Please think of **questions** you'd like answered during this workshop

Conducting Systematic Reviews: An Introduction

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Forthcoming publication in *Medical Education*

Why do a systematic review?

Hint: it's NOT a quick path to publication!

Eva: On the limits of systematicity. *Med Educ* 2008.

➔ Cook: Narrowing the focus and broadening horizons. *AHSE* 2008

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	Systematic / Quantitative	Nonsystematic / Qualitative
Purpose	Summ. lg amt data, confirm hypothesis	Generate novel insights, hypothesis generating
Classic design	Meta-analysis, RCT	Critical synthesis (review), inductive analysis
Selection	Comprehensive, systematic	Purposeful, selective
Inclusion	Similar (homogenous) population, intervention, and outcome	Perceived relevance to question; intentionally seeks dissimilar sources
Analysis	Tests of inference or meta-analysis	Qualitative (narrative)
Data presented	Single number or series of numbers	Rich, critical, insightful narrative
Attribution of differences	Differences are error (heterogeneity)	Differences suggest novel insights
Validity	Large N, homogeneity, lack of bias	Triangulation (concordant multiple sources)
Validity threats	Systematic error (bias) in sampling, heterogeneity	Researcher bias in analysis, failure to triangulate or sample to saturation
Researcher	Impartial, detached	Immersed, interactive

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Cook, AHSE 2008

The Process

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Focused question

---------- *Write protocol*

Systematic search

Inclusion / exclusion

Data abstraction

Data analysis

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Focused question

- Population
- Intervention
- Comparison
- Outcome
- Design

- Do you have an hypothesis?

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Literature search

- Information sources
  - Database
  - Files, experts
  - Hand search
- Search terms
- Restrictions (time, language, grey)
- Assistance from expert

See: Maggio, Acad Med 2011

Inclusion / Exclusion

- Defined criteria [operational, examples]
- Ideally, in duplicate
  - Pilot, pilot, pilot
- Two stages
  - Title / abstract (err on inclusion)
  - Full text (consensus "no error")

Data abstraction

- P … I … C … O … D
- Results
- Methodological quality
  - MERSQI (Reed 2007)
  - Newcastle-Ottawa (Cook 2008, 2011)

- Data abstraction form
  - Pilot, pilot, pilot
  - Refine … ***operational*** definitions

Document evolution

Reviewing Tools

- Paper
- Email, IM, teleconf
- Excel
- EndNote
- Google apps: Groups, Docs
- Purpose-built

Analysis

- **Synthesis**
  - ≠ "litany of the literature"
  - Think of **reader** … organize, interpret
  - Weaknesses, heterogeneity, gaps
- *Consider* quant. summ (meta-analysis)

What makes a good synthesis?

Focused question

Write protocol

Systematic search

Inclusion / exclusion

Data abstraction

Data analysis

Hands on practice … With neighbor →

- What did these authors do at each step?
- What could they have done better?
- Why did they make the decisions they did?
- What questions come to YOUR mind as you reflect on this example?

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Reporting

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PRISMA
www.prisma-statement.org

ACADEMIA AND CLINIC | Annals of Internal Medicine

Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement

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Editor's Note: In order to encourage dissemination of the PRISMA Statement, this article is being published in the Annals of Internal Medicine. With the journals' permission, it will be also published in PLOS Medicine, BMJ, Journal of Clinical Epidemiology, and Open Medicine. The authors jointly hold the copyright of this article. For details on further use, see the PRISMA Web site (www.prisma-statement.org).

Systematic reviews and meta-analyses have become increasingly important in health care. Clinicians read them to keep up to date with their field (1, 2), and they are often used as a starting point for developing clinical practice guidelines. Granting agencies may require a systematic review to justify the need for further primary research (3), and many health care journals are receiving in this direction (4). As with all research, the value of a systematic review depends on what was done, what was found, and the clarity of reporting. As with other publications, the reporting quality of systematic reviews varies, limiting readers' ability to assess the strengths and weaknesses of these reviews.

