Introduction to Systematic Reviews
Topics to be Introduced

1. Importance of literature syntheses
2. What are systematic reviews?
3. Steps to a systematic review:
   a) Developing the protocol
   b) Defining the review question
   c) Literature searching
   d) Study selection
   e) Risk of bias assessment
   f) Data collection
   g) Analysis & Reporting
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Evidence Informed Decision-Making

Use of current best evidence
- Health care policy
- Clinical practice

Importance
- Quality care
- Limited resources
Evidence for Decision-making

THE LD$_{50}$ OF TOXICITY DATA IS 2 KILOGRAMS PER KILOGRAM.

http://xkcd.com/1260/
Knowledge Syntheses

- Evolving science
- Varying terminology
- **Basic types reflect objectives and methods**
- Scoping reviews: Map the literature to clarify boundaries & identify gaps
- Research syntheses: Studies are analyzed and summarized
  - Narrative reviews
  - Systematic reviews

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Systematic reviews, while common in the health sciences field, are not the only type of review that exist. In their widely cited article entitled “A Typology of Reviews: An Analysis of 14 Review Types and Associated Methodologies,” Grant and Booth (2009) outline several major types of reviews, including the following (adapted from pages 94-95 in their article - see link below):

<table>
<thead>
<tr>
<th>Types of Reviews</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Label</strong></td>
</tr>
<tr>
<td>Critical review</td>
</tr>
<tr>
<td>Literature review</td>
</tr>
<tr>
<td>Mapping review/ systematic map</td>
</tr>
<tr>
<td>Meta-analysis</td>
</tr>
</tbody>
</table>

Is a systematic review the right choice for my research team?

- I Want to Do a Systematic Review
  This blog post by the Mayo Clinic Libraries outlines what makes a systematic review different from a traditional literature review. It also suggests some questions for your research team that can help you decide whether or not to embark on a systematic review.
- Quiz: What kind of review

Types of Reviews: More Resources

- Websites
  - The RAMESES Projects
    A guide to producing realistic and...
Systematic Reviews

Pre-defined, explicit methods:

– Clearly formulated research question
– Comprehensive search to identify studies
– Selection criteria for inclusion
– Data collection & critical appraisal
– Synthesis & reporting

Minimize potential biases at each step
## Types of Literature Reviews

<table>
<thead>
<tr>
<th></th>
<th>Conventional</th>
<th>Systematic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Question</strong></td>
<td>Often broad in scope</td>
<td>Often a focused clinical question</td>
</tr>
<tr>
<td><strong>Sources &amp; Searches</strong></td>
<td>Not usually specified</td>
<td>Comprehensive source and strategy explicitly stated</td>
</tr>
<tr>
<td></td>
<td>Potentially biased</td>
<td></td>
</tr>
<tr>
<td><strong>Selection</strong></td>
<td>Not usually specified</td>
<td>Criterion-based uniformly applied</td>
</tr>
<tr>
<td></td>
<td>Potentially biased</td>
<td></td>
</tr>
<tr>
<td><strong>Appraisal</strong></td>
<td>Variable</td>
<td>Rigorous critical appraisal</td>
</tr>
<tr>
<td><strong>Synthesis</strong></td>
<td>Qualitative summary common</td>
<td>Qualitative summary +/- Meta Analysis</td>
</tr>
<tr>
<td><strong>Inferences</strong></td>
<td>Sometimes evidence-based</td>
<td>Evidence-based</td>
</tr>
</tbody>
</table>
Advantages of Systematic Reviews

- Reduced likelihood of being misled
- Increased confidence about expected outcomes
- Decision-makers can focus on local applicability
- Allows stakeholders to constructively contest research evidence
Where to find systematic reviews

Who has read a systematic review?
– Where was it published?
Where to find systematic reviews, cont’d

The Cochrane Library

Search the Cochrane Library

Browse Cochrane Database of Systematic Reviews

Issue 6 of 12, June 2012

Anaesthesia & pain control (197)
Rood disorders (115)
Cancer (390)
Cold health (1429)
Complementary & alternative medicine (530)
Consumer & communication strategies (45)
Dentistry & oral health (129)
Developmental, psychosocial, & learning problems (99)
Eye care & visual health (127)

Special Collections

World No Tobacco Day
Physical activity and exercise for health and well being of older people
World Kidney Day 2012: kidneys for life

Editorial

Why should we translate Cochrane Reviews into French? A view from Cameroon

The Cochrane Collaboration is a leader in the preparation of high-quality systematic reviews, but they are prepared and available mainly in the English language. This alone greatly undermines the potential of Cochrane Reviews as building blocks for decision-making in many low- and middle-income countries, including those in Africa, where evidence about the benefits and harms of healthcare interventions is needed urgently...
Our vision
Our vision is a world of improved health where decisions about health and health care are informed by high-quality, relevant and up-to-date synthesized research evidence.

