An Introduction to Systematic Reviews

Catherine Haden, Health Liaison Librarian
Learning objectives

- What are Systematic Reviews?
- How do they differ from other types of reviews?
- Why are they important?
- How are they done?
- How do we appraise their quality?
What is a systematic review?

A systematic review is an appraisal and synthesis of primary research papers on a focused research question, which uses a rigorous and clearly documented methodology in both the search strategy and the selection of studies.

The aim is to minimise bias in the results.

The clear documentation of the process and the decisions made allow the review to be reproduced and updated.
Characteristics of a systematic review

- Focused question
- Adherence to a protocol
- Reproducible methodology
- Transparency of what is searched and where
- Comprehensive search
- Adherence to inclusion and exclusion criteria documented in the protocol.
- 2 people working on these independently avoids bias.
<table>
<thead>
<tr>
<th></th>
<th><strong>Systematic Review</strong></th>
<th><strong>Literature Review</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Question</strong></td>
<td>Focused on a single question</td>
<td>Not necessarily focused on a single question, but may describe an overview</td>
</tr>
<tr>
<td><strong>Protocol</strong></td>
<td>A peer review protocol or plan is included</td>
<td>No protocol is included</td>
</tr>
<tr>
<td><strong>Background</strong></td>
<td>Both provide summaries of the available literature on a topic</td>
<td></td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>Clear objectives are identified</td>
<td>Objectives may or may not be identified</td>
</tr>
<tr>
<td><strong>Inclusion and Exclusion Criteria</strong></td>
<td>Criteria stated before the review is conducted</td>
<td>Criteria not specified</td>
</tr>
<tr>
<td><strong>Search Strategy</strong></td>
<td>Comprehensive search conducted in a systematic way</td>
<td>Strategy not explicitly stated</td>
</tr>
<tr>
<td><strong>Process of Selecting Articles</strong></td>
<td>Usually clear and explicit</td>
<td>Not described in a literature review</td>
</tr>
<tr>
<td><strong>Process of Evaluating Articles</strong></td>
<td>Comprehensive evaluation of study quality</td>
<td>Evaluation of study quality may or may not be included</td>
</tr>
<tr>
<td><strong>Process of Extracting Relevant Information</strong></td>
<td>Usually clear and specific</td>
<td>Not clear or explicit</td>
</tr>
<tr>
<td><strong>Results and Data Synthesis</strong></td>
<td>Clear summaries of studies based on high quality evidence</td>
<td>Summary based on studies where the quality of the articles may not be specified. May also be influenced by the reviewer's theories, needs and beliefs</td>
</tr>
<tr>
<td><strong>Discussion</strong></td>
<td>Written by an expert or group of experts with a detailed and well grounded knowledge of the issues</td>
<td></td>
</tr>
</tbody>
</table>
Name that review – Systematic? Or Literature?

- Disease patterns addressed by mobile health-enabling technologies

- The Effect of Game-Based Interventions in Rehabilitation of Diabetics:

- Information and communication technology-enabled person-centered care for the “big five” chronic conditions

- Does nutritional counseling in telemedicine improve treatment outcomes for diabetes?

Literature review

Systematic Review and Meta-Analysis

Scoping review.

Systematic review and meta-analysis of results from 92 studies.
Formulate a question

Choose one of the topics below and formulate both
- A Literature review title
- Systematic review title

Topics
- Needle exchange programs
- Management of childhood asthma
- Nutrition in pregnancy
- Cancer screening programs
- Or any topic of your choice
Reading describing types of review

Why do we need them?

- A single study does not provide enough evidence to make sound treatment choices. Systematic reviews synthesize and appraise primary studies.
- Building blocks for Practice guidelines.
- Strength of weight of evidence.
Hierarchy of primary studies
Hierarchy of Levels of Evidence. Source: http://guides.is.uwa.edu.au/ACQresources
From 1956 until the late 1970s, Dr Spock’s *Baby and Child Care*, advised that infants be placed to sleep on their stomachs.

Dr Spock argued ‘There are two disadvantages to a baby’s sleeping on his back. If he vomits he’s more likely to choke on the vomitus. ..... I think it is preferable to accustom a baby to sleeping on his stomach from the start.’

This became standard practice in hospitals and millions of households. Dr Spock's advice was based on logic and common sense, but had not been tested.

Systematic reviewing of the evidence later proved that this practice had led to tens of thousands of avoidable cot deaths.

The Systematic Review process

1. Define the research question
2. Plan the review/Protocol – Prospero
3. Determine the eligibility criteria for inclusion/exclusion
4. Search for potentially eligible studies
5. Apply eligibility criteria to select studies
6. Assess risk of bias in individual studies.
7. Extract data from the included studies.
8. Synthesize the data.
9. Interpret and report the results
10. Update the review in the future
Has someone already done a systematic review on this topic?

