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Reproducibility in Systematic Reviews and Meta-Analyses

Derek K Smith, D.D.S., Ph.D.
Vanderbilt University Medical Center
Nashville, TN, USA
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Types of Reviews

- Narrative Reviews- Descriptive overview of a subject. May contain discussions of papers and their results, but the literature review is not necessarily systematic
- Systematic Reviews- Comprehensive search strategy is employed with the goal of identifying all relevant studies
- Meta-Analyses- A component of a systematic review in which statistical techniques are used to synthesize data from multiple studies into a single quantitative summary

Guidelines for Reproducibility

- A number of groups have put forward widely used guidelines for systematic reviews
  - Cochrane Collaboration
  - Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)
  - Meta-Analyses of Observational Studies in Epidemiology (MOOSE)
- Recommendations range from full methodologies to reporting guidelines

PRISMA 2009 Reporting Checklist

- A readily available review protocol
- Study eligibility criteria
- Databases searched
- Full search strategy including terms and logic
- Study selection process
- Data abstraction
- Data items
- Risk of bias assessment for each study
- Summary measures (odds ratios, risk differences, etc)
- Synthesis of results
- Risk of bias assessment across studies (publication bias)
- Additional analyses

Additional Items from MOOSE

- Qualifications of searchers
- List of citations identified and justification for any exclusion
- Method for handling abstracts and unpublished studies
- Assessment of heterogeneity
- Sensitivity analyses

ISOO 2008 Reviews

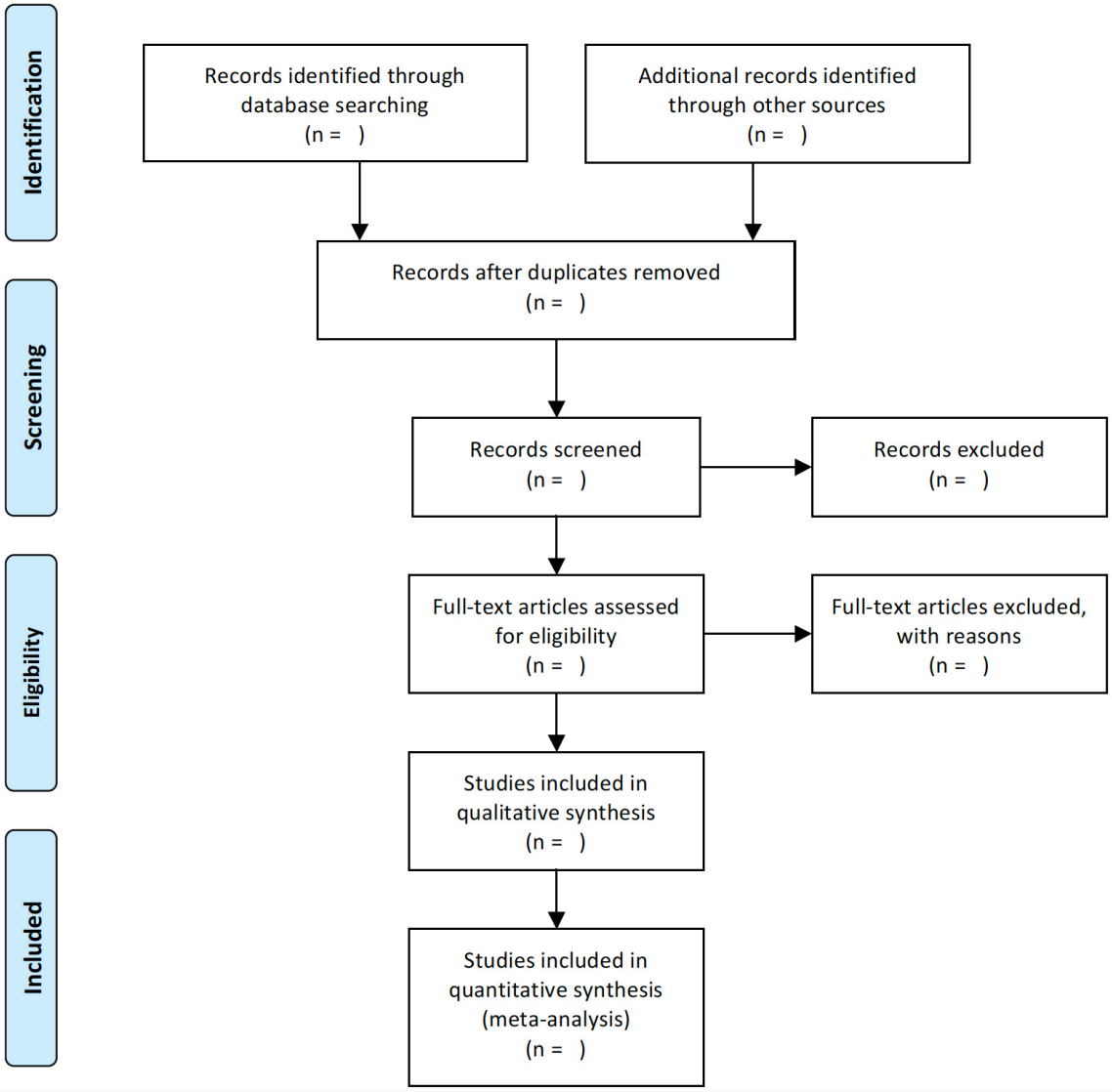
Identified the report as a systematic review
Describe the rationale for the review in the context of what is already known
Provide an expllicit statement of the questions being addressed
Full review protocol available
Specific study characteristics used for eligibility (years considered, language, etc)
Describe all information sources and databases including the last date searched
Present full electronic search strategy
State the process for selecting studies
Describe method of extracion from reports (piloted forms, independently, duplicate, etc)
List and define all variables for which data were sought and any assumptions
Describe method used for assessing risk of bias of individual studies and how this information is used in data synthesis
State principal summary measure
Describe methods of handling data and combining results including measures of consistency (I2)
Specify any assessment of risk of bias that may affect the cumulative evidence (e.g. publication bias, selective reporting)
Describe any additional analyses including sensitivity analyses
Give the numbers screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram
For each study, present characteristics for which data was extracted
Present data on the risk of bias for each study
For all outcomes present for each study a) simple summary data b) estimates with confidence intervals, ideally with a forest plot
Present results of each meta-analysis including confidence intervals and measures of consistency
Give the results of additional analyses (sensitivity, meta-regression etc)
Summarize the main findings inclucing the strength of evidence
Discuss limitations at the study and outcome level and at the review level
Provide a general interpretation of the results in the context of other evidence and implications for future research

