



BMJ Open Preoperative predictors for a successful return to sport following anterior cruciate ligament reconstruction (ACLR): a protocol for a systematic review and meta-analysis

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ABSTRACT

Introduction Return to sport (RTS) following anterior cruciate ligament reconstruction (ACLR) is the primary goal for most patients. However, the decision of when to RTS is difficult for patients and clinicians as it is based on limited available evidence. Over the past decade, a number of predictor variables have been associated with RTS after ACLR. We present a Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols compliant protocol for a systematic review and meta-analysis of preoperative predictors for RTS/preinjury levels of physical activity following ACLR.

Methods and analysis A literature search will be performed in six electronic databases (CINAHL, AMED, MEDLINE, SPORTDiscus and PsycINFO via EBSCOhost and Web of Science) from inception to December 2020. Prospective, retrospective and cross-sectional study designs will be included. To be included, studies will need to identify at least one preoperative predictor and identify the relationship between the predictor(s) and RTS/preinjury levels of physical activity following ACLR. Blinded assessment with consensus agreement will be applied for inclusion of studies, data extraction, risk of bias assessment using the Quality in Prognostic Studies tool and the Grading of Recommendations Assessment, Development and Evaluation framework. If data allows and studies are considered homogeneous, data will be pooled through a meta-analysis. If heterogeneous, a narrative synthesis will be completed. Subgroup and sensitivity analyses will be completed, where appropriate.

Ethics and dissemination Ethical permission is not required for this study. The results will be published in a peer-reviewed journal and presented at national and international conferences.

PROSPERO registration number CRD42020222567.

INTRODUCTION

Return to sport (RTS)/physical activity following anterior cruciate ligament reconstruction (ACLR) remains a complex clinical problem. Following a lengthy rehabilitation process for both patients and clinicians, the minimum time for RTS is generally considered

Strengths and limitations of this study

- A strength of this review is that it aims to complete a meta-analysis of prospective, retrospective and cross-sectional study designs, thus adopting an inclusive approach.
- An extensive search will be completed in a number of electronic databases in addition to searching the reference lists of included studies to maximise search outputs.
- By completing a thorough risk of bias assessment, results will be discussed with transparency, and the certainty of the evidence will be assessed through the use of the standardised Grading of Recommendations Assessment, Development and Evaluation framework.
- Omitting studies not published in the English language may contribute to limitations related to publication bias.
- The broad approach to the outcome of interest (return to sport/preinjury levels of physical activity) with no restriction of a time point of interest may present challenges for data syntheses.

9 months following surgery.¹ However, it is recommended that the decision is based on progression through objective criteria rather than time alone,^{2 3} with a 2016 consensus statement suggesting that RTS should be assessed on a continuum rather than a set point, with the decision shared between all stakeholders.⁴

There is currently a lack of validated guidelines for ACL rehabilitation and RTS criteria, and, therefore, best practice is unknown.^{5–8} Additionally, there is not always a clear relationship between outcomes of RTS testing and actual RTS. For example, many patients return to their preinjury activity in spite of failing RTS criteria,⁹ while others pass RTS criteria but do not make a full RTS. A number of tests are often included in RTS

criteria that are combined to form a 'test battery', with studies reporting between 10 and 20 different tests.^{5 10} It is, therefore, unsurprising that the proportion of patients who pass all these test battery components is low.⁵ Other studies have indicated that psychological factors, rather than physical, may limit RTS following ACLR.¹¹ Clinically, these points raise concerns about how RTS testing can best be used.

Returning to sport is the primary goal for most patients following surgery,^{4 12 13} who often assume this to be a realistic goal.¹⁴ However, recent studies documenting RTS/preinjury activity level outcomes report suboptimal outcomes following surgery with only 24% returning at 1 year,¹⁵ less than 45% returning at 2 years^{16 17} and 62% returning at 5 years.¹⁸ It is, therefore, clear that we have further work to do to optimise the care and outcomes for this patient population to meet their expectations of surgery and rehabilitation.

