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Cochrane Methods
Prognosis

Introducing systematic reviews of prognosis studies to Cochrane: what and how?

Karel GM Moons, Lotty Hooft, Anneke Damen

Cochrane Prognosis Methods Group (PMG)

Who are you?



Who are we?



Carl



Lotty



Anneke



Introduction

- Cochrane: reviews of intervention and DTA studies
- Personalized and precision medicine dictates
 - All about (use of) prognosis information
- Growing number of primary prognosis studies
- Systematic reviews of prognosis studies are necessary

→ Cochrane is now implementing reviews of prognosis studies



Types of prognosis studies

1. Average/overall prognosis: What is most likely course/outcome in a particular time period, of individuals within a particular health condition (traditionally having a particular disease, not necessarily)?
2. Prognostic factor studies: Which factors are associated with a specific outcome in individuals within a particular health condition?
3. Prognostic model studies: What combination of prognostic factors predict, and how well, a particular outcome in individuals within a particular health condition? Development and validation.
4. Treatment selection factors: Which factors or combination of factors (models) are predictors of (differential) effect of a particular intervention in individuals within a particular health condition.



Conducting a systematic review: generally 7 steps

1. Well-formulated review question (PICO)
2. Searching for studies
3. Selection of studies
4. Extraction of data
5. Critical appraisal/Risk of Bias
6. Synthesis of data (meta-analysis)
7. Interpretation, conclusions, recommendations

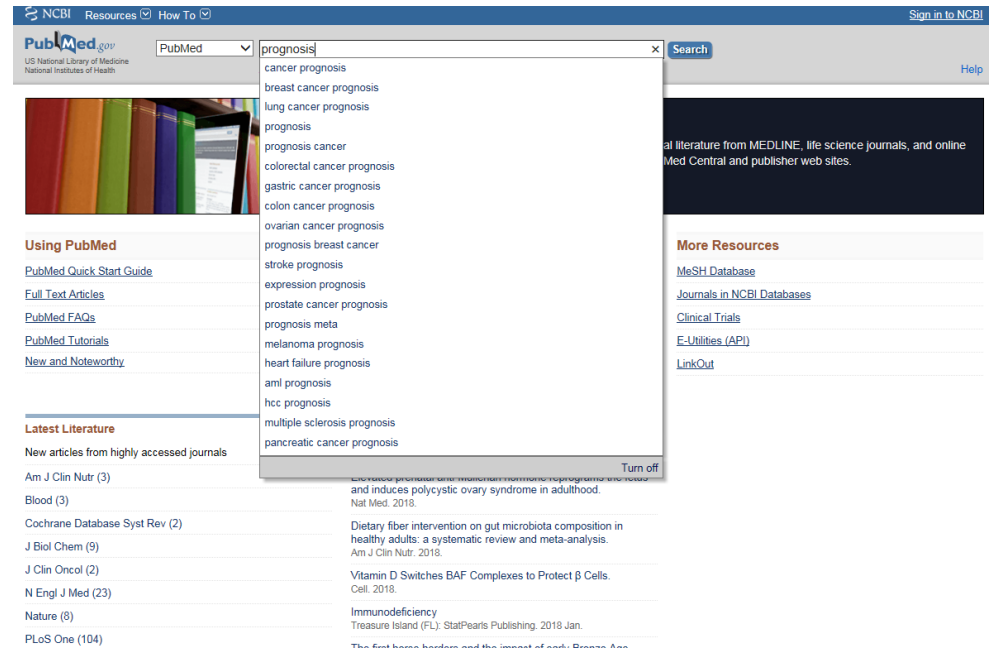
Step 1: Well-formulated review question (PICOTS)

Population	Define target population in whom prognosis is studied
Index (factor/model)	Define prognostic factor(s) or model(s) under review
Comparator	Define alternative (to the index) prognostic factors or models for the same outcome or target population, if applicable.
Outcomes	Define the health outcomes of the targeted individuals
Timing	Define moment/time-point prognosis is made (e.g. factors or models are to be used), and over what time period outcome(s) are studied
Setting	Define the intended role or setting (e.g. of the use of the prognostic factors or models)



