Prognosis Methods Group Meeting

Québec Cochrane Colloquium
September 21, 2013
Agenda

1. Introductions
2. Update on Prognosis Exemplar Review initiative
3. Updates from Exemplar Review Groups:
   a) Prognostic Factor (Hayden)
   b) Predictive Model (Pace)
   c) Overall Prognosis (Moons)
4. Discussion of ongoing methodological projects related to prognosis reviews:
   a) Risk of bias assessment of prognostic factor studies (QUIPS) (Hayden)
   b) Risk of bias and applicability assessment for prediction model studies (PROBAST) (Wolff)
   c) Development of guidance for items to report when developing or validating risk prediction models (TRIPOD) (Moons)
   d) GRADE for assessing prognostic evidence (Iorio)
   e) Literature searching for prognostic factor systematic reviews (Parker)
   f) Other
5. Discussion of other methodological needs to provide guidance for prognosis reviews
PMG Convenors

Richard Riley (UK)  
Carl Moons (Neth)  
Katrina Williams (Aus)

Sue Woolfenden (Aus)  
Jill Hayden (Can)  
Doug Altman (UK)

PMG Coordinator: Alexandra Hendry
Agenda

1. Introductions

2. **Update on Prognosis Exemplar Review initiative**

3. Updates from Exemplar Review Groups:
   a) Prognostic Factor (Hayden)
   b) Predictive Model (Pace)
   c) Overall Prognosis (Moons)

4. Discussion of ongoing methodological projects related to prognosis reviews:
   a) Risk of bias assessment of prognostic factor studies (QUIPS) (Hayden)
   b) Risk of bias and applicability assessment for prediction model studies (PROBAST) (Wolff)
   c) Development of guidance for items to report when developing or validating risk prediction models (TRIPOD) (Moons)
   d) GRADE for assessing prognostic evidence (Iorio)
   e) Literature searching for prognostic factor systematic reviews (Parker)
   f) Other

5. Discussion of other methodological needs to provide guidance for prognosis reviews
Prognosis Exemplar Reviews

• Steering Group has approved the registration & conduct of three Prognosis Exemplar Reviews
  1. Prognostic factor
  2. Risk prediction models
  3. Overall prognosis

• Goal: assess the feasibility and provide examples of these innovative types of systematic reviews

• Methodological work related to each exemplar review will inform future prognostic systematic reviews

• Process developments for conduct of innovative reviews in Cochrane
Shawn Stevenson (Aus)
Exemplar Review Coordinator
Agenda

1. Introductions

2. Update on Prognosis Exemplar Review initiative

3. **Updates from Exemplar Review Groups:**
   a) Prognostic Factor (Hayden)
   b) Predictive Model (Pace)
   c) Overall Prognosis (Moons)

4. Discussion of ongoing methodological projects related to prognosis reviews:
   a) Risk of bias assessment of prognostic factor studies (QUIPS) (Hayden)
   b) Risk of bias and applicability assessment for prediction model studies (PROBAST) (Wolff)
   c) Development of guidance for items to report when developing or validating risk prediction models (TRIPOD) (Moons)
   d) GRADE for assessing prognostic evidence (Iorio)
   e) Literature searching for prognostic factor systematic reviews (Parker)
   f) Other

5. Discussion of other methodological needs to provide guidance for prognosis reviews
Prognostic Factor Exemplar Review

- **Title**: Individual recovery expectations and prognosis of low back pain: Prognostic factor exemplar review
- **Review Team**: Hayden JA, Tougas M, Riley RD, Iles RA, Pincus T, Parker RM, Saunders R
- **Status**: 
  - Title registered with BRG
  - Protocol submitted July 2013
  - BRG Peer-review completed

*Rationale*: Important topic that will be easily understood, however also includes challenging methodological aspects for illustrating the conduct of a prognostic factor systematic review.
Individual Recovery Expectations & Prognosis of Low Back Pain