One way to improve RTS outcomes may be to identify preoperative predictive variables associated with RTS or preinjury levels of physical activity. This would allow clinicians to better address patient expectations prior to surgery and facilitate future research to develop interventions targeted at these predictive variables, improving RTS outcomes. Over the last decade, a number of risk factors have been identified with the failure to RTS following ACLR, including functional markers (eg, muscle strength and single leg hop scores), patient-reported outcomes, psychological responses and person-related factors (eg, age, gender and motivation levels).^{17 19–23} However, no study to date has collated the available evidence to identify preoperative predictors for failure to RTS. Thus, a new synthesis of the literature is warranted to help inform patients, clinicians and researchers about risk factors for poor RTS outcomes following ACLR.

Objectives

The aim of this review is to synthesise the available data to determine the preoperative predictors for a successful RTS/preinjury levels of physical activity after ACLR.

METHODS AND ANALYSIS

This systematic review protocol was drafted using the International Prospective Register of Systematic Reviews (PROSPERO) as a guideline and registered in PROSPERO (2 December 2020, https://www.crd.york.ac.uk/prospero/display_record.php?). Any changes made to the protocol will be updated in PROSPERO. The protocol was prepared in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analysis Protocols (PRISMA-P) checklist (online supplemental file 1).^{24 25}

Eligibility criteria

The eligibility criteria are prespecified by the Population-Exposure-Outcome-Study design and are described below.

Population

The population of focus will be adults aged 18–65, who have undergone a primary ACLR. However, studies will be included where participants are <18, but the mean age of the overall population is ≥18, as the authors acknowledge that a large proportion of ACL ruptures occur in adolescents. However, the main population of interest is adults, as this review is preparatory work that will contribute to intervention development for adults in a National Health Service (NHS) clinical pathway.

Exposure

To be included, studies will need to identify at least one potential preoperative predictor variable and identify the relationship between the predictor(s) and RTS/preinjury levels of physical activity. All estimates considered to determine the relationship between the predictive factor and outcome of interest will be included (eg, OR and p value). Predictive factors may be demographic (eg, age), physical (eg, quadriceps strength) or psychosocial (eg, anxiety). We aim to include any identified predictor variable in the review as available. That is, both those that do and do not have a significant relationship with the outcome of interest.

Outcome

The main outcome of interest is the success of RTS or preinjury levels of physical activity. The identified preoperative risk factors should be linked to the outcome of interest. No time limit has been defined for the reported outcome. All measures of RTS/preinjury levels of physical activity will be included (eg, participant reported [yes/no] or validated measures [Tegner, Marx scale], this list is, however, not exhaustive).

Study

This review will include human studies in the English language with full texts available. Prospective, retrospective and cross-sectional study designs will be included.

Review question

The review question is 'what preoperative factors predict a RTS or preinjury level of physical activity following ACLR?'

Timeline

The timeline for this study is presented in [table 1](#). The research question has been specified, protocol details have been registered and published via PROSPERO, the search has been started and formal screening of the search results is in progress.

Search strategy

A systematic search will be conducted in six electronic databases (CINAHL, AMED, MEDLINE, SPORTDiscus and PsycINFO via EBSCOhost and Web of Science) from inception to December 2020. Reference lists of included articles will also be examined. The search strategy includes a combination of key words in four categories: (1) ACL, (2)

Table 1 Study timeline

Review stage	Element	Status
Review question	PEOS determined	Completed November 2020
Register review	PROSPERO	Completed December 2020
Search strategy	Literature search in electronic databases and reference lists	Ongoing
Study selection	Title, abstract and full-text review	Ongoing
Data extraction	Data extraction form	Ongoing
Risk of bias	See figure 1	Ongoing
Certainty of evidence	GRADE	Planned
Analysis	Narrative/meta-analysis (sensitivity and sub-group analysis as appropriate)	Planned
Publication	Journals and conferences (international and national)	Planned

GRADE, Grading of Recommendations Assessment, Development and Evaluation; PEOS, Population-Exposure-Outcome-Study; PROSPERO, Prospective Register of Systematic Reviews.

preoperative, (3) risk factors and (4) RTS/preinjury levels of physical activity. Terms will be matched to Medical Subject Headings (MeSH) where appropriate and combined used Boolean operators. An example of the search strategy is included in online supplemental file 2.

