Systematic reviews: key principles of their development and reporting

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Systematic review

- A systematic review is a scientific investigation that focuses on a specific question and uses explicit, prespecified scientific methods to identify, select, assess, and summarise the findings of similar but separate studies.
  - A study of studies

- Objective is to summarize evidence from multiple studies using explicit methods

- It may include a quantitative synthesis (meta-analysis), depending on the available data
Key characteristics of SR

- Focused well defined research question
- Clearly stated title and objectives
- Comprehensive strategy for identification of all relevant studies (published & unpublished)
- Explicit (and justified) predefined inclusion & exclusion criteria
- Critical appraisal of studies
- Synthesis of the results of eligible studies
  - Quantitative (meta-analysis)
  - Qualitative
- Structured report
Systematic review

- A systematic identification and evaluation of all the available relevant evidence
  - always a good approach to address evidence regarding a health care issue

Meta-analysis

- Statistical combination of the numerical results of several studies
  - may be appropriate as part of a systematic review
Principles

- Systematic reviews are governed by principles of
  - methodological rigour
  - transparency
  - Reproducibility

- The same principles apply to all study types; we focus on randomised trials (RCTs)
Rationale for systematic reviews

- **To minimize bias**
  - of the reviewer, and in the research studies themselves

- **To enhance precision**
  - by including all the relevant evidence

- **To put results into context**
  - examine conflicts and understand differences

- **To help prioritize research**
  - by knowing exactly what has been done, how well, and with what findings
The systematic review process

1. Formulation of a clear question
2. Eligibility criteria for studies
3. Search for potentially relevant studies
4. Selection of studies into the review
5. Extraction of data
6. Assessment of methodological quality of included studies
7. Synthesis of findings (possibly using meta-analysis)
8. Presentation of data and results
9. Interpretation and drawing conclusions

NB: Should have a protocol
PRISMA
Flow diagram

Identification

- # of records identified through database searching
- # of additional records identified through other sources

Screening

- # of records after duplicates removed
- # of records screened
- # of records excluded

Eligibility

- # of full-text articles assessed for eligibility
- # of full-text articles excluded, with reasons

Included

- # of studies included in qualitative synthesis
- # of studies included in quantitative synthesis (meta-analysis)
Data to be extracted

- **Study design**
- **Details of interventions**
- **Patient characteristics**
- **Study methods**
  - Method of randomization
  - Blinding (participants, caregivers, assessors)
  - Method of analysis
- **Results (per group)**
  - Sample size
  - Number with each binary outcome
  - Mean and SD for each continuous outcome
  - Loss to follow up
Data extraction problems

- Poor presentation of methodology and results in papers causes many problems
  - The allocation procedure is often not stated clearly
  - Results may be given incompletely
    - Only as P value
    - For continuous outcomes SD often missing
  - It may be unclear if all randomised patients were included in the analysis

- Often not clear how to proceed when necessary information is not given
  - Contact with the authors is desirable
Outcome measures

- **BINARY OUTCOMES**
  - death
  - relapse
  - cure
  - etc
  - may be good or bad
  - may be continuous originally (e.g. pain relief)
  - any time element is ignored

- **CONTINUOUS OUTCOMES**
  - physical measurement (e.g. lung function)
  - duration (e.g. time to walk 50m, stay in hospital)
  - volume (e.g. blood loss)
  - area (e.g. pressure sore)
  - biochemical measurement
  - quality of life
  - etc

- **TIME TO EVENT OUTCOMES**
  - time to death
  - time to healing
Systematic review conduct: some key points

- **Protocol**

- **Objectives**
  - Focused well defined research question
  - Primary outcome (one)
  - Minimum number of secondary outcomes
  - Include adverse events (harms) if relevant

- **Eligibility criteria**

- **Literature search**
  - Comprehensive (electronic databases, grey literature, reference lists, personal communication, ...)

Systematic review conduct: some key points

- **Identifying eligible studies**
  - Selection of studies using predefined criteria
  - Independently done by more than one reviewer

- **Data extraction**
  - Data extraction sheet
    - Methods
    - Results
  - Independently done by more than one reviewer
Assessment of risk of bias

- Problems with the design and execution of individual studies of healthcare interventions raise questions about the validity of their findings.

- In clinical trials, biases can be broadly categorized as selection bias, performance bias, detection bias, attrition bias, reporting bias and other biases that do not fit into these categories.

- Cochrane Collaboration developed the ‘Risk of bias tool’
  - sequence generation (selection bias)
  - allocation concealment (selection bias)
  - blinding of participants and personnel (performance bias)
  - blinding of outcome assessment (detection bias)
  - incomplete outcome data (attrition bias)
  - selective outcome reporting (reporting bias)
  - other potential sources of bias
Systematic review conduct: some key points

- **Data synthesis**
  - **Qualitative**: descriptive summary
  - **Quantitative - meta-analysis**: statistical combination of data from a number of studies when there are:
    - Minimal differences between studies
    - Outcome measured in the same way
    - Data are available

- **Investigation of possible reporting bias**
  - Unpublished results

- **Interpretation**

- **Summary of findings (GRADE)**
  - Key information in a quick and accessible format
  - Relating the quality of evidence to the outcomes
Poor reporting of systematic reviews

- Good reporting of primary studies is crucial for SR development

  **BUT**

- Reviews themselves are afflicted by the problems of poor reporting
  - Moher et al. assessed epidemiological and reporting characteristics and bias-related aspects of 300 systematic reviews (of which 125 were Cochrane reviews).
  - The overall quality of reporting of key aspects of methodology was very inconsistent with particularly discouraging findings for non-Cochrane reviews.

  [Moher; *PLoS Medicine* 2007]
Reporting guidelines for systematic reviews

- Should take account of the key methodological components of a review
  - An aid for authors and reviewers

- What information should be given about the review itself?

- What information should be given about the primary studies?