Our mission
Our mission is to promote evidence-informed health decision-making by producing high-quality, relevant, accessible systematic reviews and other synthesized research evidence. Our work is internationally recognized as the benchmark for high-quality information about the effectiveness of health care.
Where to find systematic reviews, cont’d

PubMed Clinical Queries

Results of searches on this page are limited to specific clinical research areas. For comprehensive searches, use PubMed directly.

Search: atherosclerosis

Clinical Study Categories

- Category: Therapy
- Scope: Broad

Results: 5 of 24006
- Recent clinical studies of the effects of lipid-modifying therapies. Below HJ, Hwang S.

Systematic Reviews

Results: 5 of 1175
- Helicobacter pylori infection contributes to high risk of ischemic stroke: evidence from a meta-analysis.

Medical Genetics

Results: 5 of 15097
- A Genome-Wide Association Study Identifies Genetic Determinant of Plasma Partial Thromboplastin Time.

June 20, 2017 | Robin Parker

Intro Systematic Reviews
Quality Appraisal of Systematic Reviews
Quality Appraisal of Systematic Reviews

- CEBM Systematic Review Appraisal Sheet
- CASP Systematic Review Checklist
- AMSTAR: A MeaSurement Tool to Assess systematic Reviews
- PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4468143/#pone.0128754.s002
(A) Are the results of the review valid?

Screening Questions

1. Did the review address a clearly focused question?
   [ ] Yes  [ ] Can’t tell  [ ] No

   HINT: An issue can be ‘focused’ in terms of
   • The population studied
   • The intervention given
   • The outcome considered

2. Did the authors look for the right type of papers?
   [ ] Yes  [ ] Can’t tell  [ ] No

   HINT: ‘The best sort of studies’ would
   • Address the reviews question
   • Have an appropriate study design (usually RCTs for papers evaluating interventions)

Is it worth continuing?

©Critical Appraisal Skills Programme (CASP) Systematic Review Checklist 31.05.13
3. Do you think all the important, relevant studies were included?

HINT: Look for
- Which bibliographic databases were used
- Follow up from reference lists
- Personal contact with experts
- Search for unpublished as well as published studies
- Search for non-English language studies

4. Did the review’s authors do enough to assess the quality of the included studies?

HINT: The authors need to consider the rigour of the studies they have identified. Lack of rigour may affect the studies’ results. (“All that glitters is not gold” Merchant of Venice – Act II Scene 7)

5. If the results of the review have been combined, was it reasonable to do so?

HINT: Consider whether
- The results were similar from study to study
- The results of all the included studies are clearly displayed
- The results of the different studies are similar
- The reasons for any variations in results are discussed
## Table Risk of Bias

<table>
<thead>
<tr>
<th>Author Year</th>
<th>Random sequence generation</th>
<th>Allocation concealment</th>
<th>Blinding of participants and personnel</th>
<th>Blinding of outcome assessment</th>
<th>Incomplete outcome data</th>
<th>Selective outcome reporting</th>
<th>Other sources of bias</th>
<th>Overall risk of bias</th>
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<td>low</td>
<td>low</td>
<td>low</td>
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<td>low</td>
<td>low</td>
<td>low</td>
<td>low</td>
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<td>low</td>
<td>low</td>
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**Intravenous Therapy vs. Oral Rehydration Therapy**

<table>
<thead>
<tr>
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<td>low</td>
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<td>low</td>
<td>low</td>
<td>low</td>
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<td>low</td>
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<td>low</td>
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<td>low</td>
<td>low</td>
<td>low</td>
<td>low</td>
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<td>Uhlig 2009</td>
<td>unclear</td>
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<td>low</td>
<td>low</td>
<td>low</td>
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</table>