Step 2: Search for studies

- Search filters are available
 - Geersing et al, PLOS One 2012
 - Haynes et al, BMJ 2005
 - Ingui et al, J Am Med Inform Assoc 2001



Step 3: Objective selection of studies

- Not different from other types of Cochrane reviews
- However, many more deviations from the review question possible



Step 4: Objective extraction of data

OPEN ACCESS Freely available online



Guidelines and Guidance

Critical Appraisal and Data Extraction for Systematic Reviews of Prediction Modelling Studies: The CHARMS Checklist

Karel G. M. Moons^{1†*}, Joris A. H. de Groot^{1†}, Walter Bouwmeester¹, Yvonne Vergouwe¹, Susan Mallett², Douglas G. Altman³, Johannes B. Reitsma¹, Gary S. Collins³

1 Julius Center for Health Sciences and Primary Care, UMC Utrecht, Utrecht, The Netherlands, **2** Department of Primary Care Health Sciences, New Radcliffe House, University of Oxford, Oxford, United Kingdom, **3** Centre for Statistics in Medicine, University of Oxford, Botnar Research Centre, Windmill Road, Oxford, United Kingdom



Step 5: Critical appraisal of methodological quality

- Prognostic factor/predictor finding studies
 - RoB tool : **QUIPS** → J Hayden, Ann Int Med 2006 + 2013
- Prediction modelling (development and validation)
 - Critical Appraisal: **CHARMS** → K Moons, Plos Med 2014
 - Risk of Bias: **PROBAST** – under development (submitted)



RoB tools: QUIPS & PROBAST

RESEARCH AND REPORTING METHODS

Annals of Internal Medicine

Assessing Bias in Studies of Prognostic Factors

Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; Jennifer L. Cartwright, MSc; Pierre Côté, DC, PhD; and Claire Bombardier, MD

Previous work has identified 6 important areas to consider when evaluating validity and bias in studies of prognostic factors: participation, attrition, prognostic factor measurement, confounding measurement and account, outcome measurement, and analysis and reporting. This article describes the Quality In Prognosis Studies tool, which includes questions related to these areas that can inform judgments of risk of bias in prognostic research.

A working group comprising epidemiologists, statisticians, and clinicians developed the tool as they considered prognosis studies of low back pain. Forty-three groups reviewing studies addressing prognosis in other topic areas used the tool and provided feedback.

Most reviewers (74%) reported that reaching consensus on judgments was easy. Median completion time per study was 20 minutes; interrater agreement (κ statistic) reported by 9 review teams varied from 0.56 to 0.82 (median, 0.75). Some reviewers reported challenges making judgments across prompting items, which were addressed by providing comprehensive guidance and examples. The refined Quality In Prognosis Studies tool may be useful to assess the risk of bias in studies of prognostic factors.

Ann Intern Med. 2013;158:280-286.
For author affiliations, see end of text.

www.annals.org

PROBAST: a tool to assess risk of bias and applicability of prediction model studies – explanation and elaboration

Karel G. M. Moons^{1,2,*}, Robert F. Wolff^{3,*}, Richard D. Riley⁴, Penny F. Whiting^{5,6}, Marie Westwood³, Gary S. Collins⁷, Johannes B. Reitsma^{1,2}, Jos Kleijnen^{3,8}, Susan Mallett⁹



Step 6: Synthesis of data (meta-analysis)

RESEARCH METHODS AND REPORTING

A guide to systematic review and meta-analysis of prediction model performance

Thomas P A Debray,^{1,2} Johanna A A G Damen,^{1,2} Kym I E Snell,³ Joie Ensor,³ Lotty Hooft,^{1,2}
Johannes B Reitsma,^{1,2} Richard D Riley,³ Karel G M Moons^{1,2}

Article

A framework for meta-analysis of prediction model studies with binary and time-to-event outcomes

