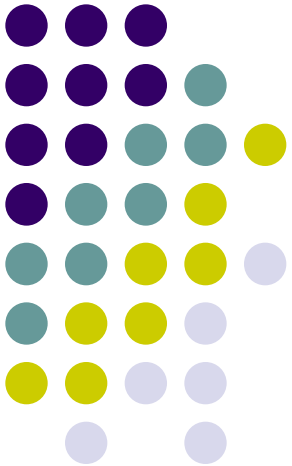
Principles & rationale for systematic review

Hilary Thomson



University of Glasgow

CHIEF SCIENTIST OFFICE

MRC|CSO Social and Public Health Sciences Unit

MRC Medical Research Council

Outline

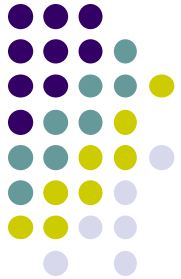
- Rationale for systematic reviews
- What is a systematic review (& what it is not)
- What systematic reviews can contribute
- Key components of a good systematic review
- Why systematic reviews of complex interventions are challenging

What is a systematic review?

Why do we need literature reviews?

- Calls for evidence
  - make use of existing research and knowledge

Why do we need literature reviews?



- Calls for evidence- make use of research and knowledge
- Information overload: an efficient method of dealing with information overload
- Deal with conflicting findings
- Best evidence: studies vary in design, soundness, population studied (etc)
- Single studies are rarely definitive
  - Synthesis of evidence allows greater confidence in findings
    - Repeated findings & consistency across different contexts, populations
    - Greater statistical power in meta-analysis with larger population

Adverse effects of doing a literature review

Non-systematic reviews

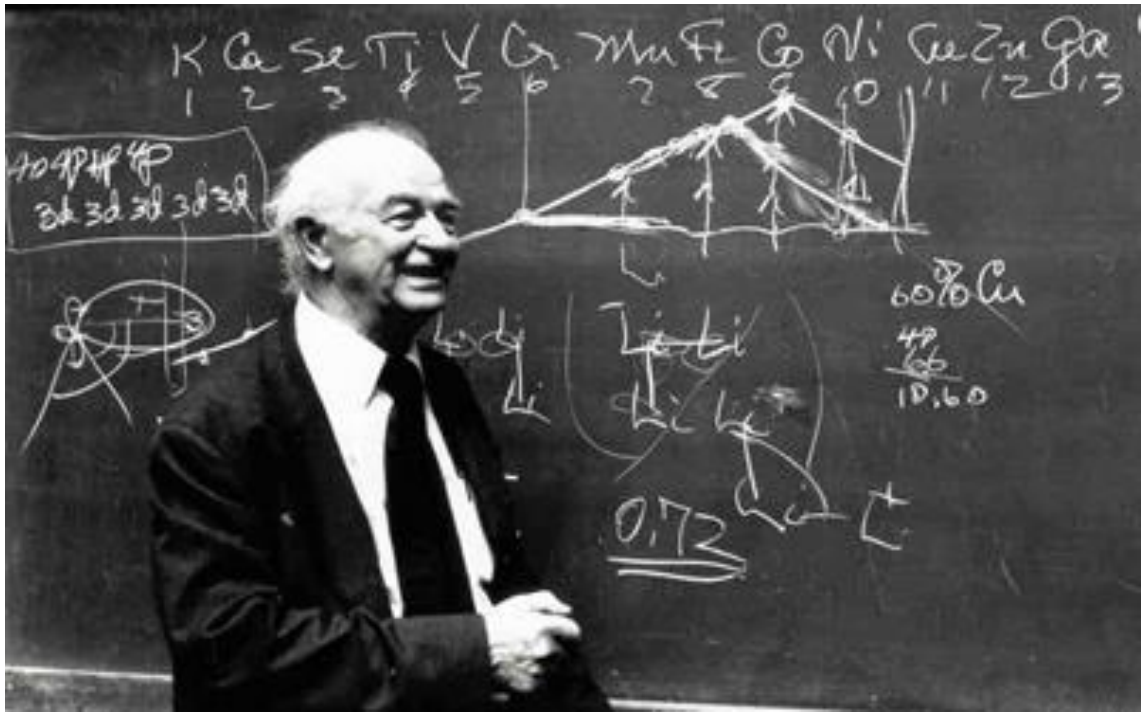
- Expert reviews- provides expert opinion on state of the field
- Introductions to papers, thesis
- Scoping reviews- map out an area identifying key literature, range of disciplines/outcomes/ interventions/evaluation…
- Rapid reviews

Not well equipped to provide comprehensive synthesis of best available evidence

Why do people take Vitamin C when they have a cold?