**Antiemetics**

<table>
<thead>
<tr>
<th>Author Year</th>
<th>Random sequence generation</th>
<th>Allocation concealment</th>
<th>Blinding of participants and personnel</th>
<th>Blinding of outcome assessment</th>
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<th>Selective outcome reporting</th>
<th>Other sources of bias</th>
<th>Overall risk of bias</th>
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<tr>
<td>Canani 2007</td>
<td>low</td>
<td>unclear</td>
<td>unclear</td>
<td>low</td>
<td>low</td>
<td>low</td>
<td>low</td>
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<tr>
<td>Henker 2007</td>
<td>low</td>
<td>unclear</td>
<td>unclear</td>
<td>low</td>
<td>low</td>
<td>low</td>
<td>low</td>
<td>low</td>
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</tbody>
</table>

**Probiotics**

<table>
<thead>
<tr>
<th>Author Year</th>
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<th>Blinding of participants and personnel</th>
<th>Blinding of outcome assessment</th>
<th>Incomplete outcome data</th>
<th>Selective outcome reporting</th>
<th>Other sources of bias</th>
<th>Overall risk of bias</th>
</tr>
</thead>
</table>
Antiemetics for reducing vomiting related to acute gastroenteritis in children and adolescents

Different review!
(B) What are the results?

6. What are the overall results of the review?

HINT: Consider

- If you are clear about the review’s ‘bottom line’ results
- What these are (numerically if appropriate)
- How were the results expressed (NNT, odds ratio etc)

7. How precise are the results?

HINT: Look at the confidence intervals, if given
### 4.3.1 Hospitalization

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>IVT Events</th>
<th>IVT Total</th>
<th>ORT Events</th>
<th>ORT Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atherly-John_2002</td>
<td>2</td>
<td>18</td>
<td>4</td>
<td>16</td>
<td>31.1%</td>
<td>0.44 [0.09, 2.11]</td>
</tr>
<tr>
<td>Listernick 1986</td>
<td>0</td>
<td>15</td>
<td>2</td>
<td>14</td>
<td>13.4%</td>
<td>0.19 [0.01, 3.60]</td>
</tr>
<tr>
<td>Spandorfer_2005</td>
<td>18</td>
<td>37</td>
<td>2</td>
<td>36</td>
<td>55.5%</td>
<td>1.59 [0.88, 2.88]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>70</strong></td>
<td><strong>66</strong></td>
<td><strong>66</strong></td>
<td><strong>66</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>0.80 [0.24, 2.71]</strong></td>
</tr>
</tbody>
</table>

Total events: 20 events on IVT, 17 events on ORT

Heterogeneity: $\tau^2 = 0.60; \chi^2 = 4.11, df = 2 (P = 0.13); I^2 = 51\%$

Test for overall effect: $Z = 0.35 (P = 0.72)$

### 4.3.2 Return to ED

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>IVT Events</th>
<th>IVT Total</th>
<th>ORT Events</th>
<th>ORT Total</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atherly-John_2002</td>
<td>0</td>
<td>18</td>
<td>0</td>
<td>16</td>
<td>Not estimable</td>
</tr>
<tr>
<td>Nager_2002</td>
<td>7</td>
<td>46</td>
<td>8</td>
<td>44</td>
<td>0.84 [0.33, 2.11]</td>
</tr>
<tr>
<td>Spandorfer_2005</td>
<td>3</td>
<td>36</td>
<td>3</td>
<td>33</td>
<td>0.92 [0.20, 4.23]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>100</strong></td>
<td><strong>93</strong></td>
<td><strong>93</strong></td>
<td><strong>93</strong></td>
<td><strong>0.86 [0.39, 1.89]</strong></td>
</tr>
</tbody>
</table>

Total events: 10 events on IVT, 11 events on ORT

Heterogeneity: $\tau^2 = 0.00; \chi^2 = 0.01, df = 1 (P = 0.92); I^2 = 0\%$

Test for overall effect: $Z = 0.38 (P = 0.70)$

Results from meta-analysis of direct comparisons of oral rehydration therapy vs. intravenous fluid therapy on the outcomes of admission to hospital from the emergency department and revisits to the emergency departments, displayed employing Forest plots.
### 1.8.1 Required IV rehydration