Check the literature:
• PubMed
• Embase
• PsycINFO etc.

Also check no one is currently working on one. Search for protocols and in registries:
• Cochrane Database Library
• Campbell Collaboration
• Joanna Briggs Institute
• PROSPERO
Starting point – 1. Define the research question

- Is the question clearly focused?
- Are there going to be primary studies on this topic?
- What types of study would answer this question?
Five steps of Evidence Based Practice

From a patient’s issue:

1. Formulate the question
2. Find the evidence
3. Appraise/Evaluate the evidence
4. Apply your findings
5. Assess the efficacy/efficiency of the practice
5 steps of Evidence Based practice

1. Formulate an answerable question – PICO (T)

PICO (T) is a method of framing a clinical question in terms of an individual patient problem so as to find relevant evidence in the literature.
What does PICO(T) stand for?

P  Population/Patient
I  Intervention/Indicator
C  Comparator/Control
O  Outcome
T  Time
PICO (T) Examples from medicine:

Aetiology and risk factors: George wants to discuss the possibility of a vasectomy. He says he has heard something about vasectomy causing an increase in testicular cancer later in life. You know that the risk of this is low but want to give him a more precise answer.

P  Population/patient  =  

I  Intervention/indicator  =  

C  Comparator/control  =  

O  Outcome  =  

‘In men, does having a vasectomy (compared to not having one) increase the risk of getting testicular cancer in the future?’
PICO (T) Examples from medicine: *Frequency or rate*: Mabel is a 6-week-old baby at her routine follow-up. She was born prematurely at 35 weeks. You want to tell the parents about her chances of developing hearing problems.

- **P** Population/patient = Infants
- **I** Intervention/indicator = Premature
- **C** Comparator/control = Full term
- **O** Outcome = Sensorial deafness

‘In infants born prematurely, compared to those born at full term, what is the subsequent lifetime prevalence of sensory deafness?’
The patient dilemma

14 year old Ruby was diagnosed with type 1 diabetes when she was 8 years old. She has had good metabolic control until recently when she took on self-management of her condition. Her parents wonder whether real time continuous monitoring (rather than her current self blood glucose monitoring) would help Ruby manage her blood glucose levels better. They are also concerned that Ruby is not monitoring her blood glucose well at school and when she is going out with her friends.

Define the research question
Define the research question

- Does real time continuous glucose monitoring (RT-CGM) facilitate better metabolic control than self blood glucose monitoring (SBGM) in adolescent patients with type 1 diabetes?

- What factors may contribute to deteriorating metabolic control in adolescents with type 1 diabetes?
## PICOTT

<table>
<thead>
<tr>
<th>Patient</th>
<th>Adolescents with type 1 diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention</strong></td>
<td>RT-CGM (real time continuous glucose monitoring)</td>
</tr>
<tr>
<td><strong>Comparison</strong></td>
<td>SBGM (self glucose monitoring)</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td>HbA1c (glycated haemoglobin) reduction</td>
</tr>
<tr>
<td><strong>Type of Question</strong></td>
<td>Therapy</td>
</tr>
<tr>
<td><strong>Type of study</strong></td>
<td>RCT</td>
</tr>
</tbody>
</table>
Sometimes there are more than 1 question

<table>
<thead>
<tr>
<th>Patient</th>
<th>Adolescents with type 1 diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenomena of Interest</td>
<td>Experiences of living with type 1 diabetes</td>
</tr>
<tr>
<td>Context</td>
<td>Home/family, school, social group, health care delivery</td>
</tr>
<tr>
<td>Outcome</td>
<td>Metabolic control</td>
</tr>
<tr>
<td>Type of Question</td>
<td>Experiential</td>
</tr>
<tr>
<td>Type of study</td>
<td>Qualitative</td>
</tr>
</tbody>
</table>
Other tools to frame the question: ECLIPSE

For Health policy/management

- **Expectation** - what is the information for?
- Client Group
- Location
- **Impact** - what is the change in the service, if any, which is being looked for? What would constitute success? How is this being measured?
- Professionals
- **Service** - for which service are you looking for information? E.G. outpatient services, nurse-led clinics, intermediate care.

Other tools to frame the question: SPICE
For qualitative evidence

- **Setting** – where?
- **Perspective** – for whom?
- **Intervention** – what?
- **Comparison** – compared with what?
- **Evaluation** – with what result?

Other tools to frame the question: SPIDER

For qualitative and mixed methods studies

- **Sample**
- **Phenomena of Interest**
- **Design**
- **Evaluation**
- **Research type**

2. Plan the review

- What is the question?
- Who is in the team?
- What are their roles?
- Develop the search strategy - what and where
- Develop the protocol and register it.
Cochrane reviews are required to be undertaken by more than one person.