• LBP is a leading cause of disability worldwide
  – No specific cause identified for most cases
  – Many treatments, but none with strong evidence of effectiveness
  – Most costs attributed to small % with prolonged disability

• Prognostic research
  – Important
  – Studies find many factors associated (conflicting results)

• Individual recovery expectations – what a patient ‘expects will occur’ with respect to health condition:
  – General outcome expectations
  – Treatment expectations
  – Self-efficacy expectations
Rationale for Selection as Exemplar

• Back pain important health condition
• Expectations is a current concept in the field
  – In-line with patient-focused research
  – Potential widespread appeal
• Potentially modifiable, providing opportunity for relevant clinical messages, if appropriate
• Complex concept
  – Supported by relevant theoretical literature
  – Heterogeneity of measurement to consider/explore
• Risk of bias, including potential confounding is important
• Studies available:
  – Existing systematic reviews do not capture all of the available literature
  – Sufficient number of longitudinal studies for meaningful syntheses
  – Available studies represent different phases of investigation, from exploratory to confirmatory
Review Project

• Funded by Canadian Institutes of Health Research

• Three components:
  – Cochrane Exemplar Review
  – Prognostic factor methodological projects:
    • Literature searching
    • Risk of bias assessment
  – Integrated knowledge translation (consumers & clinicians)

• Timeline: 12-18 months
Prognostic models for the risk of postoperative nausea and vomiting (PONV)

Registered: Mid March
Protocol submitted: Mid September
PONV Px Authors

- 5 CARG editors/2 CARG authors
- 4 content experts/2 statisticians/1 methodologist
- 5 MDs/2 PhDs
- 4 continents/4 countries
- 2 content experts published prognostic model research
- 1 content expert published large Cochrane review (PONV Prophylaxis)
Ideas for Background Section


Average Prognosis

- Multiple sources
- PONV reported in essentially all observational studies of surgical outcome
- Active Big Pharma research funding
- Large Cochrane review > 750 RCTs — usually placebo control; (update > 1000 RCTs)
- Control group event rate range (0 to 100%)
# Prognostic Factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Studies</th>
<th>Patients</th>
<th>OR</th>
<th>$I^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>20</td>
<td>90916</td>
<td>2.57 (2.32-2.84)</td>
<td>69%</td>
</tr>
<tr>
<td>History PONV/MS</td>
<td>16</td>
<td>44216</td>
<td>2.09 (1.90-2.29)</td>
<td>54%</td>
</tr>
<tr>
<td>Non smoking</td>
<td>19</td>
<td>90116</td>
<td>1.82 (1.68-1.98)</td>
<td>45%</td>
</tr>
<tr>
<td>Age (per decade)</td>
<td>9</td>
<td>70562</td>
<td>0.88 (0.84-0.92)</td>
<td>64%</td>
</tr>
</tbody>
</table>

**Other patient demographics**

**Anesthetic factors**

**Surgical factors**

Prognostic Models

• At least 10 published models

• Example

  \[ z = -0.92 + 1.28 \times \text{female sex} - 0.29 \times \text{age (decades)} - 0.74 \times \text{smoking} + 0.63 \times \text{Hx PONV/MS} + 0.26 \times \text{duration (hours)} \]

Objectives

• Identify all developed prognostic models for estimating the risk of PONV
• Describe the characteristics (statistical methods, factor identification, internal validation including discrimination and calibration, etc) of the models
• Appraise the quality (external validation including discrimination and calibration, etc) of the models
• Report and if possible meta-analyse the performance of models that have been validated in external populations
Types of Studies

• Prediction model development without external validation in independent data
• Prediction model development with external validation in independent data
• External model validation with or without model updating
• All models for the development of a PONV risk score with linked prediction probability
Methods

• Methodological quality: Adapted QUIPS?
• Data synthesis: Tabular display
  – 1) patient population, 2) number of events/sample size, 3) statistical model type, 4) outcome type, 5) number of predictor factors, 6) discrimination, 7) calibration, 8) internal validation method, and 9) presentation format of model
• GRADE: Huguet et al 2013?
• SOF?
Agenda