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Antiemetic Events</th>
<th>Placebo Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freedman_2006</td>
<td>15</td>
<td>107</td>
<td>33</td>
<td>107</td>
<td>31.5% 0.45 [0.26, 0.79]</td>
</tr>
<tr>
<td>Gouin_2012</td>
<td>7</td>
<td>74</td>
<td>9</td>
<td>70</td>
<td>15.5% 0.74 [0.29, 1.87]</td>
</tr>
<tr>
<td>Qazi_2014</td>
<td>0</td>
<td>83</td>
<td>9</td>
<td>73</td>
<td>2.1% 0.05 [0.00, 0.78]</td>
</tr>
<tr>
<td>Ramsook_2002</td>
<td>7</td>
<td>62</td>
<td>23</td>
<td>51</td>
<td>21.0% 0.25 [0.12, 0.54]</td>
</tr>
<tr>
<td>Roslund_2008</td>
<td>11</td>
<td>51</td>
<td>30</td>
<td>55</td>
<td>29.8% 0.40 [0.22, 0.70]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>377</strong></td>
<td><strong>356</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>40</td>
<td>104</td>
<td></td>
<td></td>
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</tbody>
</table>

Heterogeneity: Tau² = 0.07; Chi² = 5.69, df = 4 (P = 0.22); I² = 30%
Test for overall effect: Z = 4.36 (P < 0.0001)

### 1.8.2 Required admission

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Antiemetic Events</th>
<th>Placebo Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freedman_2006</td>
<td>4</td>
<td>107</td>
<td>5</td>
<td>107</td>
<td>16.6% 0.80 [0.22, 2.90]</td>
</tr>
<tr>
<td>Gouin_2012</td>
<td>1</td>
<td>74</td>
<td>1</td>
<td>70</td>
<td>4.8% 0.95 [0.06, 14.83]</td>
</tr>
<tr>
<td>Qazi_2014</td>
<td>1</td>
<td>82</td>
<td>0</td>
<td>83</td>
<td>3.6% 3.04 [0.13, 73.46]</td>
</tr>
<tr>
<td>Ramsook_2002</td>
<td>3</td>
<td>62</td>
<td>16</td>
<td>51</td>
<td>18.7% 0.15 [0.05, 0.50]</td>
</tr>
<tr>
<td>Stork_2006</td>
<td>2</td>
<td>46</td>
<td>9</td>
<td>44</td>
<td>13.6% 0.21 [0.05, 0.93]</td>
</tr>
<tr>
<td>Stork_2006</td>
<td>2</td>
<td>46</td>
<td>7</td>
<td>47</td>
<td>13.1% 0.29 [0.06, 1.33]</td>
</tr>
<tr>
<td>Uhlig_2009</td>
<td>10</td>
<td>117</td>
<td>13</td>
<td>107</td>
<td>29.6% 0.70 [0.32, 1.54]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>534</strong></td>
<td><strong>509</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>23</td>
<td>51</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.19; Chi² = 8.26, df = 6 (P = 0.22); I² = 27%
Test for overall effect: Z = 2.57 (P = 0.01)

### 1.8.3 Return to ED

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Antiemetic Events</th>
<th>Placebo Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
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</thead>
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<tr>
<td>Freedman_2006</td>
<td>20</td>
<td>105</td>
<td>22</td>
<td>101</td>
<td>23.0% 0.87 [0.51, 1.50]</td>
</tr>
<tr>
<td>Gouin_2012</td>
<td>11</td>
<td>74</td>
<td>18</td>
<td>70</td>
<td>20.7% 0.58 [0.29, 1.14]</td>
</tr>
<tr>
<td>Qazi_2014</td>
<td>14</td>
<td>58</td>
<td>5</td>
<td>64</td>
<td>16.1% 3.09 [1.19, 8.05]</td>
</tr>
<tr>
<td>Ramsook_2002</td>
<td>4</td>
<td>74</td>
<td>0</td>
<td>71</td>
<td>3.5% 8.64 [0.47, 157.62]</td>
</tr>
<tr>
<td>Reeves_2002</td>
<td>4</td>
<td>54</td>
<td>3</td>
<td>53</td>
<td>10.3% 1.31 [0.31, 5.57]</td>
</tr>
<tr>
<td>Roslund_2008</td>
<td>3</td>
<td>48</td>
<td>2</td>
<td>55</td>
<td>8.0% 1.72 [0.30, 9.86]</td>
</tr>
<tr>
<td>Stork_2006</td>
<td>8</td>
<td>27</td>
<td>1</td>
<td>21</td>
<td>6.5% 6.22 [0.84, 45.94]</td>
</tr>
<tr>
<td>Uhlig_2009</td>
<td>4</td>
<td>102</td>
<td>5</td>
<td>97</td>
<td>11.9% 0.76 [0.21, 2.75]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>542</strong></td>
<td><strong>532</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>68</td>
<td>56</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.31; Chi² = 14.44, df = 7 (P = 0.04); I² = 52%
Test for overall effect: Z = 0.91 (P = 0.36)