Thomas PA Debray,^{1,2}  Johanna AAG Damen,^{1,2}
Richard D Riley,³ Kym Snell,³  Johannes B Reitsma,^{1,2}
Lotty Hooft,^{1,2} Gary S Collins⁴  and Karel GM Moons^{1,2}



Statistical Methods in Medical Research

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Step 7: Interpretation, conclusions, recommendations

RESEARCH METHODS AND REPORTING

A guide to systematic review and meta-analysis of prediction model performance

Thomas P A Debray,^{1,2} Johanna A A G Damen,^{1,2} Kym I E Snell,³ Joie Ensor,³ Lotty Hooft,^{1,2} Johannes B Reitsma,^{1,2} Richard D Riley,³ Karel G M Moons^{1,2}



METHODOLOGY

Open Access

Judging the quality of evidence in reviews of prognostic factor research: adapting the GRADE framework

Anna Huguet^{1*}, Jill A Hayden², Jennifer Stinson³, Patrick J McGrath^{1,4,5,6}, Christine T Chambers^{1,4}, Michelle E Tougas¹ and Lori Wozney¹

RESEARCH METHODS & REPORTING

Use of GRADE for assessment of evidence about prognosis: rating confidence in estimates of event rates in broad categories of patients

Alfonso Iorio,^{1,2} Frederick A Spencer,² Maicon Falavigna,³ Carolina Alba,⁴ Eddie Lang,⁵ Bernard Bumand,⁶ Tom McGinn,⁷ Jill Hayden,⁸ Katrina Williams,⁹ Beverly Shea,^{10,11} Robert Wolff,¹² Ton Kujpers,¹³ Pablo Perel,¹⁴ Per Olav Vandvik,¹⁵ Paul Glasziou,¹⁶ Holger Schunemann,^{1,2} Gordon Guyatt^{1,2}



Q & A



Implementation within Cochrane

- Methods Innovation Fund → methods development (previous slides)
- Strategic Methods Fund → methods implementation
 - Training
 - Templates
- Exemplar program



Training

- 5 workshops during Cochrane Colloquium
 - Half-day precolloquium workshop (Saturday, September 15th, 14:00, fully booked)
 - Systematic reviews of prognostic studies II: risk of bias assessment in systematic reviews of prognostic studies (Sunday, September 16th, 16:00)
 - Systematic reviews of prognostic studies III: meta-analytical approaches in systematic reviews of prognostic studies (Monday, September 17th, 11:00)
 - Systematic reviews of prognostic studies IV: meta-analysis of prognostic studies using individual participant data (Tuesday, September 18th, 11:00).
 - Systematic reviews of prognostic studies I: introduction, design and protocol for systematic reviews of prognostic studies (Sunday, September 16th, 11:00)



Training

- Online course Systematic Reviews of Prognostic Research, November 19th – December 9th 2018
<http://elevatehealth.eu/online-medical-courses/systematic-reviews-of-prognostic-research>
 - Face-to-face course Systematic Review of Prognostic Studies, May 13th – 17th 2019
<http://www.msc-epidemiology.nl/courses>
- More (online) training material will be developed



Title registration form



Prognosis Studies review proposal form

Review Proposal Form

Please complete this form to outline your proposal for a Cochrane systematic review. Email the completed form to [email address], or send to [name], Managing Editor, Cochrane XXX Group, [postal address], P: +XX XXXXXXXXXX Fax: +XX XXXXXXXXXX.

Before completing this form:

- Read "Managing expectations: what does The Cochrane Collaboration expect of authors, and what can authors expect of The Cochrane Collaboration?" (see <http://community.cochrane.org/editorial-and-publishing-policy-resource/cochrane-review-development/managing-expectations>). Note: this information is particularly for systematic reviews of intervention studies. A page for prognosis reviews is under construction.)
- Note that a Cochrane review of prognosis studies clearly differs from that of intervention studies and diagnostic test accuracy studies, in, e.g., searching, data extraction, critical appraisal and meta-analysis. Step-by-step guidance to help you understanding prognosis studies and the processes of conducting a review of prognosis studies is given in the papers in the reference list below.
- Cochrane reviews of prognosis require a multidisciplinary team. Below you find several question addressing the available expertise in the author team, and whether external expertise (e.g. from information specialists or methodologists) is needed to conduct this review. If additional expertise is needed, e.g. an information specialist, or methodological or statistical expertise, please provide this request to the Prognosis Methods Group (PMG) timely.