Data collection and analysis

Data management and selection

Following the search in the listed databases, references will be exported to a referencing management software where duplicates will be removed.

Titles will be screened against the eligibility criteria by one reviewer (HC). The same reviewer will then screen abstracts for full-text review. Two reviewers (HC and BES) will independently screen full-text articles for inclusion against the eligibility criteria. Agreement will be discussed to reach consensus with a third reviewer (GL) available to solve any discrepancies where consensus cannot be reached. Reference lists of the included articles will be screened independently and agreed for inclusion following the same process as above. A PRISMA flow diagram will be used to document the selection process along with reasons for exclusion.²⁶

Data extraction

Data extraction will be completed independently by one reviewer (HC) and verified by a second reviewer against the following domains: author, year of publication, study design, sample size, participant details, preoperative predictors and their relationship with RTS or preinjury level of physical activity (eg, OR and p value), outcome measure used and time point of reported outcome. If additional data are needed about a particular study, the corresponding author will be contacted to obtain the required detail.

Quality assessment

A quality assessment will be carried out on all studies independently by two reviewers (HC and BES). The Quality in Prognostic Studies (QUIPS) tool is suggested to assess risk of bias in prognostic factor studies.^{27–29} It comprises

of six domains with a number of facilitatory questions in each to allow a rating of low, moderate and high risk of bias to be made. The six domains assessed are shown in [figure 1](#) with the full QUIPS tool available in online supplemental file 3.

Disagreements between the review authors regarding the risk of bias in particular studies will be resolved by discussion, with the involvement of a third review author (GL) if necessary.

When the risk of bias assessment is complete, the level of consensus will be evaluated using Cohen's kappa statistic as follows: (1) none to slight 0.01–0.2, (2) fair 0.21–0.4, (3) moderate 0.41–0.6, (4) substantial 0.61–0.8, (5) almost perfect 0.81–1.00.³⁰ All studies that met the inclusion criteria will be included in the review regardless of methodological quality. The methodological quality of

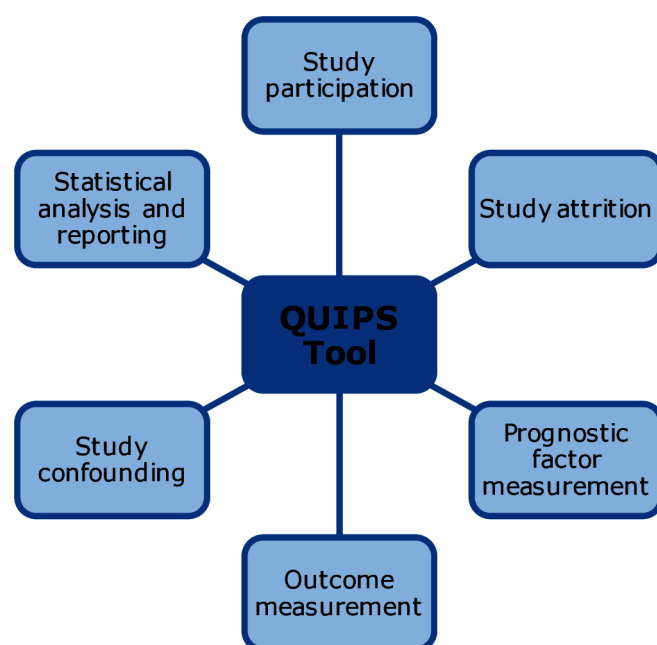


Figure 1 Six domains assessed in the QUIPS tool. QUIPS, Quality in Prognostic Studies.

the included studies will be considered in the interpretation and discussion of the results.

Sensitivity analysis

Where relevant, a sensitivity analysis will be completed to ensure that results are interpreted and discussed appropriately. Studies judged to be at high risk of bias will be excluded and compared with the meta-analysis results where all studies are included. Further sensitivity analysis may be completed as appropriate, where the meta-analysis will be rerun according to study design (eg, prospective and retrospective methodology) and time point for return (eg, 1 year and 2 years).