1. Introductions
2. Update on Prognosis Exemplar Review initiative
3. Updates from Exemplar Review Groups:
   a) Prognostic Factor (Hayden)
   b) Predictive Model (Pace)
   c) Overall Prognosis (Moons)
4. Discussion of ongoing methodological projects related to prognosis reviews:
   a) Risk of bias assessment of prognostic factor studies (QUIPS) (Hayden)
   b) Risk of bias and applicability assessment for prediction model studies (PROBAST) (Wolff)
   c) Development of guidance for items to report when developing or validating risk prediction models (TRIPOD) (Moons)
   d) GRADE for assessing prognostic evidence (Iorio)
   e) Literature searching for prognostic factor systematic reviews (Parker)
   f) Other
5. Discussion of other methodological needs to provide guidance for prognosis reviews
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.

Well-conducted prognostic research is important for clinical decision making. It informs patients about possible outcomes, identifies risk groups for stratified management, and helps target specific prognostic factors for modification (1). However, previous research shows many methodological shortcomings in the design and conduct of studies that address prognosis (2–4).

Critical appraisal of prognostic studies is essential to assess and identify biases sufficiently large to distort study results. A tool to guide such critical appraisal would help reviewers conducting systematic reviews, clinical practice guidelines, research syntheses, and readers of such studies.

During assessment of risk domains should be considered when bias in studies of prognostic factors: study participation, fine prompting items for assessing bias domains and proposed ratings for the bias assessments as they considered prognosis studies of low back pain.

During an in-person workshop in 2006 that included working group members and other participants, a facilitator presented issues of agreement or dissent related to assessment of the bias domains. Through an iterative process of discussion and voting, workshop participants reached consensus on the wording of prompting items to guide ratings of high, moderate, or low risk of bias related to the

**Table:** A summary of the bias domains, prompting items and ratings of the QUIPS tool (reproduced from Hayden et al., 2013\textsuperscript{62}); a copy of the full QUIPS tool is available at www.annals.org.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Optimal Study or Characteristics of Unbiased Study</strong></td>
<td>The study sample adequately represents the population of interest.</td>
<td>The study data available [i.e. participants not lost to follow-up] adequately represent the study sample.</td>
<td>The prognostic factor (PF) is measured in a similar way for all participants.</td>
<td>The outcome of interest is measured in a similar way for all participants.</td>
<td>Important potential confounding factors are appropriately accounted for.</td>
<td>The statistical analysis is appropriate and all primary outcomes are reported.</td>
</tr>
<tr>
<td><strong>Prompting Items and Considerations</strong></td>
<td>a. Adequate participation in the study by eligible individuals</td>
<td>a. Adequate response rate for study participants</td>
<td>a. A clear definition or description of the PF is provided</td>
<td>a. A clear definition of the outcome is provided</td>
<td>a. All important confounders are measured</td>
<td>a. Sufficient presentation of data to assess the adequacy of the analytic strategy</td>
</tr>
<tr>
<td></td>
<td>b. Description of the source population or population of interest</td>
<td>b. Description of attempts to collect information on participants who dropped out</td>
<td>b. Method of PF measurement is adequately valid and reliable</td>
<td>b. Method of outcome measurement is adequately valid and reliable</td>
<td>b. Clear definitions of the important confounders measured are provided</td>
<td>b. Strategy for model building is appropriate and is based on a conceptual framework or model</td>
</tr>
<tr>
<td></td>
<td>c. Description of the baseline study sample</td>
<td>c. Reasons for loss to follow-up are provided</td>
<td>c. Continuous variables are reported or appropriate cut-points are used</td>
<td>c. Measurement of all important confounders is adequately valid and reliable</td>
<td>c. The method and setting of confounding measurement are the same for all study participants</td>
<td>c. The selected statistical model is adequate for the design of the study</td>
</tr>
<tr>
<td></td>
<td>d. Adequate description of the sampling frame and recruitment</td>
<td>d. Adequate description of participants lost to follow-up</td>
<td>d. The method and setting of measurement of PF is the same for all study participants</td>
<td>d. The method and setting of outcome measurement is the same for all study participants</td>
<td>d. Appropriate methods of imputation are used for missing PF data</td>
<td>d. There is no selective reporting of results</td>
</tr>
<tr>
<td></td>
<td>e. Adequate description of the period and place of recruitment</td>
<td>e. There are no important differences between participants who completed the study and those who did not</td>
<td>e. Adequate proportion of the study sample has complete data for the PF</td>
<td>e. Important potential confounders are accounted for in the study design</td>
<td>e. Appropriate methods of imputation are used for missing PF data</td>
<td>e. Important potential confounders are accounted for in the analysis</td>
</tr>
<tr>
<td></td>
<td>f. Adequate description of inclusion and exclusion criteria</td>
<td>f. Adequate description of participants who completed the study and those who did not missing PF data</td>
<td>f. Appropriate methods of imputation are used for missing PF data</td>
<td>f. Important potential confounders are accounted for in the study design</td>
<td>f. Important potential confounders are accounted for in the analysis</td>
<td></td>
</tr>
</tbody>
</table>