PRISMA Reporting for Updates

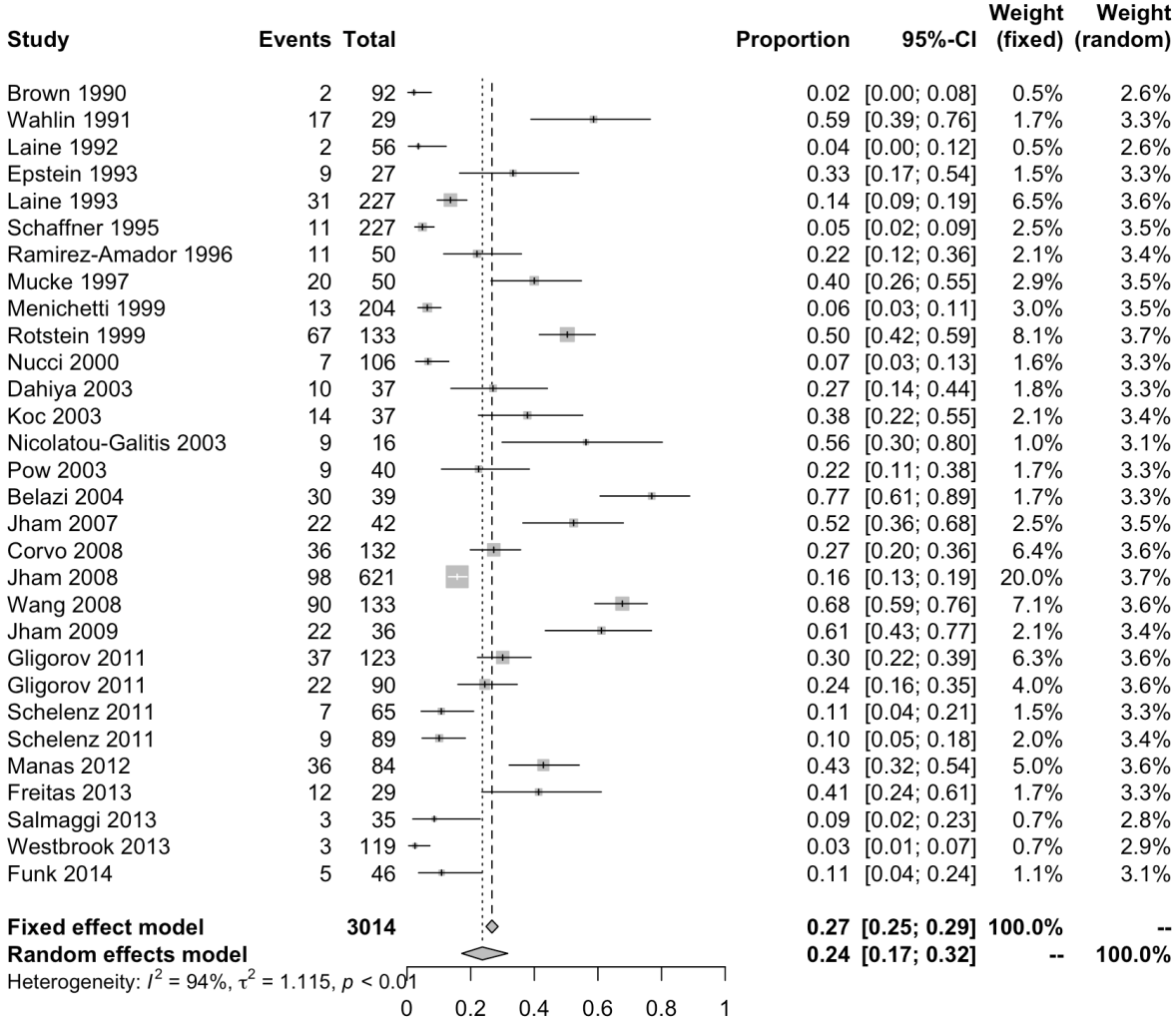
- Publish a full protocol for each study
- Include the last date included databases were searched
- Give the full electronic search strategy
- Describe how bias is assessed
- Define all items abstracted from papers
- Measures of consistency

- Consider sensitivity analyses
- Give the number screened, excluded, and the reason for any exclusions in a *flow diagram*
- Present the characteristics of each study included in tabular form
- Present the risk of bias for each study
- For each study present the data abstracted in a *forest plot*
- Present the results of each meta-analysis with a confidence interval and a *measure of consistency*
- Discuss limitations at the study outcome and *review level*

PRISMA Flow Diagram



Forest Plot Example



Bias Assessment- MASCC/ISOO scoring

1) Representativeness:	Multi-institution, consecutive patients representative of underlying population 2 Single institution, consecutive patients, representative of underlying population 1 Convenience sample 0
2) Ascertainment bias	CT: daily or weekly assessment 2 RT: >4 assessments during or after RT CT: >1 assessment per cycle, <weekly assessment 1 RT: 2–4 assessments during or after RT CT: 1 assessment per cycle 0 RT: 1 assessment during or after RT
3) Misclassification bias:	Prospective (patient or professional) 1 Retrospective (patient recall) 0
4) Examiner bias:	Blinded 1 Unblinded 0
5) Oral complication assessment validity:	Standard validated scale 2 Well-defined, study-specific scale 1 Not defined 0
6) Estimate precision:	Sample size sufficient to estimate a prevalence of 20% within: ±5% ($n \geq 250$) 2 ±10% ($50 < n < 250$) 1 Greater than 10% ($n \leq 50$) 0

Proposals for Improved Reproducibility

- Publish a protocol for each review section with specific details about how the review will be conducted, what will be assessed, search strategy, data abstraction methods, and statistical analysis plan.
- Consider tailoring bias assessment to the type of study being examined (i.e. Blinding should not be a concern in a retrospective review)
- Evaluate bias and precision separately
- Design a customized database for each review that regulates how data is entered, keeps track of who makes changes to the database and when, is readily available to reviewers through the web, and exports the data in easy to analyze format
- Achieve improved fidelity by having reviewers do a short training session and evaluating a test paper