…**Nobel Laureate** Linus Pauling's 1986 book *"How to live longer and feel better"*, in which he reviews the literature and concludes that

"*…we should be getting 200 times the amount of vitamin C that the Food and Nutrition Board recommends*"

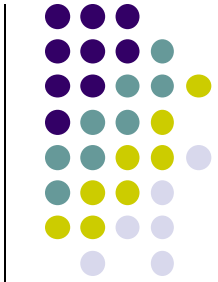


Testing Pauling's claims about Vitamin C & colds

- Exhaustive search of databases, and hand searches of journals and special collections,
- Identifyied 61 trials- 15 methodologically sound
- Even in megadoses Vitamin C cannot prevent a cold, though it might shorten its duration if already infected
- Pauling's review did not mention 5 of the "top 15" studies, and two others were referred to only in passing
- A haphazard review, even one carried out by an expert, can be very misleading

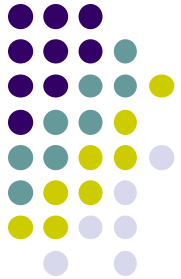
Knipschild P. Some examples of systematic reviews. In: Chalmers I, Altman D, editors. *Systematic reviews*. London: BMJ Publishing Group, 1995.

Why you *should* do a non-systematic review



- Easier
- Quicker/cheaper
- Can do it on your own
- Get the answer you want

Why do we need systematic reviews?



- Limit bias in selection & interpretation of existing evidence
- Focussed approach to managing overwhelming amount of evidence, publications
- Systematic & transparent method for:
  - Identifying relevant evidence
  - Assessing quality/validity of relevant evidence
  - Drawing conclusions based on best available evidence

What is a systematic review?

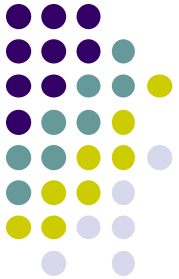
- Systematic reviews are “hypothesis-testing” – they need to answer a clear, specific question

- Key elements of a systematic review:
  - ***Identify:*** *comprehensive searches within pre-set limits*
  - ***Appraise:*** *assess validity of evidence*
  - ***Synthesis****: may be statistical (meta-analysis) or narrative*

What is a systematic review?

- **Hypothesis testing:** addressing clear review question with pre-specified primary outcomes
- **Transparent scientific method**- agreed methods, replicable, transparent, follows a protocol to limit scope for bias
- **Comprehensive** (within defined criteria- not necessary to include everything)- not a partial or biased selection of studies
- **Objective**- formal, using a range of methods to limit reviewer bias- **more than one** reviewer for independent selection & appraisal of evidence
- Conclusions based on the “best evidence”

What is a systematic review?



- ***Comparable to primary research***
  - Designed to test hypothesis: needs clearly defined and answerable question which can be addressed given resources/time
  - Review protocol
  - Minimise selection bias- selection of studies using protocol and two reviewers
  - Each included study is a case- data is extracted/collected and assessed for validity
  - Methods need to be transparent- carefully recorded
  - Detailed analysis
  - Examination of explanatory variables- what works for whom and in what circumstances
  - Able to assess validity of final synthesis
  - Dedicated resources and specialist skills

Steps in a systematic review

- Define question
- Write protocol
- Develop & conduct searches
- Screen for eligible studies
- Assess study quality
- Extract findings
- Synthesis
- Prepare summaries for users

Define hypothesis

Plan in advance

Determine population

Recruitment

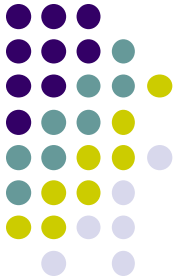
Ensure data validity

Data collection

Analysis

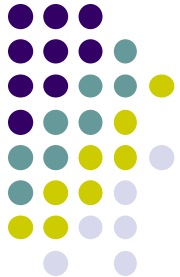
Disseminate

What do you think about systematic reviews?



- Application & limitations
  - what kind of research can be included?
  - what kind of questions can be addressed?
  - how are the data synthesised?

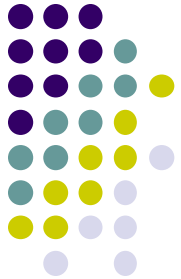
Some myths about systematic reviews?