Several empirical studies evaluated the quality of review reports. In 1987, Mulrow examined 50 review articles published in four leading medical journals in 1985 and 1986 and found that none met all eight explicit scientific criteria, such as a quality assessment of included studies (5). In 1987, Sacks and colleagues (6) evaluated the adequacy of reporting of 83 meta-analyses on 23 characteristics in six domains. Reporting was generally poor between one and 16 characteristics (median: five characteristics) were adequately described (mean = 2.7). A 1996 update of this study found little improvement (7).

In 1996, to address the suboptimal reporting of meta-analyses, an international group developed a guidance called the QUOROM Statement (QUality Of Reporting Of Meta-analyses), which focused on the reporting of meta-analyses of randomized, controlled trials (8). In this article, we summarize a revision of these guidelines, renamed PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses), which have been updated to address several conceptual and practical advances in the science of systematic reviews (Box 1).

See also:
Web-Only
Related Exploration and Elaboration article
Downloadable template Table S1 and Figure S1
Conversion of graphics into slides

TERMINOLOGY

The terminology used to describe a systematic review and meta-analysis has evolved over time. One reason for changing the name from QUOROM to PRISMA was the desire to encompass both systematic reviews and meta-analyses. We have adopted the definitions used by the Cochrane Collaboration (9). A systematic review is a review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyze data from the studies that are included in the review. Statistical methods (meta-analysis) may or may not be used to analyze and summarize the results of the included studies. Meta-analysis refers to the use of statistical techniques in a systematic review to integrate the results of included studies.

DEVELOPING THE PRISMA STATEMENT

A three-day meeting was held in Ottawa, Ontario, Canada, in June 2005 with 29 participants, including representatives from the clinical epidemiology, biostatistics, and a statistician. The objective of the Ottawa meeting was to revise and expand the QUOROM checklist and flow diagram, as needed.

The executive committee completed the following tasks: prior to the meeting: a systematic review of studies examining the quality of reporting of systematic reviews, which provided empirical evidence for the need to revise the original and other articles that might inform the meeting, especially in relation to modifying checklist items. An international survey of review authors, consumers, and groups commissioning or using systematic reviews and meta-analyses was completed, including the International Network of Agencies for Health Technology Assessment (INAHTA) (10) and the Guidelines International Network (GIN) (11). This survey asked about items in QUOROM, including the utility of the existing checklist items. The results of these activities were presented during the meeting and are summarized on the PRISMA Web site (www.prisma-statement.org).

Table 1. Checklist of Items to Include When Reporting a Systematic Review or Meta-Analysis

Section/Topic	Item #	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

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Introduction

- Be brief
- Highlight previous reviews
  - Limitations → gap

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Methods

- Describe each step of process (separate headings)

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Results

- Trial flow (ref diagram)
- Study characteristics
- Study quality
- Synthesis (* remember to synthesize *)
- Tables:
  - 1. List all studies (salient data)
  - 2. Quality of all studies
- Fig: Meta-analysis, themes, framework

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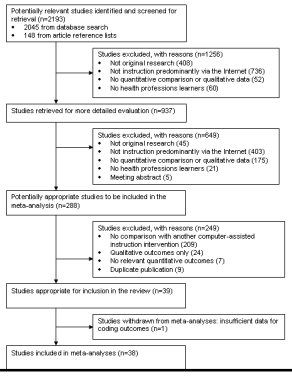
Flow diagram



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Discussion

- Summary
- Limitations
- Integration with previous reviews
- Implications

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Abstract

- Background (or Context)
- Question (or Objective)
- Data sources
- Study selection
- Data extraction
- Data synthesis
- Conclusions

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A taste of meta-analysis

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Meta-analysis
Why?

- Are results similar?
- What is overall best estimate?
- How precise is this estimate?
- Can dissimilarities be explained?

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Meta-analysis
Should I try?