Test for subgroup differences: Chi² = 11.50, df = 2 (P = 0.003), I² = 82.6%
Exploring heterogeneity

From CEBM Systematic Review Appraisal Sheet

Heterogeneity can be assessed using the “eyeball” test or more formally with statistical tests, such as the Cochran Q test. With the “eyeball” test one looks for overlap of the confidence intervals of the trials with the summary estimate. In the example above note that the dotted line running vertically through the combined odds ratio crosses the horizontal lines of all the individual studies indicating that the studies are homogenous. Heterogeneity can also be assessed using the Cochran chi-square (Cochran Q). If Cochran Q is statistically significant there is definite heterogeneity. If Cochran Q is not statistically significant but the ratio of Cochran Q and the degrees of freedom (Q/df) is > 1 there is possible heterogeneity. If Cochran Q is not statistically significant and Q/df is < 1 then heterogeneity is very unlikely. In the example above Q/df is <1 (0.92/4= 0.23) and the p-value is not significant (0.92) indicating no heterogeneity.

Note: The level of significance for Cochran Q is often set at 0.1 due to the low power of the test to detect heterogeneity.
8. Can the results be applied to the local population?

☐ Yes  ☐ Can’t tell  ☐ No

HINT: Consider whether

- The patients covered by the review could be sufficiently different to your population to cause concern
- Your local setting is likely to differ much from that of the review

9. Were all important outcomes considered?

☐ Yes  ☐ Can’t tell  ☐ No

HINT: Consider whether

- Is there other information you would like to have seen

10. Are the benefits worth the harms and costs?

☐ Yes  ☐ Can’t tell  ☐ No

HINT: Consider

- Even if this is not addressed by the review, what do you think?
Topics to be Introduced

1. Importance of literature syntheses
2. What are systematic reviews?
3. Steps to a systematic review:
   a) Developing the protocol
   b) Defining the review question
   c) Literature searching
   d) Study selection
   e) Risk of bias assessment
   f) Data collection
   g) Analysis & Reporting
Why would YOU conduct a systematic review?

Justification for research project (often prerequisite to grant proposal)

Project for a research block or thesis
  – Good chance of publication

Your supervisor tells you to do a systematic review!
Publication

Where do systematic reviews get published?

General medical/health profession journals: *BMJ*, *CMAJ*, *Annals of Internal Medicine*, *Nursing Research*, etc.

Specialty topic journals: *Cancer*, *Circulation*, etc.

Cochrane Database of Systematic Reviews
Conducting a systematic review will also...

Give you an excellent grasp of the state of research on a topic of interest to you
- Helps identify gaps in the existing research
- Highlights best practices

Increases your understanding of how research is conducted and reported
- The critical appraisal and assessment of bias used in conducting a systematic review will increase your ability to conduct rigorous, well-reported research
Many meta-analysis studies include the phrase “we searched Medline, EMBASE, and Cochrane for studies...”

This has led to meta-meta-analyses comparing meta-analysis methods.


We performed a meta-meta-meta-analysis of these meta-meta-analyses.