- Like non-systematic review only bigger- more comprehensive
- Only include randomised trials
- Most useful for clinical questions about drugs
- Most useful for questions about what works
- Only deal with outcomes- not able to consider what works for who and in what circumstance
- Searches do not need information science expertise
- Conclude with a meta-analysis

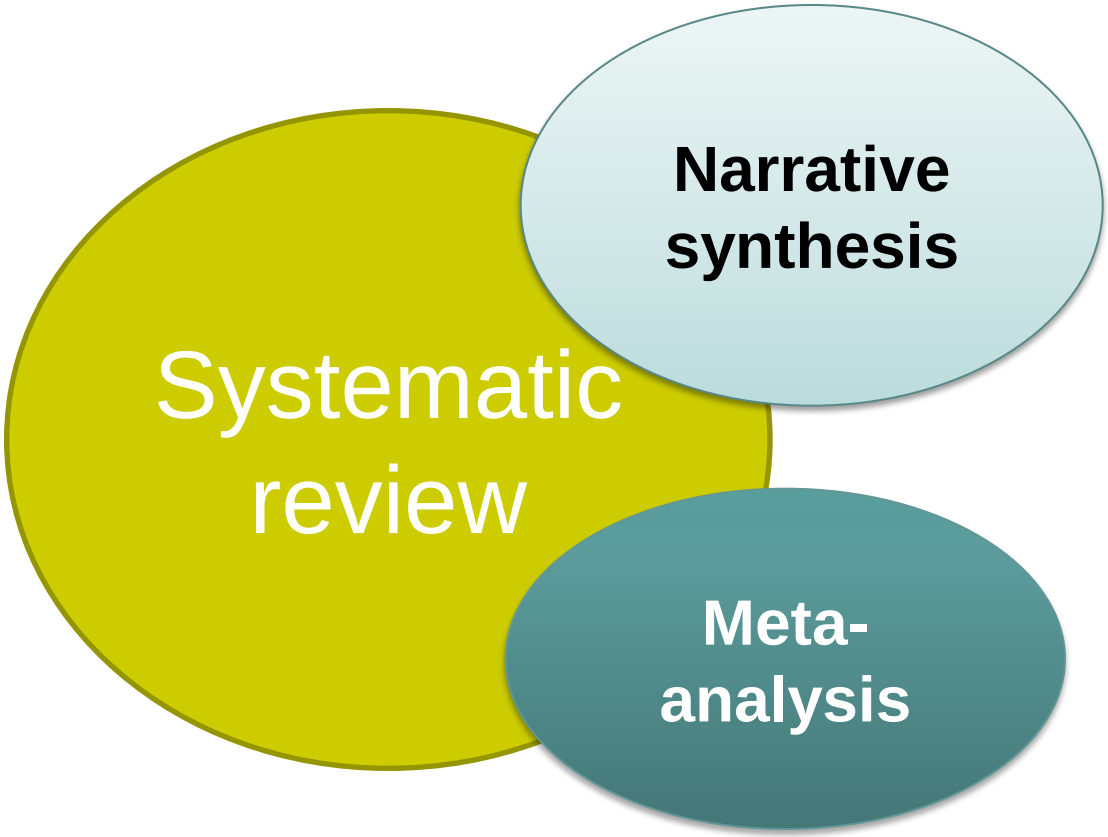
Petticrew M: Systematic reviews from astronomy to zoology: myths and misconceptions. *BMJ 2001, 322(7278):98-101.*

Value of a systematic review approach



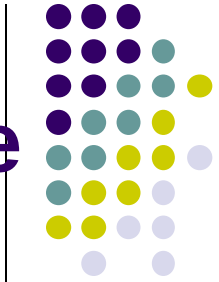
- Focussed question- developed for application in practice
- Minimises bias in selection & interpretation of evidence
- Transparent & replicable
- Prioritises evidence according to study quality

How data are synthesised



- Data synthesis is part of a systematic review
- Systematic review is not a method of synthesis
- Type of synthesis will depend on type of data being reviewed

What systematic review can contribute



- Establishes what is known (and what is unknown) & how it is known
  - Provide map of knowledge & nature of research on a topic
- Drawing on collection of studies to develop body of evidence allows greater confidence in repeated findings
  - Meta-analysis across studies allows for greater statistical power and precision of final effect estimate
- Systematically examine reasons for variations across studies
  - Positive impacts of housing improvements in New Zealand but not in UK

Approaches to reviews

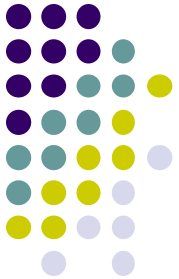
- Aggregative
  - Synthesis of similar data to test hypothesis
  - Deductive
  - Likened to adding stones to build a cairn

- Configurative
  - Synthesis of data with some level of commonality but incorporates high level of variation- used to generate hypothesis
  - Inductive
  - Likened to mosaic- contrasts create image

- Most reviews will involve a mix of approaches (especially of complex interventions)

What makes a good systematic review?