"Statistical tests cannot compensate for lack of common sense, clinical acumen, and biological plausibility"

– Lau 1997

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Systematic review ≠ meta-analysis

- Can have integrative systematic review
  - "Realist review"
  - Systematic critical review

Meta-analysis
Estimate effect – common metric

- Binary (pass, death, complication)
  - Odds ratio
- Continuous (score, rating, rate)
  - [standardized] mean difference = "effect size" (Cohen d, Hedges g)
  - r

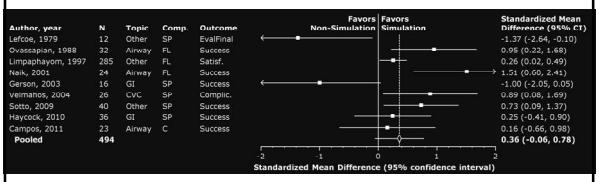
Meta-analysis
Estimate common effect

- Fixed effects
  - All variance due to random sampling around "true"
  - (Large sample → error disappears)
- Random effects
  - Some error due to diff. population / context / intervention / outcome
  - (Error persists even with lg sample)

Meta-analysis
Estimate common effect

- Study weights
  - Function of sample size and ES
  - *(Does NOT include the variance of the individual study)*
- Random effects ADDS between-study variance

- **→ "Pooled estimate" and CI**



Forest plot: standard (list all studies)

Meta-analysis
Estimate & explore inconsistency

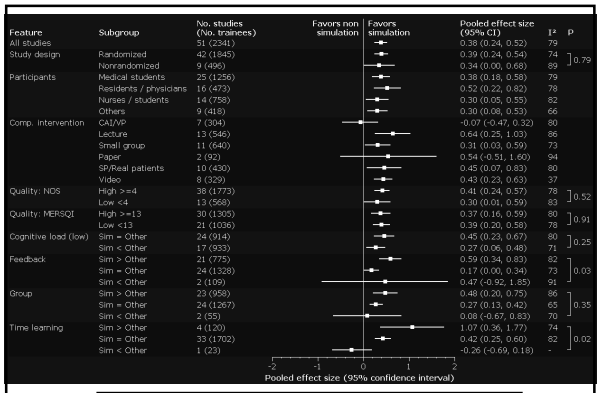
- Aka heterogeneity
- I^2 ("I squared"): >50% is "high"
  - (also a function of N … large sample = higher I^2)

See: Higgins, BMJ 2003

- Explanatory covariates
  - Treatment-subgroup interaction
  - Meta-regression (~ANOVA)

Meta-analysis
Estimate & explore inconsistency

- Subgroup vs Sensitivity analysis
- Subgroup: classify, analyze in groups
  - 17 studies total, ES = 0.49
  - 9 RCT, ES = 0.31
  - 8 observational, ES = 0.55
    - P=0.02 for difference (interaction)
- Sensitivity: classify, delete (ignore) 1 grp
  - 9 RCT, ES = 0.31

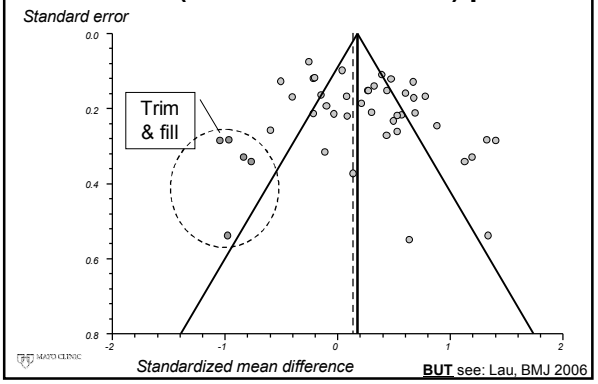


Forest plot: List subgroup analyses

Meta-analysis
Estimate & explore bias

- Study quality (methods)
  - Low-qual → bias? (Cook, Med Educ 2011)
  - Handle it?
    - Subgroup / meta-regression
    - Sensitivity analysis (delete)
- Publication bias (small / neg studies unpublished)
  - Detect? ***NO GOOD WAY***! (Funnel plot)
  - Handle it? No good way (trim & fill)

Funnel ("bias assessment") plot



BUT see: Lau, BMJ 2006

Meta-analysis in medical education?

- The future is bright … but still in the future
- We need common
  - Conceptual frameworks
  - Interventions (operational)
  - Outcomes

Additional References

- Cook & West. Conducting Systematic Reviews in Medical Education: A Stepwise Approach. In press, *Medical Education*
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  - 126:376; 127:380, 531, 820, 989
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