How to read a Systematic Review

**FAST**

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Massive heart attack

A Systematic Review is a review of a clearly formulated question that uses systematic and explicit methods to identify, select and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review.

Most reviews do not pass minimum criteria

A study of 158 reviews*

– Only 2 met all 10 criteria
– Median was only 1 of 10 criteria met

* McAlister Annals of Intern Med 1999
Is the review any good?
FAST appraisal

- Question – What is the PICO?
- Finding
  - Did they find most studies?
- Appraisal
  - Did they select good ones?
- Synthesis
  - What to they all mean?
- Transferability of results

What is your question?
Search for a systematic review
Does the PICO of the review fit that of your question?

Do pedometers increase activity and improve health?
A Systematic Review

- Population
- Intervention
- Comparison
- Outcome(s)

Using Pedometers to Increase Physical Activity and Improve Health

Find: what is your search strategy?
- Databases?
- Terms?
- Other methods?

Do yourself then
Get neighbour’s help

FIND: Did they find all Studies?
- Check for existing systematic review?
- Good initial search
  - Terms (text and MeSH)
  - At least 2 Databases: MEDLINE, EMBASE, CINAHL, CCTR, ...
- Plus a Secondary search
  - Check references of relevant papers & reviews and
  - Find terms (words or MeSH terms) you didn’t use
  - Search again! (snowballing)

Is finding all published studies enough?

- Negative studies less likely to be published than ‘Positive’
- How does this happen?
- Follow-up of 737 studies at Johns Hopkins*
  - Positive SUBMITTED more than negative (2.5 times)

*Dickersin, JAMA, 1992

METHODS
Data Sources and Search Strategies

In collaboration with a professional librarian, we developed individualized search strategies for 2 databases, MEDLINE (January 1986 to February 2007), and EMBASE (January 1986 to February 2007). We used search terms such as pedometer, activity monitor, and step counter. We also reviewed the bibliographies of retrieved articles and relevant conference proceedings and contacted experts in exercise physiology for additional studies.
Registered vs Published Studies
Ovarian Cancer chemotherapy: single v combined

<table>
<thead>
<tr>
<th></th>
<th>Published</th>
<th>Registered</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. studies</td>
<td>16</td>
<td>13</td>
</tr>
<tr>
<td>Survival ratio</td>
<td>1.16</td>
<td>1.05</td>
</tr>
<tr>
<td>95% CI</td>
<td>1.06-1.27</td>
<td>0.98-1.12</td>
</tr>
<tr>
<td>P-Value</td>
<td>0.02</td>
<td>0.25</td>
</tr>
</tbody>
</table>

Simes, J. Clin Oncol, 86, p1529

Publication Bias: Solution

• All trials registered at inception,
  • The National Clinical Trials Registry: Cancer Trials
  • National Institutes of Health Inventory of Clinical Trials and Studies
  • International Registry of Perinatal Trials
• Meta-Registry of trial Registries
  – www.controlled-trials.com

Which are biased? Which OK?

1. All positive studies
2. All studies with more than 100 patients
3. All studies published in BMJ, Lancet, JAMA or NEJM
4. All studies registered studies

Flowchart

- 345 identified
- 254 screened
- 31 retrieved in full
- 14 RCTs included
- 91 duplicates
- 223 not relevant
- 17 excluded
**APPRAISE & select studies**

Did they select only the good quality studies?

**Assessment: How can you avoid biased selection of studies?**

- Assessment and selection should be:
  - Standardized “Objective” OR
  - Blinded to Results

* assessment of quality blind to study outcome

**Synthesis: pooling the results**

**What is a meta-analysis?**

Optional part of a systematic review

Systematic reviews → Meta-analyses

there’s a label to tell you what the comparison is and what the outcome of interest is
At the bottom there’s a horizontal line. This is the scale measuring the treatment effect.

For each study there is an ID.

The data for each trial are here, divided into the experimental and control groups.

This is the % weight given to this study in the pooled analysis.

The pooled analysis is given a diamond shape where the widest bit in the middle is located at the calculated best guess (point estimate), and the horizontal width is the confidence interval.

Note on interpretation

If the confidence interval crosses the line of no effect, this is equivalent to saying that we have found no statistically significant difference in the effects of the two interventions.

The vertical line in the middle is where the treatment and control have the same effect – there is no difference between the two.

The data shown in the graph are also given numerically.

The label above the graph tells you what statistic has been used.

The table below contains the data for each study, divided into the experimental and control groups.

<table>
<thead>
<tr>
<th>Study</th>
<th>Pool Management</th>
<th>Control</th>
<th>Chi-Square</th>
<th>p-Value</th>
<th>Weight</th>
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<tbody>
<tr>
<td>Miller 1993</td>
<td>0.03</td>
<td>1.24</td>
<td>2.14</td>
<td>8.29</td>
<td>0.10</td>
</tr>
<tr>
<td>Miller 1999</td>
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</table>
Meta-analysis (Forest) plot

The figure on the right is from Figure 3. See if you can answer the following questions about this plot.

1. How many studies are there?
2. How many studies favour treatment?
3. How many studies are statistically significant?
4. Which is the largest study?
5. Which is the smallest study?
6. What is the combined result?

Weighting studies

- More weight to the studies which give us more information
  - More participants
  - More events
  - More precision
- Weight is proportional to the precision

Transferable? Use in my patients

Is the AVERAGE effect similar across studies?

- If NO, then WHY?
  - Study methods - biases
  - PICO
- If YES, then 2 questions
  - Effect in different individuals?
  - Which version of treatment?

If we just add up the columns we get 34.3% vs 32.5%, a RR of 1.06, a higher death rate in the steroids group.

From a meta-analysis, we get RR=0.96, a lower death rate in the steroids group.
Are these trials different?

Risk of SIDS and sleeping position

Cumulative meta-analysis

When did we know that sleeping position affected mortality?

Conclusion

**EBM and Systematic Review**

- **EBM (quick & dirty)**
  - Ask Question
  - Search
  - Appraise
  - Apply
  - Time: 90 seconds
  - < 20 articles
  - **This patient survives!**

- **Systematic Review**
  - Ask Question
  - Search ++++ x 2
  - Appraise x 2
  - Synthesize
  - Apply
  - Time: 6 months, team
  - < 2,000 articles
  - **This patient is dead**

Find a systematic review!! (and appraise it FAST)
Pros and cons of systematic reviews

- Advantages
  - Larger numbers & power
  - Robustness across PICO(s)

- Disadvantages
  - May conclude small biases are real effects