All very well in theory



- Not bias free
- Not fully transparent
  - Room for interpretation in assessments

Most “systematic reviews” aren’t systematic

- The validity of 480 systematic review and meta-analyses using a simple scale was assessed
  - Thorough search
  - Appraisal of study quality
  - Assessment of heterogeneity

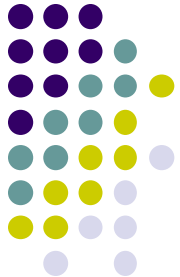
- 26% met all three the criteria

Petticrew M, Song F, Wilson P, Wright K *International Journal of Technology Assessment in Health Care* 2000; 15(4)671-8.

Marks of a good systematic review

- Essential characteristics- transparent & replicable
  - Clear & focussed review question
  - Search strategy described
  - Comprehensive searching of all included sources
  - Two reviewers to select included studies
  - Two reviewers to assess quality of included studies
  - Justification for method of synthesis- meta-analysis or narrative
  - Synthesis reflects quality of included studies- less weight given to studies with high levels of bias
  - Results & characteristics of individual studies to accompany final conclusions of synthesis- tables, forest plots etc

Markers of a well conducted systematic review

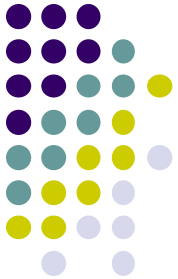


- Shea B, Grimshaw J, Wells G, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. *BMC Medical Research Methodology 2007;7(1):10.*

- Reporting standards
  - Moher D, Liberati A, Tetzlaff J, Altman DG, for the Prisma Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ 2009;339(jul21_1):b2535-.*
  - Wong G, Greenhalgh T, Westhorp G, Buckingham J, Pawson R. RAMESES publication standards: realist syntheses. *BMC Medicine 2013;11(1):21.*
  - Stroup D; Berlin JA; Morton SC; Olkin I; G. David Williamson, PhD; Rennie D, MD; Moher D; Becker BJ; Sipe TA; Thacker SA; for the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group. Meta-analysis of Observational Studies in Epidemiology. A Proposal for Reporting JAMA. 2000;283(15):2008-2012. doi: 10.1001/jama.283.15.2008

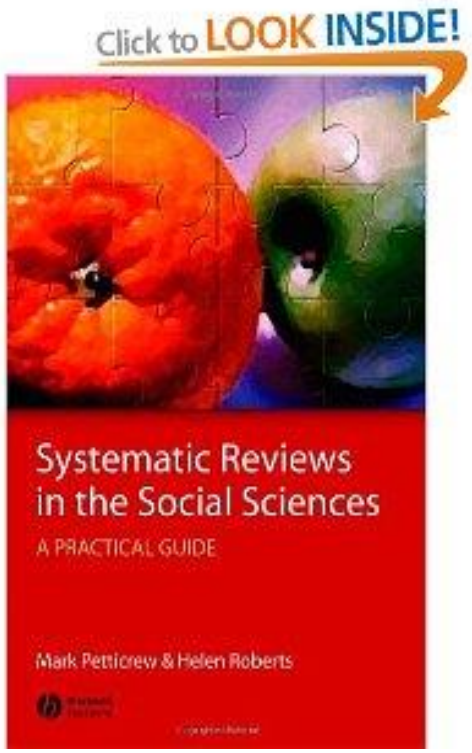
Why systematic reviews of complex interventions are challenging

Why systematic reviews of complex interventions are challenging



- Broad questions
  - Not conceptually appropriate to only look at outcomes- complex data extraction
  - Need to include broad range of study designs & data types
    - Issues around assessment of study quality and synthesis
- Difficult to identify grey literature
- Complex interventions
  - Intervention: multi-components, interactions, delivery and components vary within and between studies
  - Potential multiple confounders & interactions
- Heterogeneity limits potential for meta-analysis & appropriate synthesis

Reading



Petticrew M, Roberts H. *Systematic reviews in the social sciences: a practical guide. Oxford: Blackwell, 2006.*