Undertaking a literature review: Developing a research question and searching the literature

Spyros Kitsiou, PhD
Assistant Professor
Department of Biomedical and Health Information Sciences
College of Applied Health Sciences
University of Illinois at Chicago
Learning objectives

At the completion of this seminar, you should be able to:

1. Formulate a review question
2. Develop eligibility criteria for the selection of studies
3. Translate the research question into relevant research concepts, key terms, and controlled vocabularies
4. Develop a search query for different databases (e.g. MEDLINE, CENTRAL, EMBASE, and CINHAL)
Steps of a literature review

• Develop the review question and eligibility criteria
• Plan methods and develop a protocol
• Search for studies
• Apply eligibility criteria for the selection of studies
• Extract data
• Assess risk of bias in included studies (if applicable)
• Analyze and present results
• Interpret results and formulate conclusions
<table>
<thead>
<tr>
<th>Review Type</th>
<th>Overarching Goal</th>
<th>Scope</th>
<th>Search strategy</th>
<th>Primary sources</th>
<th>Explicit study selection</th>
<th>Quality appraisal</th>
<th>Synthesis methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Narrative review</td>
<td>Summarization of prior knowledge</td>
<td>Broad</td>
<td>Selective</td>
<td>Conceptual and empirical studies</td>
<td>No</td>
<td>No</td>
<td>Narrative summary</td>
</tr>
<tr>
<td>Descriptive or mapping review</td>
<td>Summarization of prior knowledge</td>
<td>Broad</td>
<td>Representative</td>
<td>Empirical studies</td>
<td>Yes</td>
<td>No</td>
<td>Frequency analysis</td>
</tr>
<tr>
<td>Critical review</td>
<td>Critical synthesis</td>
<td>Broad</td>
<td>Selective or representative</td>
<td>Conceptual or empirical</td>
<td>Yes/No</td>
<td>Not essential</td>
<td>Critical interpretive methods</td>
</tr>
<tr>
<td>Theoretical review</td>
<td>Explanation building Theory development</td>
<td>Broad</td>
<td>Comprehensive</td>
<td>Conceptual and empirical studies</td>
<td>Yes</td>
<td>No</td>
<td>Content analysis &amp; interpretive methods</td>
</tr>
<tr>
<td>Scoping review</td>
<td>Summarization of prior knowledge</td>
<td>Broad</td>
<td>Comprehensive</td>
<td>Conceptual and empirical studies</td>
<td>Yes</td>
<td>Not essential</td>
<td>Content or thematic analysis</td>
</tr>
<tr>
<td>Systematic review (with or without meta-analysis)</td>
<td>Data aggregation or integration</td>
<td>Narrow</td>
<td>Exhaustive</td>
<td>Empirical studies</td>
<td>Yes</td>
<td>Yes</td>
<td>Met-analysis, vote counting, or qualitative synthesis</td>
</tr>
<tr>
<td>Realist Review</td>
<td>Explanation building</td>
<td>Narrow</td>
<td>Iterative &amp; purposive</td>
<td>Conceptual and empirical</td>
<td>Yes</td>
<td>Yes</td>
<td>Mixed methods</td>
</tr>
<tr>
<td>Overview of SRs (Umbrella review)</td>
<td>Summarization of multiple systematic reviews</td>
<td>Narrow</td>
<td>Exhaustive</td>
<td>Systematic reviews</td>
<td>Yes</td>
<td>Yes</td>
<td>Met-analysis, vote counting, or qualitative synthesis</td>
</tr>
</tbody>
</table>


Developing the review question(s)

• Essential first step for your review
• Guides many aspects of your methods
  • Type of review (e.g. systematic review, scoping review, narrative review)
  • Eligibility criteria
  • Search strategy
  • Data collection and analysis
• Think carefully in advance
• Address a question of importance and relevance
• Address real choices faced in decision making
• Are there any similar reviews?
# A broad or narrow research question?