Proposed title

Choose one of the formats below. See also the generic guidance on defining a review question for prognosis studies in the CHARMS checklist.

- Incidence of [outcome] within [time] in [population]
- [Prognostic factors] for predicting incidence of [outcome] in [population]
- Prediction of [outcome] in [population] using [prognostic factors]
- Prognostic models for predicting [outcome] in [population]
- Predictive performance of [prognostic model] for predicting [outcome] in [population]
- Added value of [prognostic factor] on top of [existing prognostic factors/prognostic model] for predicting [outcome] in [population]
- [Predictive factors] predicting the [outcome of treatment] in [population]
- [Factors / Models] predicting differential treatment response in [population]
- [Factors / Models] for predicting treatment response in [population]

Contact person

Name:

Email:

Short description of review proposal

Provide brief but enough information to make sure that the clinical context and the actual question that is being asked is clear for non-content experts as well.

For explicit guidance to help filling in this title registration form and for the conduct of the review, from framing the review question, search strategy, study in/exclusion criteria, critical appraisal, risk of bias assessment, meta-analysis and reporting, please see the papers mentioned in the reference list below.

Type of prognosis review

Indicate what type of review you are going to perform (double click to check a box). See PROGRESS series in the reference list.

- Overall prognosis
- Prognostic factors
- Prognostic models
- Predictive/Treatment selection factors

Motivation for the review

For example, is this going to be part of a PhD thesis; is it part of a larger project; is it particularly topical at the present time?

Background

- i) The clinical problem. A short description of the existing clinical pathway of the targeted individuals/patients; their starting condition and moment of prognostication (time point in the clinical pathway); what prognostic outcomes are relevant to the targeted individuals. For predictive factor reviews also refer to the role of treatment.
- ii) Why is this review relevant, including how might the results of the review be used: e.g., the prognostic or predictive factor(s) or model(s) under review may be used to determine treatment allocation or abstention, decide on closer follow-up or monitoring, etc. Reference to an existing systematic review on this topic outside Cochrane is helpful.

Review objective(s)

What is the review question, according to the PICOTS format? (see Box 1 in the paper of Debray et al, BMJ 2017, see reference list below.)

Primary objective:

Secondary objective(s):

Participants / setting

Short outline of the targeted population and clinical setting, to be included and excluded for the review.

Protocol template



Protocol Cochrane Review Prognosis Studies

*Prognosis exemplar protocols are published in the Cochrane Library using the “Flexible (Prognosis)” type. The Prognosis Methods Group recommends inclusion of specific sub-headers relevant to the type of prognostic review being undertaken. This document includes the recommended sub-headers for exemplar reviews of prognostic model(s). See at the end of this document relevant references that may be helpful when writing the protocol.

Header*	Description
Title	Choose preferably one of the following formats: Incidence of [outcome] within [time] in [population] [Prognostic factors] for predicting incidence of [outcome] in [population] Prediction of [outcome] in [population] using [prognostic factors] Prognostic models for predicting [outcome] in [population] Performance of [prognostic model] for predicting [outcome] in [population] Added/Incremental value of [prognostic factor] on top of [existing prognostic factors/prognostic model] for predicting [outcome] in [population] [Predictive factors] predicting the [outcome of treatment] in [population] [Factors / Models] predicting differential treatment response in [population] [Factors / Models] for predicting treatment response in [population]
Authors	List names and affiliations of all authors.
Contact person	List name and contact details

