Supplemental file 2: Quality in prognostic studies (QUIPS) tool.

Overall Acceptable Quality (++) Moderate Bias

QUIPS tool components		
Biases	**Issues to consider for judging overall rating of "Risk of bias"**	**Explanation**
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.	
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).	High Quality (+++) Low Bias
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)	Low Quality (+) High Bias
Recruitment period	Period of recruitment is adequately described	High Quality (+++) Low Bias
Place of recruitment	Place of recruitment (setting and geographic location) are adequately described	High Quality (+++) Low Bias
Inclusion and exclusion criteria	Inclusion and exclusion criteria are adequately described (e.g., including explicit diagnostic criteria description).	High Quality (+++) Low Bias
Adequate study participation	There is adequate participation in the study by eligible individuals	Acceptable Quality (++) Moderate Bias
Baseline characteristics	The baseline study sample (i.e., individuals entering the study) is adequately described for key characteristics (LIST).	High Quality (+++) Low Bias
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.**	High Quality (+++) Low Bias
. 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.	High Quality (+++) Low Bias
Attempts to collect information on participants who dropped out	Attempts to collect information on participants who dropped out of the study are described.	Low Quality (+) High Bias
Reasons and potential impact of subjects lost to follow-up	Reasons for loss to follow-up are provided.	Low Quality (+) High Bias
Outcome and prognostic factor information on those lost to follow-	Participants lost to follow-up are adequately described for key characteristics (LIST).	Low Quality (+) High Bias

up	There are no important differences between key characteristics (LIST) and outcomes in participants who completed the study and those who did not.	Low Quality (+) High Bias
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.**	Acceptable Quality (++) Moderate Bias
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).	Low Quality (+) High Bias
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).	Acceptable Quality (++) Moderate Bias
	Continuous variables are reported or appropriate cut-points (i.e., not data-dependent) are used.	High Quality (+++) Low Bias
Method and Setting of PF Measurement	The method and setting of measurement of PF is the same for all study participants.	High Quality (+++) Low Bias
Proportion of data on PF available for analysis	Adequate proportion of the study sample has complete data for PF variable.	High Quality (+++) Low Bias
Method used for missing data	Appropriate methods of imputation are used for missing 'PF' data.	High Quality (+++) Low Bias
PF Measurement Summary	***PF* is adequately measured in study participants to sufficiently limit potential bias.**	Acceptable Quality (++) Moderate 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.	High Quality (+++) Low Bias
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).	High Quality (+++) Low Bias
Method and Setting of Outcome Measurement	The method and setting of outcome measurement is the same for all study participants.	High Quality (+++) Low Bias
Outcome Measurement Summary	***Outcome of interest* is adequately measured in study participants to sufficiently limit potential bias.**	High Quality (+++) Low 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.	Low Quality (+) High Bias
Definition of the confounding factor	Clear definitions of the important confounders measured are provided (e.g., including dose, level, and duration of exposures).	Low Quality (+) High Bias

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).	Low Quality (+) High Bias

Method and Setting of Confounding Measurement	The method and setting of confounding measurement are the same for all study participants.	High Quality (+++) Low Bias
Method used for missing data	Appropriate methods are used if imputation is used for missing confounder data.	Low Quality (+) High Bias
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).	Low Quality (+) High Bias
	Important potential confounders are accounted for in the analysis (i.e., appropriate adjustment).	Low Quality (+) High Bias
Study Confounding Summary	**Important potential confounders are appropriately accounted for, limiting potential bias with respect to the relationship between *PF* and *outcome*.**	Low Quality (+) High Bias
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	High Quality (+++) Low Bias
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.	High Quality (+++) Low Bias
	The selected statistical model is adequate for the design of the study.	High Quality (+++) Low Bias
Reporting of results	There is no selective reporting of results.	High Quality (+++) Low Bias
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.**	High Quality (+++) Low Bias
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.		

Ratings:

High bias: The relationship between the PF and outcome is very likely to be different for participants and eligible nonparticipants

Moderate bias: The relationship between the PF and outcome may be different for participants and eligible nonparticipants

Low bias: The relationship between the PF and outcome is unlikely to be different for participants and eligible nonparticipant

Scottish Intercollegiate Guidelines Network: rating a quality of Cohort Studies;

Rate the overall methodological quality of the study, using the following as a guide: **High quality** (+++): Majority of criteria met, little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (++): Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (+): Either most criteria not met, or significant flaws relating to key aspects of study design.