GRADE

The certainty of evidence for each prognostic factor will be derived using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework.^{31 32} The overall certainty of evidence will be rated as high, moderate, low or very low. GRADE ratings will be assigned by two reviewers (HC and BES) and disagreements will be resolved through consensus with a third reviewer available as needed (GL).

Data synthesis strategy

Clinical heterogeneity will be assessed through visual examination of the data extraction table on details related to participant characteristics (eg, sex, age), risk factors (eg, Anterior Cruciate Ligament Return to Sport After Injury [ACL-RSI] score, laxity, physical activity level and smoking [list not exhaustive]), RTS/preinjury levels of physical activity outcomes (eg, participant reported [yes/no] or validated measures [Tegner, Marx scale]), data points (eg, data collected at 6 months postsurgery, 12 months or 2 years), study design (eg, retrospective or prospective) and process (eg, retrospective data analysed from an existing database or prospective study carried out at orthopaedic clinic) in the included studies. The data extraction table will be independently verified by a second reviewer. If heterogeneous, data will be assessed narratively.

If at least two studies are deemed to be capturing the same risk factor within similar populations, statistical heterogeneity will be assessed using the I^2 statistic where 0%–25% is low, 26%–74% is moderate and 75% and over high statistical heterogeneity.³³ If data allow and studies are considered homogenous, data will be pooled through a meta-analysis. The random effects model will be used for high statistical heterogeneity³⁴ and a fixed effects model for low statistical heterogeneity.³⁵

Publication bias will be assessed by an asymmetry test.³⁶ All data analysis will be performed using the OpenMeta-Analyst software.³⁷

Subgroup analysis

Subgroup analysis may be performed, if possible, according to the predictors associated with a RTS compared with those associated with a return to preinjury level of physical activity. It is acknowledged that there

is a lack of consensus regarding the terminology used when reporting return to physical activity outcomes.⁵ Based on our scoping exercise, studies frequently report this outcome differently (eg, RTS, return to preinjury levels of physical activity and return to performance), and this has, therefore, been considered by the research team to ensure that all relevant literatures are reviewed. Further analysis may be performed, as appropriate, to compare population groups (eg, athletes vs recreational participants).

Patient and public involvement

No patient or public involvement is planned for the design and execution of this review. However, patient/public participation may be sought to aid with dissemination of the review findings.

As this review will only be focusing on the currently published literature, ethics approval is not required. Results from this systematic review will be published in a peer-reviewed journal. Where relevant, the results will also be presented at appropriate national and international conferences.

DISCUSSION

The present review will use rigorous methodology to provide a review of preoperative predictors for successful RTS/physical activity following ACLR. The findings will help improve research and clinical practice, enabling highlighted risk factors to be further explored and understood. Acknowledging pertinent prognostic indicators prior to surgery will allow clinicians to begin exploring and investigating these with patients to improve education regarding the surgical pathway and provide a clearer indication for returning to sport or preinjury levels of physical activity. The results will also help direct future research towards the development of targeted interventions for identified predictors with aim to improve RTS success.

As a result of the risk of bias assessment and GRADE approach, our review may also identify the strengths and limitations of research in this field and provide insights into future research areas. Findings will be disseminated widely to maximise the impact of the results to help a wide audience of patients, healthcare professionals and all other relevant stakeholders.

Strengths and limitations

A strength of this review is that it aims to complete a meta-analysis of prospective, retrospective and cross-sectional study designs, thus adopting an inclusive approach. An extensive search will be completed in a number of electronic databases in addition to the reference lists of included studies to maximise search outputs. By completing a thorough risk of bias assessment that has been customised to the aims of the review, results will be discussed with transparency. Further certainty of the evidence will be assessed using the GRADE approach.

The review will omit studies not published in the English language, which may contribute to limitations related to publication bias.