Protocol template

Background [Fixed, level 1 heading]	
Description of the health condition and context [Fixed, level 2 heading]	<p>A description of the targeted health condition and clinical context for which the (overall) prognosis or prognostic/predictive factor or model under review is intended (frequency, severity, and possible treatments). A health condition can for example be people undergoing surgery, having a certain disease or diagnosis, being pregnant, or healthy individuals of the general population within a certain age range.</p> <p>Also clearly define the moment of prognostication or prediction in the targeted population. For example, within two weeks after receiving a certain diagnosis, the day of intensive care admission, being 3 months pregnant, or visiting the emergency department with a trauma.</p> <p>If there are existing Cochrane reviews of interventions or diagnostic tests for the targeted health condition they should be cross-referenced here.</p>
Description of the prognostic / predictive model(s) / factor(s) [Fixed, level 2 heading]	<p>Not applicable for reviews on overall prognosis. Clearly state in which of the types of prognosis studies you are interested: prognostic factor, prognostic model, or predictive factor (see PROGRESS series for definitions, see below for references). Describe the factor(s) or model(s) under review in more detail.</p>
Health outcomes [Fixed, level 2 heading]	<p>Description of the health outcomes that are being studied in the targeted population – e.g. the outcomes of the overall prognosis or that are to be predicted by the factor(s)/model(s) under review.</p> <p>Also clearly define the time horizon (relative to the moment of prognostication or prediction) of the outcome occurrence, e.g., 30 day mortality, one or five year incidence of disease recurrence, or even lifelong incidence of certain outcome events.</p>
Why it is important to do this review [Fixed, level 2 heading]	<p>Explain the rationale for the review and why the prognosis questions being asked are important.</p>
Objectives [Fixed, level 1 heading]	
Primary objectives [Optional, level 2 heading]	<p>State the review question, including a table in the PICOTS format. (See Box 1 in the paper of Debray et al, BMJ 2017, and Table 1 of the CHARMS guidance Moons et al, PLOS Med 2014). The PICOTS format consists of the following elements:</p> <ul style="list-style-type: none"> • Population—define the target population in which the overall prognosis or factor(s)/model(s) will be used.

	<ul style="list-style-type: none"> • Intervention (model/factor)—define the factor(s)/model(s) under review. • Comparator—if applicable, one can address competing factor(s)/model(s) for the factor(s)/model(s) under review. • Outcome(s)—define the outcome(s) of interest that is/are studied for the overall prognosis estimation or predicted with the factor(s)/model(s). • Timing—define when and over what time period the outcome occurrence is studied or predicted. • Setting—define the intended setting (role) of the overall prognosis estimation or of the factor(s)/model(s).
Secondary objectives [Optional, level 2 heading]	<p>Reviews that investigate multiple prognosis questions may categorise their objectives as ‘Primary Objectives’ and ‘Secondary Objectives’. For example, the primary objectives may be to quantify the added predictive value of several biomarkers to an existing prognostic model; the secondary objective may be to compare the performance of this existing prognostic model to the performance of the biomarkers alone.</p> <p>Secondary objectives related to investigating heterogeneity between study results should not be listed under this subheading but under the next subheading.</p>
Investigation of sources of heterogeneity between studies [Fixed, level 2 heading]	<p>Heterogeneity investigations explore factors which may affect, e.g. the overall prognosis or the prognostic accuracy of factors or models. These explorations are essential because they provide a framework by which the observed heterogeneity may be explained a priori and to provide a more clinically useful review. For example, the predictive performance of a certain prognostic model for predicting 10-year cardiovascular disease outcomes in adults above 40 in the general population may vary when different definitions of cardiovascular disease outcomes are applied, when different age ranges, ethnic groups or genders have been studied, or when different study designs were used in the prognostic model studies.</p>