<table>
<thead>
<tr>
<th></th>
<th>Narrow</th>
<th>Broad</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Examples</strong></td>
<td>• Peer education interventions for HIV prevention in young men</td>
<td>• Interventions for HIV prevention</td>
</tr>
<tr>
<td></td>
<td>• Text-messaging interventions for improving physical activity</td>
<td>• Behavioral interventions for improving physical activity in people at high risk of CVD</td>
</tr>
<tr>
<td><strong>Advantages</strong></td>
<td>• Easy to write</td>
<td>• Comprehensive</td>
</tr>
<tr>
<td></td>
<td>• Easy to read</td>
<td>• Generalizable</td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
<td>• May be selectively defined</td>
<td>• Complex</td>
</tr>
<tr>
<td></td>
<td>• Need multiple reviews</td>
<td>• May miss subgroup effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Overview of reviews may be preferable</td>
</tr>
</tbody>
</table>
Frameworks for developing the review question

• PICO(S)
  • population, intervention, comparison, outcomes, study design

• CIMO
  • (context, intervention, mechanisms, outcomes)
PICO Framework

• **Population**: health condition/diagnosis, age, gender, ethnicity

• **Intervention**: type, dose, intensity, timing, location, context, alone or in combination with other interventions

• **Comparison**: define specific active comparisons in much detail. Be clear what you mean “usual care” or “no intervention”. Can remain open to any comparisons found

• **Outcomes**: identify meaningful outcomes used in studies of related topics and key time points, including measurement options.
Review objective

• A precise statement of the primary objective
• Usually one sentence
• May also include specific objectives relating to different
  • participant groups
  • comparisons of interventions
  • outcome measures

To assess the effects of [intervention or comparison] for [health problem] for/in [types of people, disease or problem and setting if specified].
Some examples of review objectives...

• To assess the effects of self-monitoring mobile apps in patients with diabetes

• To assess the effectiveness of hip protectors for preventing hip fractures in older people

• To assess the impact of structured telephone support on hospital readmissions in recently discharged patients (< 30 days) with chronic heart failure

• To assess the impact of structured telephone support in patients with chronic heart failure

• To assess the methodological quality of systematic reviews of HIV interventions
Group exercise #1

Formulate your own research question/objective using the PICO framework
Developing eligibility criteria

• Eligibility criteria are a combination of aspects of the review question plus specification of the types of studies that have addressed these questions (e.g. randomized controlled trials)

• The participants, interventions and comparisons in the clinical question usually translate directly into eligibility criteria for the review

• Outcomes usually are not part of the criteria for including studies
Review objective:

- To review randomized controlled trials of non-invasive home telemonitoring interventions compared to standard practice for people with heart failure, in order to quantify the effects of these interventions over and above usual care

Inclusion criteria:

- Population: Adults (aged 18 years and over) of either sex, any age or ethnic group, with a definitive diagnosis of heart failure
- Intervention: [Description of] non-invasive home telemonitoring
- Comparison: “Usual care” consisted of standard post-discharge care without intensified attendance at cardiology clinics or clinic-based heart failure disease management program, or home visits
Eligibility assessment form

Caffeine for daytime drowsiness

Eligibility checklist

Study ID: __________________________

Screened by: __________________________

1. Study design
   Is the study a randomised controlled trial?
   - Yes
   - No (exclude)
   - Can't tell

2. Participants
   Did the study include adults undergoing normal daily activities?
   - Yes
   - No (exclude)
   - Can't tell

   Did the study include adults reporting symptoms of daytime drowsiness (e.g. reduced alertness, fatigue or lowered mood)?
   - Yes
   - No (exclude)
   - Can't tell

   Did the study include participants under conditions of sleep deprivation?
   - Yes (exclude)
   - No
   - Can't tell

   Did the study include participants taking stimulants?
   - Yes (exclude)
   - No
   - Can't tell

   Did the study include participants with a psychiatric disorder, chronic fatigue or narcolepsy syndrome?
   - Yes (exclude)
   - No
   - Can't tell