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Contributors HC, GL and BES contributed to the development of the protocol and provided feedback on the study design and methods. GL and BES were responsible for ensuring statistical descriptions were accurate. HC wrote the manuscript. All authors (HC, GL and BES) have read and approved the final manuscript. BS is guarantor of the study.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study does not involve human participants.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information. Study results of the systematic review will be published in another article.

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Supplementary File 1 – PRISMA-P 2015 Checklist

Section and topic	Item No	Checklist item	Page No.
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1 (title)
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	n/a
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	1
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Support:			
Sources	5a	Indicate sources of financial or other support for the review	1
Sponsor	5b	Provide name for the review funder and/or sponsor	n/a
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	n/a
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	3
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	3-4
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	4

Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5 + Supp File 2
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	5
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	5
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	5
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	4-5
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	4
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	5-6
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	6-7
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2 , Kendall's τ)	6-7
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	6-7
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	6-7
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	5-6
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	6

Supplementary File 2 – Search Strategy

Category	ACL	Preoperative	Prognostic factors	RTS/preinjury level
MeSH Heading	Anterior cruciate ligament	Preoperative Period	Risk factors	Return to sport
Alternatives		Preop*	Risk	Return to preinjury level
		Pre-op*	Predictor	Return to physical activity
		Periop*	Prognostic	Return to Performance

All terms in each category will be combined with OR. All terms across categories will be combined with AND as follows:

1. Anterior cruciate ligament
2. ACL
3. 1 OR 2
4. Preoperative period
5. Preop*
6. Pre-op*
7. Periop*
8. 5 OR 6 OR 7
9. Risk factors
10. Risk
11. Predictor
12. Prognostic
13. 9 OR 10 OR 11 OR 12
14. Return to sport
15. Return to preinjury level
16. Return to physical activity
17. Return to performance
18. 14 OR 15 OR 16 OR 17
19. 3 AND 8 AND 13 AND 18

Supplementary File 3 – QUIPS Tool

QUIPS Risk of Bias Assessment Instrument for Prognostic Factor Studies

Modified from: Hayden JA, Côté P, Bombardier C. Evaluation of the Quality of Prognosis Studies in Systematic Reviews. Annals of Internal Medicine. 2006;144:427-437, with the assistance of the QUIPS-LBP Working Group.

Author and year of publication				
Study identifier				
Reviewer				
Biases	Issues to consider for judging overall rating of "Risk of bias"	Study Methods & Comments	Rating of reporting	Rating of "Risk of bias"
Instructions to assess the risk of each potential bias:	These issues will guide your thinking and judgment about the overall risk of bias within each of the 6 domains. Some 'issues' may not be relevant to the specific study or the review research question. These issues are taken together to inform the overall judgment of potential bias for each of the 6 domains.	Provide comments or text excerpts in the white boxes below, as necessary, to facilitate the consensus process that will follow.	Click on each of the blue cells and choose from the drop down menu to rate the adequacy of reporting as yes, partial, no or unsure.	Click on the green cells; choose from the drop-down menu to rate potential risk of bias for each of the 6 domains as High, Moderate, or Low considering all relevant issues
1. Study Participation	Goal: To judge the risk of selection bias (likelihood that relationship between PF and outcome is different for participants and eligible non-participants).			
Source of target population	The source population or population of interest is adequately described for key characteristics (LIST).			
Method used to identify population	The sampling frame and recruitment are adequately described, including methods to identify the sample sufficient to limit potential bias (number and type used, e.g., referral patterns in health care)			
Recruitment period	Period of recruitment is adequately described			
Place of recruitment	Place of recruitment (setting and geographic location) are adequately described			
Inclusion and exclusion criteria	Inclusion and exclusion criteria are adequately described (e.g., including explicit diagnostic criteria or "zero time" description).			
Adequate study participation	There is adequate participation in the study by eligible individuals			
Baseline characteristics	The baseline study sample (i.e., individuals entering the study) is adequately described for key characteristics (LIST).			