This ensures that tasks such as selection of studies for eligibility and data extraction can be performed by at least two people independently, increasing the likelihood that errors are detected.

(Cochrane Handbook of Systematic Reviews 2.3.4.1 The importance of a team )

AND REDUCES RISK OF BIAS
**The protocol**

Publication of a protocol for a review prior to knowledge of the available studies reduces the impact of review authors’ biases, promotes transparency of methods and processes, reduces the potential for duplication, and allows peer review of the planned methods (Light 1984).

(Cochrane Handbook of Systematic Reviews)

What makes a review systematic (as opposed to unsystematic) is the use of an explicit and auditable protocol for review.

If what makes a review systematic is adherence to a protocol, what makes a review unsystematic is simply that it does not adhere to a protocol.

Register your review

PROSPERO

Joanna Briggs Institute

Cochrane Library
3. Determine the eligibility criteria for inclusion/exclusion

Aspects of the clinical question

- What condition
- Which population
- Which treatments
- What types of studies address these questions
What is the appropriate study?

<table>
<thead>
<tr>
<th>QUESTION</th>
<th>STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>Cross-sectional study of those suspected of having disease</td>
</tr>
<tr>
<td>Aetiology</td>
<td>Basic science</td>
</tr>
<tr>
<td></td>
<td>Prospective cohort</td>
</tr>
<tr>
<td></td>
<td>Case-control</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Prospective cohort</td>
</tr>
<tr>
<td>Treatment</td>
<td>Randomised controlled/clinical trial</td>
</tr>
</tbody>
</table>
What exclusion/inclusion criteria would you consider for these questions?

Does real time continuous glucose monitoring (RT-CGM) facilitate better metabolic control than self blood glucose monitoring (SBGM) in adolescent patients with type 1 diabetes?

What factors may contribute to deteriorating metabolic control in adolescents with type 1 diabetes?
What exclusion/inclusion criteria would you consider for these questions?

Does real time continuous glucose monitoring (RT-CGM) facilitate better metabolic control than self blood glucose monitoring (SBGM) in adolescent patients with type 1 diabetes?

Types of study: RCTs

Population: adolescents with type 1 diabetes

Treatments: real time continuous glucose monitoring (RT-CGM) or self blood glucose monitoring (SBGM)

What factors may contribute to deteriorating metabolic control in adolescents with type 1 diabetes?

Types of study: qualitative research studies

Population: adolescents with type 1 diabetes

Outcome metabolic control factors

Specific social settings
4. Search for eligible studies

- Where, what and how? – consult a specialist
- Were the relevant studies identified?
- Which databases were searched? Were all the appropriate databases searched?
- Were there any date range/language applied?
- Was the grey literature searched?
- Were reference lists followed up?
- Were experts in the field consulted?
- Who did the searching?
- How good were the search strategies?
- Were they accurately reported?
Document the search

Use the PRISMA flow chart to document the literature found and the winnowing process.

Make a table of your searches.
Cut and paste the searches to ensure your report them accurately

Save your searches in the databases – easy editing and UPDATING.

Also include: the date the searches were run, the database names and platforms, the date range of the databases.
The searches should be reproducible

The strategy will be in the methodology and the full searches documented in an Appendix
Example Search Methodology

An extensive search for relevant studies was carried out on the 8th of January 2014 using the following electronic databases; Medline (via Ebscohost), PsycINFO (via Ebscohost), CINAHL (via Ebscohost), Web of Science, Scopus and ERIC (via Ebscohost). Searches were conducted to identify papers that contained the following key words: ("daytime sleep" OR nap* OR "day?sleep" OR "sleep consolidation") AND (cognition OR behavio?r OR "physical health" OR "night sleep") AND (child* OR infant OR bab*). The search strategies were developed in consultation with a Health Liaison Librarian. The exact search terms and limiters used for each database are listed in the online supplementary material Table S1. Reference lists from papers identified by searches were also examined to identify potential papers for inclusion.
Search strategy:

Sensitivity versus precision - a balancing act between finding all relevant literature yet still being able to sift through it.

Which study type answers the question and how this can inform the search
Search strategy:
Techniques to ensure all vocabulary has been identified

- Use Subject Headings where available *as well* as key words, (e.g. MESH in PubMed)
- Mine the Subject Headings to be sure you capture all relevant keywords
- Use text mining tools to help identify other relevant keywords, such as [PubMed](https://pubmed.ncbi.nlm.nih.gov/) [PubReminer](https://www.ncbi.nlm.nih.gov/pubreminer/)
- Keep notes of relevant vocabulary from your reading
Search needs sometimes inform which version of a database you use

- Would proximity operators improve the search? *If yes then use MedLine OVID not PubMed.*

E.g. ADJ find terms next to each other in specified order. ADJn finds terms in any order with n words between them.
Clinical Trial registries: why search them?