**Ratings**

- **HIGH:** The relationship between the PF and outcome is very likely to be different for participants and eligible non-participants
- **MODERATE:** The relationship between the PF and outcome may be different for participants and eligible non-participants
- **LOW:** The relationship between the PF and outcome is unlikely to be different for participants and eligible non-participants

*Prompting items are to guide the user's judgment about bias for each domain and are taken together to inform the overall judgment of potential bias, and facilitate consensus between reviewers for each of the 6 domains. Some items may not be relevant to the specific study or the review research.
# QUIPS Risk of Bias Assessment Instrument for Prognostic Factor Studies


<table>
<thead>
<tr>
<th>Biases</th>
<th>Issues to consider for judging overall rating of &quot;Risk of bias&quot;</th>
<th>Study Methods &amp; Comments</th>
<th>Rating of reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Instructions to assess the risk of each potential bias:</td>
<td>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.</td>
<td>Provide comments or text excerpts in the white boxes below, as necessary, to facilitate the consensus process that will follow.</td>
<td>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 orange cell to assess the risk as High, Moderate, or Low.</td>
</tr>
</tbody>
</table>

## 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).

<table>
<thead>
<tr>
<th>Source of target population</th>
<th>The source population or population of interest is adequately described for key characteristics (LIST).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method used to identify population</td>
<td>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)</td>
</tr>
<tr>
<td>Recruitment period</td>
<td>Period of recruitment is adequately described.</td>
</tr>
<tr>
<td>Place of recruitment</td>
<td>Place of recruitment (setting and geographic location) are adequately described.</td>
</tr>
<tr>
<td>Inclusion and exclusion criteria</td>
<td>Inclusion and exclusion criteria are adequately described (e.g., including explicit diagnostic criteria or <em>zero time</em> description)</td>
</tr>
<tr>
<td>Adequate study participation</td>
<td>There is adequate participation in the study by eligible individuals</td>
</tr>
<tr>
<td>Baseline characteristics</td>
<td>The baseline study sample (i.e., individuals entering the study) is adequately described for key characteristics (LIST).</td>
</tr>
<tr>
<td>Summary Study participation</td>
<td>The study sample represents the population of interest on key characteristics, sufficient to limit potential bias of the observed relationship between PF and</td>
</tr>
</tbody>
</table>

## 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).

<table>
<thead>
<tr>
<th>Proportion of baseline sample available for analysis</th>
<th>Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attempts to collect information on participants who dropped out</td>
<td>Attempts to collect information on participants who dropped out of the study are described.</td>
</tr>
</tbody>
</table>
Further Testing of QUIPS