3. Interventions
   Did the intervention group receive a preparation or dose of caffeine (e.g. instant, brewed or espresso coffee, tea, cola, chocolate, intravenous or pill)?
   - Yes
   - No (exclude)
   - Can't tell

   Did the control group also receive a preparation or dose of caffeine?
   - Yes (exclude)
   - No
   - Can't tell

Should this study be included in the review?
   - INCLUDE
   - EXCLUDE
   - Can't tell
A rigorous approach to searching

• Reviews require an extensive search - MEDLINE is not enough!
• a limited search may find an unrepresentative set of studies
  • Incomplete results
  • Selection bias
  • Reduced generalizability
• Balance sensitivity with efficiency
A rigorous approach to searching
Sources to search

- Bibliographic databases likely to identify the majority of your studies
  - Cochrane Central Register of Controlled Trials (CENTRAL)
  - MEDLINE
  - EMBASE
  - and others (e.g. CINHAL, PsycINFO)

- Other sources
  - Grey literature databases (e.g. PROQUEST)
  - Trial registries (clinicaltrials.gov)
  - Conference abstracts and proceedings (known conference related to your topic)
  - Reference lists, citations, and related articles
  - Dissertation databases
  - Unpublished and ongoing studies (contact field experts and colleagues) – very important to minimize bias
How do databases index articles?

• Controlled vocabulary (e.g. Medical Subject Headings – MeSH terms)
• Titles and abstracts only – not full-text article
• Authors, affiliations, keywords, journals/publishers
• Other identifiers (e.g. study design/publication type, language, dates)

Be aware
• Lag time between publication and indexing of an article
• Overlapping of databases – leads to duplicate references returned
• Each database has its own search engine
• MEDLINE can be accessed either via PubMed or Ovid
Constructing a good search strategy

• Don’t try this alone. Always consult your librarian!
• Reviews (especially systematic reviews) require complex, rigorous search strategies
• This session is an introduction to basic principles only
Structure of a search strategy

• Based on your research objective and eligibility criteria
• Start with the 2 or 3 most important concepts
• Focus on those most likely to be found in title & abstract

P  participants
I  intervention
C  comparison
O  outcomes
S  study design
## Step 1: Developing main concepts

<table>
<thead>
<tr>
<th>Population</th>
<th>Intervention</th>
<th>Study Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main concept</td>
<td>Main concept</td>
<td>Main concept</td>
</tr>
</tbody>
</table>
Step 1: Developing main concepts and search terms

Example:
“To review randomized controlled trials of non-invasive home telemonitoring compared to standard practice for people with heart failure, in order to quantify the effects of these interventions over and above usual care”

<table>
<thead>
<tr>
<th>Population</th>
<th>Intervention</th>
<th>Study Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main concept</td>
<td>Main concept</td>
<td>Main concept</td>
</tr>
</tbody>
</table>
Step 1: Developing main concepts and search terms

Example:
“To review randomized controlled trials of non-invasive home telemonitoring compared to standard practice for people with heart failure, in order to quantify the effects of these interventions over and above usual care”

<table>
<thead>
<tr>
<th>Population</th>
<th>Intervention</th>
<th>Study Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main concept</td>
<td>Main concept</td>
<td>Main concept</td>
</tr>
<tr>
<td>Heart failure</td>
<td>Telemonitoring</td>
<td>Randomized controlled trial</td>
</tr>
</tbody>
</table>
Step 2: Turning concepts into search terms

- Aim for high **sensitivity**
  - express each concept in as many ways as possible
  - minimize the risk of missing a relevant study
  - will lead to lower precision – find a balance

- Use both **text words** and **controlled vocabulary** (e.g. MeSH terms)

- preliminary searching may help test your strategy

- strategies must be translated for **every** database or interface
• Include synonyms, related terms, opposites (if necessary), international terms, alternative spellings, plurals
  • e.g. telehealth, telemonitoring, telemedicine, telecare
  • Brain injury, head injury, skull injury, skull fracture

