PCORI Methodology Standards: Academic Curriculum
Step 5: Evaluate Study Quality and Applicability

- Decide how evaluation of study quality and applicability will be used
  - To inform users about risk of bias and applicability of evidence
  - To determine eligibility of studies
  - To give more or less weight to studies
  - To improve future research

- Focus on most important aspects of quality and applicability

- Right: Example of a “Risk of bias summary” figure

<table>
<thead>
<tr>
<th>Type of bias</th>
<th>Assessment criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selection bias and confounding</td>
<td>Randomization, allocation concealment and sequence generation in randomized controlled trials (RCTs); control of confounders in cohort studies; case matching in case-control studies</td>
</tr>
<tr>
<td>Performance bias</td>
<td>Fidelity to protocol, co-interventions, unintended interventions</td>
</tr>
<tr>
<td>Attrition bias</td>
<td>Completeness of follow-up and outcome data, intention-to-treat analysis with appropriate handling of missing data</td>
</tr>
<tr>
<td>Detection bias</td>
<td>Blinding of outcome assessors, bias in inferential statistics, validity/reliability of measures</td>
</tr>
<tr>
<td>Reporting bias</td>
<td>Selective outcome reporting; compare results to prespecified methods</td>
</tr>
<tr>
<td>Sponsor bias</td>
<td>Any bias resulting from influence of sponsor</td>
</tr>
</tbody>
</table>
Precision

- Sample size and statistical power
  - Number of subjects needed for power to detect important difference
  - If control group response is 20%, type I error 0.05, and type II error 0.20, you need 40 in each group to have 80% power to detect absolute difference of 15%

- Clinical importance versus statistical significance
  - Minimally important difference
Applicability (External Validity)

- Consider PICOTS
  - Population
  - Interventions
  - Comparisons
  - Outcomes
  - Timing
  - Setting

- Use subgroup analysis and meta-regression

- Use epidemiological studies and surveys to assess representativeness of studies in the review

- Consider feasibility and acceptability
  - Use SUPPORT tool* to assess applicability

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Potential Causes of Bias and Error in Evaluating Study Quality and Applicability

- **Bias**
  - Evaluator influenced by conflict of interest
  - Evaluator influenced by another reviewer

- **Error**
  - Inadequate specification of assessment criteria
  - Limited reliability of assessment instruments
  - Inadequate training and auditing
What Can Be Done to Minimize Bias and Error in Evaluating Study Quality and Applicability?

- Use established instruments with independent dual review
  - For RCTs:
    - Jadad criteria—based on three main questions (randomization, blinding, follow-up), with good inter-rater reliability
    - Cochrane risk of bias tool—covers the risk of bias domains in detail without generating a score (http://www.cochrane-handbook.org/)
  - For observational studies, assess risk of bias domains with:
    - Downs and Black tool (*J Epidemiol Commun Health*, 1998, 52(6), 377-384)
    - Newcastle Ottawa tool (www.ohri.ca/programs/clinical_epidemiology/oxford.htm)
    - ACROBAT-NRSI (www.riskofbias.info)

- Establish quality control process with a plan to reconcile discrepancies
Standard 2.1: Establish a team with appropriate expertise and experience to conduct review
   - Include expertise in systematic review methods

Standard 2.3: Ensure user and stakeholder input as review is designed and conducted
   - Protect independence of team to make final decisions about design, analysis, and reporting

Standard 2.4: Manage bias and conflict of interest for individuals providing input
   - Require individuals to disclose conflict of interest and professional or intellectual bias
   - Exclude input from individuals whose conflict of interest or bias would diminish credibility in eyes of intended users
Relevant IOM Standards for Evaluating Study Quality and Applicability

- **Standard 2.6: Develop a systematic review protocol**
  - Describe context and rationale for review from decision-making and research perspective
  - Describe study screening and selection criteria (inclusion and exclusion)
  - Describe which outcomes, time points, interventions and comparisons will be addressed
  - Describe search strategy for identifying relevant evidence
  - Describe procedures for study selection and data extraction, and how to identify and resolve disagreement between researchers in study selection and data extraction
  - **Describe approach to critically appraising studies**
  - Describe method for evaluating body of evidence, including quantitative and qualitative synthesis
  - Describe and justify planned analyses of differential treatment effects according to subgroups, how intervention is delivered, or how outcome measured
  - Describe proposed timetable
Relevant IOM Standards for Evaluating Study Quality and Applicability

**Standard 3.6: Critically appraise each study**

- Systematically assess the risk of bias, using predefined criteria
- Assess the relevance of the study’s populations, interventions, and outcome measures
- Assess the fidelity of the implementation of interventions