Systematic reviews and meta-analysis

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Why consider a systematic review?

• Evidence about an intervention or a risk factor taken from different studies can be conflicting.
• Methods are needed to assess all available information in an unbiased way, in order to:
  • Guide practice
    – Does an intervention work?
    – In whom does it work?
    – At what dose?
  • Identify evidence gaps
  • Guide further research
Non–systematic

• provide an overview of the literature on a topic, but
• do not provide unbiased answers to research questions.

Systematic

• highly structured, à priori research question/hypotheses; designed to reduce bias
• attempt to collate all relevant empirical evidence to answer a specific research question
The Research Question: PICO(T)

- **People**, patients or population - who are you asking the question about?
- **Intervention** – in what intervention (or exposure or factor) are you interested?
- **Control or comparison** - what are you comparing the intervention to?
- **Outcome** - what outcome are you interested in measuring?
- **Time** - and at what time points?

*Take home message 1: THE RESEARCH QUESTION IS THE FOUNDATION*
Steps in Review Process

- Research question/hypothesis (PICOT)
- Search for data
- Select studies against pre-specified eligibility criteria (based on PICOT)
- Assess risk of bias in studies
- Data synthesis (narrative and/or meta-analysis)

Take home message 2: WRITE ALL THIS DOWN IN A PROTOCOL BEFORE YOU START!
• Reduces bias: each methodological decision can alter findings and create bias

• Prospective registration possible 
  http://www.crd.york.ac.uk/PROSPERO/

• Some journals require it (as for RCTs)
• international not–for–profit organisation
• provides up–to–date information about the effects of health care by synthesising the best available evidence into systematic reviews.
• focus on quality of reviews and accessibility of information.

Cochrane Library: http://www.thecochranelibrary.com
Cochrane Handbook: http://handbook.cochrane.org/

Take home message 3: THE COCHRANE HANDBOOK IS INDISPENSABLE
• Identify data sources
  – Which databases?
  – Trial registers?
  – Unpublished data?
  – Reference list of included papers

• Develop search strategy based on PICO
Research Question: To determine the effectiveness of vitamin D supplementation for improving bone mineral density in children.
• If not very experienced, make use of a clinical librarian
• Cochrane has filters for study design (see handbook)
• Check for reviews of same intervention and/or similar outcome measures for tips
• Run in stages – if too many hits not specific enough, if not enough then too narrow and likely to miss studies
Three stages
• all against pre-set criteria
• all by at least 2 reviewers independently
• compare results at end of each stage
• all decisions documented
• if needed – information from authors and/or third reviewer to adjudicate
Flow of information through phases of a systematic review

• Independent with comparison between reviewers to reduce errors
• Use a predesigned and pilot tested proforma
• Relevant study and participant characteristics
• Outcome data
• Commonest are straightforward (in theory!)
  – N, means and SD for continuous data
  – numbers with and without outcome for dichotomous outcomes
• Less common: ordinal data, counts and rates calculated from counting the number of events that each individual experiences; and time-to-event (typically survival) data
• SDs not reported
• Studies using mix of continuous and dichotomous measures of same outcome
• Studies using different methods of measuring a continuous outcome
• Studies reporting in subgroups separately
• Data in figures, not in tables
• Etc, etc, etc
• These issues can be dealt with...
• See Cochrane Handbook...
• May need statistical advice and/or advice from an experienced systematic review author...

Take home message 4: SEEK THE ADVICE YOU NEED!
1. The research question is the foundation
2. Write and register a protocol before commencing your review
3. The Cochrane Handbook is indispensable
4. Seek the advice you need!