• Truncation and wildcards * $ ?
  • Telemonitor* = telemonitor, telemonitors, telemonitoring
  • But beware – car* = cars (but also carcinoma)

• Phrases can be put in quotes or you can use proximity operators
  • e.g. “home telemonitoring”

• Proximity operators – NEAR, NEXT, ADJ
  • Ovid (ADJ): Liver ADJ3 cancer = liver cancer, liver and bowel cancer
  • Cochrane Library: The ‘NEAR’ operator will find the search terms within six words of each other
  • Cochrane Library: The ‘NEXT’ operator is more sensitive (i.e. retrieves more hits) than the alternative method of phrase searching using quotation marks
  • Note: if you are using PubMed to search Medline, PubMed does not use proximity operators. If you want to use proximity operators, you must use Ovid
Controlled Vocabulary

• standardized subject terms assigned by indexers
  • Medline and Cochrane Library use MeSH terms
  • EMBASE uses the EMTREE
  • identifies relevant articles even if different terms are used for the same concept
  • ‘explode’ to include all narrower terms
  • caution – indexers may not be subject experts, and authors may not describe their study very well

• check the terms applied to relevant papers for ideas

• use database tools to map words to subject terms

• controlled vocabulary must be translated for each database
Step 2: Turning concepts into search terms

Example:
“To review randomized controlled trials of non-invasive home telemonitoring compared to standard practice for people with heart failure, in order to quantify the effects of these interventions over and above usual care”

<table>
<thead>
<tr>
<th>Population</th>
<th>Intervention</th>
<th>Study Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main concept</td>
<td>Main concept</td>
<td>Main concept</td>
</tr>
<tr>
<td>Heart failure</td>
<td>Telemonitoring</td>
<td>Randomized controlled trial</td>
</tr>
<tr>
<td>Synonyms/search terms</td>
<td>Synonyms/search terms</td>
<td>Synonyms/search terms</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>Telehealth</td>
<td>Controlled clinical trial</td>
</tr>
<tr>
<td></td>
<td>Telemedicine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Telecare</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Telemetry</td>
<td>Random allocation</td>
</tr>
</tbody>
</table>
Step 2: Turning concepts into search terms

Heart Failure
1. Heart Failure [MeSH Term]
2. heart failure
3. cardiac failure
4. Telemedicine [MeSH Term:noexp]
5. Remote consultation [MeSH Term]
6. telecare
7. telemonitor*

Telemonitoring

All MeSH Categories
Diseases Category
Cardiovascular Diseases
Heart Diseases
Heart Failure
Cardio-Renal Syndrome
Dyspnea, Paroxysmal
Edema, Cardiac
Heart Failure, Diastolic
Heart Failure, Systolic

All MeSH Categories
Information Science Category
Information Science
Telecommunications Media
Telemedicine
Remote Consultation
Telepathology
Teleradiology
Telerhabilitation
Group exercise #2
Create your own search terms for your review question/objective
Step 4: Selecting search fields and filters

Each database has its own set of filters. Below are some of the most frequently used filters:

- **Ovid** - `.tw.` searches in title/abstract; `.ti.` searches only in the title; `.ab.` searches only in the abstract; `.pt.` searches in the publication type field

- **PubMed** - `[Title/Abstract]` searches only in the title and abstract; `[Text Word]` searches in the title, abstract, and keywords; `[Publication Type]` searches for specific publication type articles (e.g. RCTs)

- **Cochrane Library** - `:ti,ab,kw` searches in the title, abstract, and keywords; `:pt` searches the type of publication
Step 5: Study design filters

• A set of search terms to limit your results to specific study designs (e.g. RCTs)

• Research has been done to identify the most sensitive and efficient search terms

• Select according to:
  • database and interface to be searched
  • study designs needed for your review

• **Do not use an RCT filter when searching CENTRAL**
Step 5: Study design filters