- Within prognostic factor exemplar project
- Reliability testing:
  - Between raters
  - Between consensus agreements (teams)
- Validity:
  - Association between study/domain ROB ratings and prognostic factor effect size
- Collaboration opportunity:
  - Ongoing or upcoming prognostic factor review
  - Willingness to assess risk of bias in duplicate
PROBAST
Prediction model risk of bias assessment tool

Robert Wolff¹, Penny Whiting¹, Susan Mallett², Richard Riley³, Marie Westwood¹, Jos Kleijnen¹,⁴, Karel Moons⁵

¹ Kleijnen Systematic Reviews Ltd, York, United Kingdom
² University of Oxford, United Kingdom
³ University of Birmingham, United Kingdom
⁴ University of Maastricht, The Netherlands
⁵ University of Utrecht, The Netherlands

www.systematic-reviews.com  o  robert@systematic-reviews.com
Systematic reviews of prediction model studies

• Numerous methodology reviews in recent years:
  • Collins et al. J Clin Epidemiol. 2013
  • Mallett et al. BMC Med. 2010
  • Steyerberg et al. Epidemiology 2010

• Conclusions from methodology reviews:
  • (Very) poor reporting
  • (Very) poor methods
  • Each SR: own search strategy, own checklist data extraction. Hardly ever risk of bias assessment
Prediction model studies Risk Of Bias Assessment Tool

Other initiatives:
- TRIPOD statement: reporting of studies developing or validating multivariable prediction model
- Checklist for data extraction and framing SR question

Development of PROBAST

Delphi procedure using 42 panel members (see last slide)

Feedback from workshop yesterday
Which prediction model studies?

**Predictive factor studies** - which predictors contribute to prediction of particular prognostic/diagnostic outcome - preferring multivariable modelling – aim not to develop a prediction model for individualised predictions

(Hayden et al. 2013 Ann Intern Med)

**Model development studies** – to develop prediction model(s) from data at hand: identify important predictors; estimate multivariable predictor weights; construct model for individualised predictions; quantify predictive performance in development set; internal validation.

**Model validation studies** – test (validate) predictive performance of previously developed model in participant data other than development set – sometimes combined in development study – sometimes followed by updating/revision model

**Model impact studies** – quantify effect/impact actually using model on participant, physician behaviour and management; on health outcomes or effectiveness of care - hence using the model → comparative

QuIPS 2 – assessing bias in studies of prognostic factors (Comparative, intervention studies – different risk assessment)

Cochrane Risk of Bias tool

Structure of PROBAST

- Conform QUADAS-2 (Whiting et al. 2011 Ann Intern Med)
- Domain based: each with section risk of bias and applicability

- Risk of bias: extent to which primary study results in unbiased estimates of model performance (e.g. coefficients, calibration, discrimination or (re)classification) for intended use and target population.
- Applicability: extent to which model from a primary study matches the review question.
Domains of PROBAST