Methods: we searched Medline, EMBASE, and Cochrane for the phrase “we searched Medline, EMBASE, and Cochrane for the phrase “we searched Medline, EMBASE and

Life Goal #28: get a paper rejected with the comment “too meta”

http://xkcd.com/1447/
Important resource for conducting a SR

http://dal.ca.libguides.com/systematicreviews

Intro Systematic Reviews
Topics to be Introduced

1. Importance of literature syntheses
2. What are systematic reviews?
3. Steps to a systematic review:
   a) Developing the protocol
   b) Defining the review question
   c) Literature searching
   d) Study selection
   e) Risk of bias assessment
   f) Data collection
   g) Analysis & Reporting
Topics to be Introduced

1. Importance of literature syntheses
2. What are systematic reviews?
3. Steps to a systematic review:
   a) Developing the protocol
      b) Defining the review question \[\text{Done}\]
      c) Literature searching \[\text{Done}\]
      d) Study selection
      e) Risk of bias assessment
      f) Data collection
      g) Analysis & Reporting \[\text{Planned}\]
Prospective register of Systematic Reviews

PROSPERO
International prospective register of systematic reviews

Home
Register a review
My PROSPERO records
My details
Search PROSPERO
Search CRD databases
About PROSPERO
Help with registration
Support for PROSPERO
References and resources
Contact
Disclaimer

PROSPERO latest news
CRD is pleased to announce that PROSPERO now contains over 1000 registrations. The 1000th record is for a systematic review of the accuracy of first trimester ultrasound in the diagnosis of ectopic pregnancy. The review is being undertaken by clinical researchers at the University of Nottingham in the UK and can be found at www.crd.york.ac.uk/PROSPERO

Register your review protocol details
Registration is free and open to anyone undertaking systematic reviews of the effects of interventions and strategies to prevent, diagnose, treat, and monitor health conditions, for which there is a health related outcome.

http://www.crd.york.ac.uk/PROSPERO/
Example Timeline - Systematic Review

- **Protocol**: 3-6 months
- **Search**: 1-2 months
- **Study Selection**: 2-3 months
- **Risk of bias assessment**: 3-4 months
- **Data extraction**: 1-2 months
- **Analysis and reporting**: 2-3 months

Total duration: 1-2 years
Defining the Review Question

- Important to clearly specify
- Practical relevance
- Relevant stakeholders
  - Who are they?
  - What do they want to know?
## Broad vs. Narrow Questions: Example

<table>
<thead>
<tr>
<th>Review Question</th>
<th>Number of studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects of audit and feedback (A&amp;F)</td>
<td>85</td>
</tr>
<tr>
<td>Effects of A&amp;F to improve chronic diseases</td>
<td>18</td>
</tr>
<tr>
<td>Effects of A&amp;F to improve chronic diseases within primary care</td>
<td>14</td>
</tr>
<tr>
<td>Effects of A&amp;F to improve diabetes care within primary care</td>
<td>3</td>
</tr>
</tbody>
</table>
Framework to define the Question

P

I

C

O
Framework to define the Question

Population of interest

Intervention (or Exposure)

Comparisons

Outcomes
Importance of the Review Question

- Transparency
- Minimizes bias
- Facilitates subsequent steps:
  - Search strategy
  - Selection of studies
  - Planning the analysis
  - Reporting of results
More examples of review questions – beware!

Example – What antibiotic is best for treating UTIs?
Challenges – not specific regarding intervention, comparison, and key outcomes
Solutions – compare two specific drugs, or one compared to several (or no treatment); specify severity of condition and outcomes of interest (eg. presence of bacteria in culture, reduced duration of symptoms, recurrence)
Improved question

Do prophylactic antibiotics help prevent recurrent UTIs in healthy, non-pregnant women?

Topics to be Introduced

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   d) Study selection
   e) Risk of bias assessment
   f) Data collection
   g) Analysis & Reporting
Literature Searching

• Key factor distinguishing systematic review from narrative review

• Comprehensive & systematic
  – Minimize bias
  – Identify as many relevant studies as possible

• Trade-off:
  – Sensitivity
  – Specificity
Phases of the Literature Search

Identify existing systematic reviews
  – E.g. the Cochrane Library; Experts

Scoping search
  – Initial search on small range of databases

Comprehensive, systematic search
  – Full search; multiple sources

Update the search during the review process

Watch Yale video tutorials:
http://library.medicine.yale.edu/tutorials/subjects/systematic-reviews
Sources for Locating Studies

Electronic bibliographic databases (e.g. Medline, EMBASE, CINAHL, Cochrane Library)