- Cochrane highly sensitive search strategy for RCTs

<table>
<thead>
<tr>
<th>Sensitivity-maximising version, MEDLINE (PubMed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. randomized controlled trial [pt]</td>
</tr>
<tr>
<td>2. controlled clinical trial [pt]</td>
</tr>
<tr>
<td>3. randomized [tiab]</td>
</tr>
<tr>
<td>4. placebo [tiab]</td>
</tr>
<tr>
<td>5. drug therapy [sh]</td>
</tr>
<tr>
<td>6. randomly [tiab]</td>
</tr>
<tr>
<td>7. trial [tiab]</td>
</tr>
<tr>
<td>8. groups [tiab]</td>
</tr>
<tr>
<td>9. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8</td>
</tr>
<tr>
<td>10. animals [mh] NOT humans [mh]</td>
</tr>
<tr>
<td>11. #9 NOT #10</td>
</tr>
</tbody>
</table>
Boolean Operators

OR – to expand search

AND – to narrow search
Step 4: Bringing it all together
Step 4: Bringing it all together

<table>
<thead>
<tr>
<th>Population</th>
<th>Intervention</th>
<th>Study design</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td>OR</td>
<td>OR</td>
</tr>
<tr>
<td>heart failure [tiab]</td>
<td>Telecare [tiab]</td>
<td>Controlled clinical trial [pt]</td>
</tr>
<tr>
<td>OR</td>
<td>OR</td>
<td>OR</td>
</tr>
<tr>
<td>Cardiac Failure [tiab]</td>
<td>Telemonitor* [tiab]</td>
<td>Placebo [tiab]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clinical trials as topic [mesh: noexp]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ranodomly [tiab]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trial [ti]</td>
</tr>
</tbody>
</table>
Sample MEDLINE Strategy using the PubMed interface

1. Heart Failure [Mesh:noexp]
2. heart failure [tiab]
3. cardiac failure [tiab]
4. or/1-3
5. Telemedicine [Mesh:noexp]
6. telecare [tiab]
7. telemonitor* [tiab]
8. #5 OR #6 OR 7
9. randomized controlled trial [pt]
10. controlled clinical trial [pt]
11. randomized [tiab]
12. placebo [tiab]
13. drug therapy [sh]
14. randomly [tiab]
15. trial [tiab]
16. groups [tiab]
17. #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16
18. animals [mh] NOT humans [mh]
19. #17 NOT #18
20. #4 AND #8 AND #19

Heart Failure

Telemonitoring

RCTs
Limits and restrictions

• To avoid bias, do not limit by:
  • Language
  • Year – unless there is a clear point (e.g. cell phones were not available in the 70s or 80s)
  • Format – may be additional information about a study in letters, etc.
Screening and selection process

- Cochrane Library (n = 3095)
- Medline (PubMed) (n = 1526)
- Embase (n = 2586)
- CINAHL (EBSCOhost) (n = 788)

Duplicate citations excluded (n = 2354)
Citations excluded as not relevant to the overview (n = 5681)

Citations screened after duplicates removed (n = 5741)

Full-text articles retrieved and reviewed for eligibility (n = 50)

Total number of full-text articles retrieved and assessed for inclusion (n = 64)

Additional references identified through hand-searching of the references of the retrieved articles (n = 4)

Full-text articles excluded (n = 41):
- Not RCT (n = 11)
- Involved adult patients (n = 19)
- Not an ED-based intervention (n = 2)
- Intervention was not aimed at improving PCP follow-up visits (n = 9)

Final number of articles (n = 23)
Final number of studies (RCTs) (n = 16)
Take home messages

• Work closely with a librarian and/or an expert in search strategies for literature reviews to develop your search query
• Plan a systematic search, balancing sensitivity, precision, and efficiency
• Think about the key concepts of your question, and how they might be described
• Search strategy must be translated for every database and interface
• Start with CENTRAL, MEDLINE and EMBASE – then consider other appropriate sources
• Manage and keep careful records of your search strategies