Protocol template

Methods <small>[Fixed, level 1 heading]</small>	<p>The Methods section in a protocol should be written in the future tense. In the methods section, authors should clearly describe the selection criteria for considering studies for the review, the methods used to identify relevant studies, the process used for selection of studies and collecting data and how the methodological quality (risk of bias) of the included studies is assessed. The methods section should thus address the PICOTS (see above) in detailed form. A methodologist/statistician may best write the section for describing the statistical analysis and data synthesis. In addition, information about how to investigate sources of heterogeneity and any pre-planned sensitivity analyses should be described clearly here.</p> <p>The following addresses details for specific subheadings of the methods section.</p>
Criteria for considering studies for this review <small>[Fixed, level 2 heading]</small>	<p>The eligibility criteria required for studies to be included in the review must be clearly stated. More details are given below. An overview of items to consider when formulating the in- and exclusion criteria is presented in Table 1 of the CHARMS guidance (Moons et al, PLOS Med 2014). The CHARMS checklist is originally developed for reviews of prognostic model studies, but the items are also relevant to reviews of the other three types of prognosis studies.</p>
Types of studies <small>[Fixed, level 3 heading]</small>	<p>State eligible study designs, and provide a justification for the choice.</p> <p>For example, will you include (non-randomised) cohort studies (both prospective and retrospective), registries, prognosis studies based on RCT data, case-control studies, etc.</p> <p>If studies are excluded on the basis of publication status or language of publication, explain and justify this. Also other eligibility criteria not relating to population, predictors, and outcome, can be listed here (e.g. criteria related to analyses).</p>
Targeted population <small>[Fixed, level 3 heading]</small>	<p>State eligibility criteria for participants, including any criteria around setting, definition of the targeted population, demographic factors, and how studies including subsets of relevant participants are handled.</p> <p>Planned subgroup analyses related to participant characteristics should not be listed here but rather under "Subgroup analysis and investigation of heterogeneity" (see below).</p>
Types of prognostic / predictive factor(s) or model(s) <small>[Optional, level 3 heading]</small>	<p>Describe the prognostic/predictive factors or models under review. For prognostic models, describe if you will include studies in which models are developed, externally validated, extended with</p>

	<p>additional predictors, or a combination of those.</p> <p>Describe for example, if you are only interested in models including certain types of predictors, e.g. noninvasive predictors, predictors available before surgery, or predictors measured in using a specific measurement method. For prognostic/predictive factors, describe if you are interested in one or more specific factors, or for example in all blood biomarkers, or imaging based predictors for a certain outcome. Other covariates can also be listed here.</p> <p>This heading is not applicable to reviews of overall prognosis.</p>
Types of outcomes to be predicted <small>[Fixed, level 3 heading]</small>	<p>Describe the health outcomes that are being studied in the targeted population, including definitions, measurement methods, and timing of outcome measurement.</p> <p>For example, if you are interested in the composite outcome of cardiovascular disease, describe what you will do with studies that only have a single component like myocardial infarction as outcome.</p> <p>State whether studies will be excluded based on the time horizon, e.g. if you are interested in 10-year predictions, what will you do with studies with 1-month predictions or with 5-year predictions.</p>
Search methods for identification of studies <small>[Fixed, level 2 heading]</small>	
Electronic searches <small>[Fixed, level 3 heading]</small>	<p>Based on the review question, the search strategy should be formulated. Below this heading, the methods used to identify studies should be summarized. The bibliographic databases searched, the dates and periods searched and any constraints, such as language, should be stated. The full search strategies for each database should be listed in an appendix. Unfortunately, prognosis studies are not labelled as such and therefore, searching for prognosis studies is often more difficult compared to RCTs. Researchers often end with many hits, in fear of missing something. To narrow the number of results, several search filters have been developed for searching prognostic studies (Haynes et al, BMJ 2005; Ingui et al, J Am Med Inform Assoc 2001) that were validated and updated by Geersing et al (Geersing et al, PLOS One 2012).</p>
Searching other resources <small>[Optional, level 3 heading]</small>	<p>List 'grey' literature sources, such as reports and conference proceedings. If journals are specifically hand-searched for the review, this should also be noted. List people (for example, researchers, experts) and/or organisations who will be contacted. List any other sources, which may include, for example, reference</p>