Specialized registers of trials (CENTRAL, Cochrane review group registries)

Hand-searching relevant journals

Reference lists
  - Other reviews
  - Included studies

Grey literature
  - Pharmaceutical companies
  - Internet

Personal communication
  - suggestions from experts
  - contacting study authors
Developing the Database Search Strategy

• Get help from a health librarian
• Review question components: PICO
• Subject headings and free text:
  – Exemplar articles & reviews
  – Cochrane Review Groups
• Boolean operators (AND, OR, NOT)
• Study design filters
### Concept Map for Constructing Search Strategies

**Search statement - I am looking for articles to answer the question:**

After writing out the question, underline the key concepts. Decide how the concepts will be combined together using the **AND** and **OR** Boolean operators. Concepts to be **ANDed** go across the grid and concepts to be **ORed** go down the grid.

Fill in the grid with the key concepts and possible synonyms for each concept. Add subject headings first (where applicable).

<table>
<thead>
<tr>
<th>Concept 1</th>
<th>AND</th>
<th>Concept 2</th>
<th>AND</th>
<th>Concept 3</th>
<th>AND</th>
<th>Concept 4</th>
<th>AND</th>
<th>Concept 5</th>
</tr>
</thead>
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</table>

**Synonyms**

<table>
<thead>
<tr>
<th>OR</th>
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<th>OR</th>
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<th>OR</th>
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<th>OR</th>
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<th>OR</th>
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</tbody>
</table>

**Screening Criteria (Limits):**
Meet with a health sciences librarian to help develop and refine your search strategies!

The librarian can also serve as a peer-reviewer to confirm that there are no errors or oversights in your final search strategies.
Search strategy translated to multiple databases

<table>
<thead>
<tr>
<th>MEDLINE (OVID) and Central (OVID)*</th>
<th>EMBASE (OVID)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Acupuncture/ or acupuncture.mp.</td>
<td>1. exp ACUPUNCTURE/ or acupuncture.mp.</td>
</tr>
<tr>
<td>4. electroacupuncture/ or electroacupuncture.mp. [mp=title, original title, abstract, name of substance word, subject heading word]</td>
<td></td>
</tr>
<tr>
<td>5. moxibustion.mp. [mp=title, original title, abstract, name of substance word, subject heading word]</td>
<td></td>
</tr>
<tr>
<td>6. medicine, oriental traditional/ or medicine, chinese traditional/</td>
<td></td>
</tr>
<tr>
<td>7. Oriental Traditional Medicine.mp. [mp=title, original title, abstract, name of substance word, subject heading word]</td>
<td></td>
</tr>
<tr>
<td>8. Chinese traditional medicine.mp. [mp=title, original title, abstract, name of substance word, subject heading word]</td>
<td></td>
</tr>
<tr>
<td>9. or/1-8</td>
<td></td>
</tr>
<tr>
<td>10. arthritis.mp. [mp=title, original title, abstract, name of substance word, subject heading word]</td>
<td></td>
</tr>
<tr>
<td>11. arthritis/ or exp osteoarthritis/</td>
<td></td>
</tr>
<tr>
<td>12. osteoarthritis.mp. [mp=title, original title, abstract, name of substance word, subject heading word]</td>
<td></td>
</tr>
<tr>
<td>13. exp clinical trial/</td>
<td></td>
</tr>
<tr>
<td>14. exp randomized controlled trial/</td>
<td></td>
</tr>
<tr>
<td>15. randomized.ab.</td>
<td></td>
</tr>
<tr>
<td>16. placebo.ab.</td>
<td></td>
</tr>
</tbody>
</table>
Final Search Strategy

Complete & finalized at the protocol stage

Describe in detail:
  – Allow replication
  – Facilitate update -> save searches and set alerts!