1. Participant selection
2. Outcome
3. Predictors
4. Sample size and flow
5. Analysis
PROBAST group

Doug Altman, University of Oxford  
Patrick Bossuyt, University of Amsterdam  
Gary Collins, University of Oxford  
Nancy Cook, Harvard University  
Gennaro D’Amico, Ospedale V Cervello  
Thomas Debray, University of Utrecht  
Jon Deeks, University of Birmingham  
Joris de Groot, University of Utrecht  
Emanuele di Angelantonio, University of Cambridge  
Tom Fahey, Royal College of Surgeons in Ireland  
Paul Glasziou, Bond University  
Frank Harrell, Vanderbilt University  
Jill Hayden, Dalhousie University  
Martin Heymans, University of Amsterdam  
Lotty Hooft, University of Amsterdam  
Chris Hyde, Peninsula Technology Assessment Group  
John Ioannidis, Stanford University  
Alfonso Iorio, McMaster University  
Stephen Kaptoge, University of Cambridge  
Jos Kleijnen*, Kleijnen Systematic Reviews  
Andre Knottnerus, University of Maastricht  
Mariska Leeflang, University of Amsterdam  
Susan Mallett*, University of Oxford  
Karel Moons*, University of Utrecht  
Frances Nixon, NICE  
Michael Pencina, University of Boston  
Pablo Perel, London School of Hygiene and Tropical Medicine  
Bob Philips, CRD  
Heike Raatz, University of Basel  
Hans Reitsma, University of Utrecht  
Rob Riemersma, Kleijnen Systematic Reviews  
Richard Riley*, University of Birmingham  
Maroeska Rovers, University of Utrecht  
Anne Rutjes, University of Bern  
Willi Sauerbrei, University of Freiburg  
Stefan Sauerland, IQWiG  
Fülöp Scheibler, IQWiG  
Rob Scholten, University of Amsterdam  
Ewoud Schuit, University of Utrecht  
Ewout Steyerberg, University of Rotterdam  
Toni Tan, NICE  
Gerben ter Riet, University of Amsterdam, Danielle van der Windt, Keele University  
Yvonne Vergouwe, University of Rotterdam  
Andrew Vickers, Memorial Sloan-Kettering CC  
Marie Westwood*, Kleijnen Systematic Reviews  
Penny Whiting*, Kleijnen Systematic Reviews  
Robert Wolff*, Kleijnen Systematic Reviews  
Angela Wood, University of Cambridge  

* denotes steering group members
introducing
GRADE for PROGNOSIS

Alfonso Iorio on behalf of the GRADE Prognosis working group
The journey:

1. ATG 9
2. Baseline risk*
3. Guidance paper

We have features for every step of the way

(*) Spencer, F. BMJ, 345(nov14 1), e7401–e7401
# Prognostic papers - definitions

<table>
<thead>
<tr>
<th>Study type</th>
<th>Study Goal</th>
<th>Examples in the field of atrial fibrillation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline risk</td>
<td>Establish the typical risk in a broadly defined population</td>
<td>Risk of bleeding in patients with atrial fibrillation receiving vitamin K antagonists</td>
</tr>
<tr>
<td>Risk factor</td>
<td>Establish how a particular patient characteristic influences risk</td>
<td>Influence of age on the risk of bleeding in patients with atrial fibrillation</td>
</tr>
<tr>
<td>Prognostic model</td>
<td>Development of a full prognostic model simultaneously considering a number of prognostic factors and classifying patients into various levels of risk</td>
<td>CHADS2 and CHADS-VASC for the risk of stroke HAS-BLED, HEMORRHAGE for the risk of bleeding</td>
</tr>
</tbody>
</table>
• Systematic reviewers in prognostic fields

• Systematic reviews of
  • absolute risk of events
  • in broadly defined populations
    and
  • methodologically sound
    • Measuring heterogeneity
    • Reporting RoB assessment

Which needs? Which best strategy?
Draft status
Summary concepts

• GRADE’s approach defines quality of evidence as confidence in effect estimates; the conceptualization can be readily applied to bodies of evidence addressing risk estimates in broadly defined populations.

• In the field of prognosis, observational studies begin as high quality evidence.
Summary concepts

• The **five domains** GRADE considers in rating down confidence in estimates of effect, i.e. risk of bias, imprecision, inconsistency, indirectness and publication bias, **also apply to prognostic studies**.

• GRADE's **criteria for rating up** quality may also apply, but are rarely relevant.
Summary concepts

• The **five domains** GRADE considers in rating down confidence in estimates of effect, i.e. risk of bias, imprecision, inconsistency, indirectness and publication bias, *also apply to prognostic studies*.