Review template

- Under development



Q & A



Exemplar program

- 17 exemplars

Type	Number
Overall prognosis	3
Prognostic factor	8
Prognostic model	6
Predictive factor	1

- 10 protocols registered
- 7 titles registered
- First full review published September 1st, 2018



Protease activity as a prognostic factor for wound healing in venous leg ulcers (Review)

Westby MJ, Dumville JC, Stubbs N, Norman G, Wong JKF, Cullum N, Riley RD




Exemplar program

CRG	Number
Airways	1
Anaesthesia	1
Back and Neck	1
Breast Cancer	2
Developmental, Psychosocial and Learning Problems	2
Haematological Malignancies	2
Heart	1
Inflammatory Bowel Disease and Functional Bowel Disorders	1
Kidney and Transplant	1
Metabolic and Endocrine Disorders Group	1
Neuro-oncology	2
Upper Gastrointestinal and Pancreatic Diseases Group	1
Vascular	1
Wounds	1



Exemplar program

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+ Rheumatology 1

+ Child health 1

Cochrane Reviews 7747

Type: **Prognosis** ✕

10 Cochrane Prot

Cochrane Database of Systematic Reviews
Issue 8 of 12, August 2017

Select all (10) E

Order by: Relevancy ▾

- 1 **Prognosis**
Kurinchi Selvan
- 2 **Prognosis meta-analysis**
Nicole Sko
- 3 **Prognosis**
Maggie J W
- 4 **Interim review**
Nicole Sko
Trivella
- 5 **Prognosis**
therapie
Yet H Khor,

- 6 **Intermediate hyperglycaemia as a predictor for the development of type 2 diabetes: prognostic factor exemplar review**
Bernd Richter, Bianca Hemmingsen, Maria-Inti Metzendorf, Yemisi Takwoingi
 Prognosis Protocol 12 May 2017
- 7 **Individual recovery expectations and prognosis of outcomes in non-specific low back pain: prognostic factor exemplar review**
Jill A Hayden, Michelle E Tougas, Richard Riley, Ross Iles, Tamar Pincus
 Prognosis Protocol 2 September 2014
- 8 **Prediction models for the risk of postoperative nausea and vomiting**
Nathan Leon Pace, John Carlisle, Leopold HJ Eberhart, Peter Kranke, Marialena Trivella, Anna Lee, Michael H Bennett
 Prognosis Protocol 26 September 2014
- 9 **Overall prognosis of preschool autism spectrum disorder diagnoses**
Amanda Brignell, Natalia Albein-Urios, Susan Woolfenden, Andrew Hayden, Alfonso Iorio, Katrina Williams
 Prognosis Protocol 24 August 2017
- 10 **Mammographic density, endocrine therapy and breast cancer risk: a prognostic and predictive biomarker review**
Emma C Atakpa, Mangesh A Thorat, Jack Cuzick, Adam R Brentnall
 Prognosis Protocol 10 August 2018

Yes, I would like to do a Cochrane prognosis review!

- Check our website:
<https://methods.cochrane.org/prognosis/>
- Contact Toby Lasserson (tlasserson@cochrane.org)
- Contact Cochrane Review Group
- We are there to help you
 - As reviewer
 - Or as author