• Reduces publication bias
• Informs decision as to whether systematic review is required
• Identifies studies that could be included on completion
• Potential to increase number of studies synthesized
Study registers

- **Australian New Zealand Clinical Trials Registry** Covers trials being undertaken in Australia, New Zealand on the therapeutic areas of pharmaceuticals, surgical procedures, preventive measures, lifestyle, devices, treatment and rehabilitation strategies and complementary therapies.

- **ClinicalTrials.gov** Database of federally and privately supported clinical trials conducted in the United States and around the world.

- **UK CRN Study Portfolio**

- **EU Clinical Trials Register**

- **Chinese Clinical Trial Registry** A register for trials supported by Chinese Evidence-Based Medicine Center, Ministry of Health of the People's Republic of China, West China Hospital, Sichuan University, and is a member of Ottawa Statement Group.

- **Clinical Trials Registry India**

- **Internet Portal of the German Clinical Trials Register (DRKS)**

- **ISRCTN Register** The ISRCTN is a numeric system for the unique identification of randomised controlled trials worldwide.

- **Netherlands Trial Register**

- **Pan African Clinical Trials Registry**

- **Current Controlled Trials**

- **WHO International Clinical Trials Registry Platform**
Managing the literature

Use **EndNote** to:

- Remove **duplicates**.
- Make **Groups** of studies excluded and included.
- Rank the studies.
- Run find full text function.

For titles we don’t hold use **Document Delivery**
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8. Synthesize the data.
9. Interpret and report the results
10. Update the review in the future
Selection of papers. *Non-randomised controlled trials, non-controlled trials, retrospective studies, case series, case studies presented as on-line supplemental material.

*Non-randomised controlled trials, non-controlled trials, retrospective studies, case series, case studies presented as on-line supplemental material.
Criteria for considering studies for this review

**Types of studies**
We included randomised controlled trials (RCTs), controlled clinical trials (CCTs), cohort studies, case-control studies, time-series studies, case cross-over studies, ecological studies, self controlled case series, mixed RCT and time-series (see Appendix 1).

**Types of participants**
Healthy children up to 15 years of age.

**Types of interventions**
Vaccination with any combined MMR vaccine given in any dose, preparation or time schedule compared with do nothing or placebo.

**Types of outcome measures**

*Primary outcomes*
Effectiveness: clinical and/or confirmed cases of measles, mumps or rubella.

Safety: serious systemic adverse events. All those which have been hypothesised so far (thrombocytopenic purpura, parotitis, joint and limb symptoms, Crohn's disease, ulcerative colitis, autism and aseptic meningitis), plus encephalitis/encephalopathy, febrile seizure, asthma, leukaemia, hay fever, type 1 diabetes, gait disturbance, demyelinating diseases, bacterial or viral infection.

*Secondary outcomes*
Local reactions (for example, soreness and redness at the site of inoculation) and systemic reactions (for example, fever, rash, vomiting and diarrhoea) following MMR vaccination.

Systematic review process

• 5. Apply eligibility criteria to select studies
• 6. Assess risk of bias in individual studies.
• 7. Extract data from the included studies.
• 8. Synthesize the data.
• 9. Interpret and report the results
• 10. Update the review in the future
Guides for reporting systematic reviews

- Cochrane Handbook for Systematic Reviews of Interventions
- Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)
- Systematic reviews: CRDs guidance for undertaking systematic reviews in Health Care
How to appraise a Systematic review

- **CASP**: Critical Appraisal Skills Programme Checklists
- Critically Appraised Topics: Generic systematic reviews (DARE; ACP Journal club)
- **SIGN**: Scottish Intercollegiate Guidelines Network (based on AMSTAR)
- **CEBM**: Centre for Evidence Based Medicine Appraisal Sheets (www.cebm.net)
Critical Appraisal of a systematic review

Scenario: As Carolyn suffers from hypertension she has a diet high in antioxidants, eating foods such as vegetables, fruits and nuts. She likes to reward herself occasionally by eating chocolate and has recently heard that it has antioxidant properties and beneficial flavonoids. She would like to know what effect eating chocolate has on blood pressure. Carolyn would like some reliable information on the topic.

- Read the Systematic Review supplied and use the CASP checklist provided to evaluate it.
- Report back to the group the strengths and weakness of each review.
Questions?

Systematic Reviews Subject Guide

For further advice on Systematic reviews contact your Liaison Librarian