• GRADE's **criteria for rating up quality** may also apply, but are rarely relevant.
Summary concepts

• Guidance in applying these concepts to systematic reviews of prognostic studies provides a practical, useful approach to determine confidence in estimates of prognosis in broad populations.
## Systematic reviews

<table>
<thead>
<tr>
<th>N</th>
<th>Reference</th>
<th>Disease</th>
<th>Outcome</th>
<th>Design</th>
<th>N</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Lopes C</td>
<td>Atrial Fibrillation</td>
<td>Bleeding</td>
<td>Any</td>
<td>51</td>
<td>342699</td>
</tr>
<tr>
<td>2</td>
<td>Januel JM</td>
<td>Orthopedic Surgery</td>
<td>VTE</td>
<td>RCT, Obs</td>
<td>47</td>
<td>44844</td>
</tr>
<tr>
<td>3</td>
<td>Arcelus J</td>
<td>Anorexia Nervosa</td>
<td>Death</td>
<td>Obs</td>
<td>36</td>
<td>166642</td>
</tr>
<tr>
<td>4</td>
<td>Mohan KM</td>
<td>First Stroke</td>
<td>Stroke rec</td>
<td>Registries</td>
<td>13</td>
<td>9115</td>
</tr>
<tr>
<td>5</td>
<td>Yousef</td>
<td>Barrett Esophagus</td>
<td>Cancer</td>
<td>Obs</td>
<td>47</td>
<td>11279</td>
</tr>
<tr>
<td>6</td>
<td>Obeyesekere</td>
<td>Asympt pre-excitation</td>
<td>Sudden death</td>
<td>Any</td>
<td>20</td>
<td>1869</td>
</tr>
<tr>
<td>7</td>
<td>Su Y</td>
<td>Hemodialysis</td>
<td>HCV infec</td>
<td>Obs</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Desai TK</td>
<td>Barrett esophagus</td>
<td>Cancer</td>
<td>Obs</td>
<td>57</td>
<td>11434</td>
</tr>
<tr>
<td>9</td>
<td>Avina-Z JA</td>
<td>Rheumatoid Arthritis</td>
<td>CVE</td>
<td>CCohort</td>
<td>14</td>
<td>41490</td>
</tr>
<tr>
<td>10</td>
<td>Kaw R</td>
<td>CABG induced Afib</td>
<td>Death</td>
<td>Obs</td>
<td>11</td>
<td>40112</td>
</tr>
<tr>
<td>11</td>
<td>Lin KJ</td>
<td>Healthy population</td>
<td>Peptic ulcer</td>
<td></td>
<td>31</td>
<td></td>
</tr>
</tbody>
</table>
Is the CI precise?

YES → Inconsistency?

NO → Inconsistency?

YES → Rate down due to Inconsistency

NO → Rate down due to precision

Rate down due to imprecision

Inconsistency if fixed-effects model employed or OIS criteria not met.

YES → Rate down due to inconsistency and imprecision

NO → Rate down due to inconsistency only

Key message: if the CI is imprecise, we need to evaluate the inconsistency first
Risk of bias

• We suggest the use of available instruments

  – Quality in Prognosis Study (QUIPS)$^{12}$
  – Modified version of the Newcastle Ottawa (NO) scale$^{13, 14}$
  – Chapter 13 of the Cochrane Handbook for Systematic Reviews$^{15}$
1. Introductions
2. Update on Prognosis Exemplar Review initiative
3. Updates from Exemplar Review Groups:
   a) Prognostic Factor (Hayden)
   b) Predictive Model (Pace)
   c) Overall Prognosis (Moons)
4. Discussion of ongoing methodological projects related to prognosis reviews:
   a) Risk of bias assessment of prognostic factor studies (QUIPS) (Hayden)
   b) Risk of bias and applicability assessment for prediction model studies (PROBAST) (Wolff)
   c) Development of guidance for items to report when developing or validating risk prediction models (TRIPOD) (Moons)
   d) GRADE for assessing prognostic evidence (Iorio)
   e) Literature searching for prognostic factor systematic reviews (Parker)
   f) Other
5. Discussion of other methodological needs to provide guidance for prognosis reviews