Summary Study participation	The study sample represents the population of interest on key characteristics, sufficient to limit potential bias of the observed relationship between PF and outcome.			
2. Study Attrition	Goal: To judge the risk of attrition bias (likelihood that relationship between PF and outcome are different for completing and non-completing participants).			
Proportion of baseline sample available for analysis	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate.			
Attempts to collect information on participants who dropped out	Attempts to collect information on participants who dropped out of the study are described.			
Reasons and potential impact of subjects lost to follow-up	Reasons for loss to follow-up are provided.			
Outcome and prognostic factor information on those lost to follow-up	Participants lost to follow-up are adequately described for key characteristics (LIST).			
	There are no important differences between key characteristics (LIST) and outcomes in participants who completed the study and those who did not.			
Study Attrition Summary	Loss to follow-up (from baseline sample to study population analyzed) is not associated with key characteristics (i.e., the study data adequately represent the sample) sufficient to limit potential bias to the observed relationship between PF and outcome.			
3. Prognostic Factor Measurement	Goal: To judge the risk of measurement bias related to how PF was measured (differential measurement of PF related to the level of outcome).			
Definition of the PF	A clear definition or description of 'PF' is provided (e.g., including dose, level, duration of exposure, and clear specification of the method of measurement).			
Valid and Reliable Measurement of PF	Method of PF measurement is adequately valid and reliable to limit misclassification bias (e.g., may include relevant outside sources of information on measurement properties, also characteristics, such as blind measurement and limited reliance on recall).			
	Continuous variables are reported or appropriate cut-points (i.e., not data-dependent) are used.			
Method and Setting of PF Measurement	The method and setting of measurement of PF is the same for all study participants.			
Proportion of data on PF available for analysis	Adequate proportion of the study sample has complete data for PF variable.			

Method used for missing data	Appropriate methods of imputation are used for missing 'PF' data.			
PF Measurement Summary	PF is adequately measured in study participants to sufficiently limit potential bias.			
4. Outcome Measurement	Goal: To judge the risk of bias related to the measurement of outcome (differential measurement of outcome related to the baseline level of PF).			
Definition of the Outcome	A clear definition of outcome is provided, including duration of follow-up and level and extent of the outcome construct.			
Valid and Reliable Measurement of Outcome	The method of outcome measurement used is adequately valid and reliable to limit misclassification bias (e.g., may include relevant outside sources of information on measurement properties, also characteristics, such as blind measurement and confirmation of outcome with valid and reliable test).			
Method and Setting of Outcome Measurement	The method and setting of outcome measurement is the same for all study participants.			
Outcome Measurement Summary	Outcome of interest is adequately measured in study participants to sufficiently limit potential bias.			
5. Study Confounding	Goal: To judge the risk of bias due to confounding (i.e. the effect of PF is distorted by another factor that is related to PF and outcome).			
Important Confounders Measured	All important confounders, including treatments (key variables in conceptual model: LIST), are measured.			
Definition of the confounding factor	Clear definitions of the important confounders measured are provided (e.g., including dose, level, and duration of exposures).			
Valid and Reliable Measurement of Confounders	Measurement of all important confounders is adequately valid and reliable (e.g., may include relevant outside sources of information on measurement properties, also characteristics, such as blind measurement and limited reliance on recall).			
Method and Setting of Confounding Measurement	The method and setting of confounding measurement are the same for all study participants.			
Method used for missing data	Appropriate methods are used if imputation is used for missing confounder data.			
Appropriate Accounting for Confounding	Important potential confounders are accounted for in the study design (e.g., matching for key variables, stratification, or initial assembly of comparable groups).			
	Important potential confounders are accounted for in the analysis (i.e., appropriate adjustment).			

Study Confounding Summary	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the relationship between <i>PF</i> and <i>outcome</i> .			
6. Statistical Analysis and Reporting	Goal: To judge the risk of bias related to the statistical analysis and presentation of results.			
Presentation of analytical strategy	There is sufficient presentation of data to assess the adequacy of the analysis.			
Model development strategy	The strategy for model building (i.e., inclusion of variables in the statistical model) is appropriate and is based on a conceptual framework or model.			
	The selected statistical model is adequate for the design of the study.			
Reporting of results	There is no selective reporting of results.			
Statistical Analysis and Presentation Summary	The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid or spurious results.			