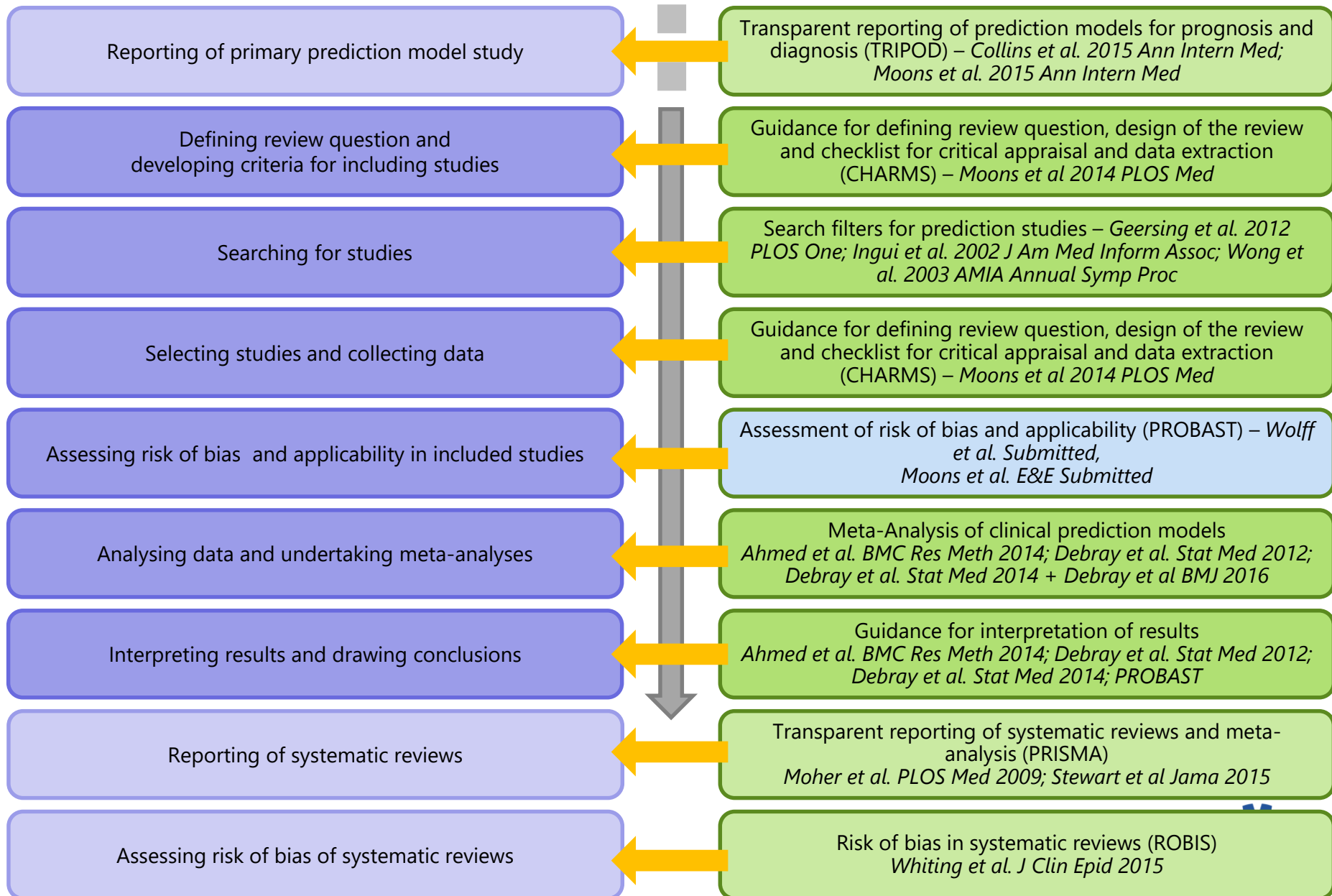


Our SMF team



Q & A





Reporting guideline prediction modeling studies

Annals of Internal Medicine RESEARCH AND REPORTING METHODS

Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD): The TRIPOD Statement

Gary S. Collins, PhD; Johannes B. Reitsma, MD, PhD; Douglas G. Altman, DSc; and Karel G.M. Moons, PhD *Ann Intern Med.* 2015;162:55-63. doi:10.7326/M14-0697

Annals of Internal Medicine RESEARCH AND REPORTING METHODS

Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD): Explanation and Elaboration

Ann Intern Med. 2015;162:W1-W73. doi:10.7326/M14-0698

Karel G.M. Moons, PhD; Douglas G. Altman, DSc; Johannes B. Reitsma, MD, PhD; John P.A. Ioannidis, MD, DSc; Petra Macaskill, PhD; Ewout W. Steyerberg, PhD; Andrew J. Vickers, PhD; David F. Ransohoff, MD; and Gary S. Collins, PhD

www.tripod-statement.org