Document throughout the search process:
  – Sources
  – Strategies
  – Time periods
  – Any restrictions
Topics to be Introduced

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   d) Study selection
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   f) Data collection
   g) Analysis & Reporting
Study Selection Criteria

Decisions about study inclusion/exclusion:
- Based on design
- NOT results

Standardized process (decision rules)
- Transparent
- Guide decisions
- Produce consistent results

Operationalize PICO *a priori*

Studies (not reports) are unit of interest
Study Selection Process

Separate step from collecting data
Pilot test selection criteria
Phases of selection:
  – Initial screen (Title & Abstract)
  – Detailed screen (Full text)

Two reviewers with consensus
  – Each reviewer: Yes, No, Unclear
  – Include notes & comments

Track excluded articles & reasons

Consider using Systematic Review Management Software such as Covidence!!
Study Selection: Additional issues

Uncertain inclusion (after full review)
- Information from other publications of the same study
- Contact the study author

Non-English language publications
- Risk of bias if excluded (some topic areas)
- Capture in the search
- Translation assistance
Topics to be Introduced

1. Importance of literature syntheses
2. What are systematic reviews?

3. Steps to a systematic review:
   a) Developing the protocol
   b) Defining the review question
   c) Literature searching
   d) Study selection
   e) Risk of bias assessment
   f) Data collection
   g) Analysis & Reporting
Risk of Bias Assessment

Component of ‘Quality Assessment’
Internal validity of included studies
Assessment of key potential biases
Validity of included studies will influence:
  – Analysis & results
  – Interpretation
What is bias?

• Systematic error or deviation from the truth in results or inferences

• Can operate in either direction:
  – Underestimation
  – Overestimation of true treatment effect

• Results of the review could be misleading if risk of bias is not considered

• Empirical evidence:
  – Flaws in design, conduct, analysis lead to bias
Incorporating Risk of Bias Assessments

- Not appropriate to ignore potential biases
- Explore the impact of individual bias domains
- Include in analyses
  - Primary analysis restricted to studies with low Risk of Bias
    - Sensitivity analyses may include higher risk studies
Topics to be Introduced

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   c) Literature searching
   d) Study selection
   e) Risk of bias assessment
   f) **Data collection**
   g) Analysis & Reporting
Data collection

A priori determine:
- ‘Who’ (two people, independent), and
- ‘How’ (process) to minimize bias

Data extraction form:
- Paper or electronic
- Develop information and instructions
- Pilot test

Study characteristics:
- PICO information
- Potential sources of heterogeneity
Topics to be Introduced

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   f) Data collection
   g) Analysis & Reporting
Overview of Analysis

- Different analytical methods:
  - Qualitative synthesis
  - Meta-analysis
  - Meta-regression
- Strengths & limitations with each
- Methods should be pre-specified and justified
Quantitative Synthesis

Systematic Review ≠ Meta-analysis

*Systematic reviews:* use well-defined protocol and methodological principles to attempt to reduce bias
  – Can be qualitative or quantitative

*Meta-analysis:* statistical analysis of a collection of independent studies
  – Quantitative part of *SOME* systematic reviews
Why perform a Meta-analysis?

Synthesis: Estimate overall measure of treatment effect
- Combine data from primary studies
- Improve precision of estimate of treatment effect
- Improve statistical power

Exploratory: Assess between-study differences
- Exploring heterogeneity
- Assess sensitivity to study characteristics
- Generate new hypotheses
When is Meta-analysis NOT appropriate?

• If studies are clinically diverse
  – Results may be meaningless
  – Genuine differences may be obscured

• Not appropriate to pool if important differences:
  – Population
  – Intervention
  – Comparisons
  – Outcomes

• Presence of serious publication or reporting biases
Reporting Results

Tables and figures
Forest plots to illustrate results of individual studies and meta-analyses (Review Manager software)

Discussion in context
- Benefits & harms
- Completeness and applicability of evidence
- Quality of the evidence

Implications for practice & for research

Use PRISMA checklist to guide in reporting:
http://www.prisma-statement.org/
Where to go for more assistance

Systematic literature searching and overview of evidence synthesis process and tools:

– Health Librarians at Dalhousie’s W. K. Kellogg Health Sciences Library (students and faculty)

– [http://dal.ca.libguides.com/systematicreviews](http://dal.ca.libguides.com/systematicreviews)
More assistance, cont’d
Statistics/meta-analyses:
– RMU/Faculty of Medicine Biostatistics
Consultants:
  • Steve Doucette
  • Kara Thompson

http://www.cdha.nshealth.ca/discovery-innovation/research-centres-and-facilities/research-methods-unit
Questions?

Contact information:
Robin Parker,
robin.parker@dal.ca
OR
ugmelib@dal.ca

Thank you!