13TH ISPRM WORLD CONGRESS – ISPRM 2019

Cochrane rehabilitation workshop: Apply CochRane Evidence with Confidence (ACREC)

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Trusted evidence.
Informed decisions.
Better health.
Disclosure

I have no conflicts of interest with anything in this presentation
How to read and understand systematic reviews?

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Trusted evidence.
Informed decisions.
Better health.
REAL LIFE SETTING – PHYSICANS AND SCIENCE

• less time to read what others have written
• selection, reading and critical appraisal - necessary to stay up to date
• this is also demanded by the precepts of evidence-based medicine
• interpretation and evaluation - require understanding of the statistical methodology
• in scientific surrounding not all terms are used correctly


Practicing EBM - five essential steps:

1. converting information needs into answerable questions
2. finding the best evidence with which to answer the questions
3. critical appraisal of the evidence for its validity and usefulness
4. applying the results of the appraisal into clinical practice
5. evaluating performance

What Is Evidence-Based Medicine?

Clinical Judgment

EBM

Relevant Scientific Evidence

Patients’ Values and Preferences

**Systematic Reviews**

Clear Search strategy  
Locate all relevant published and unpublished studies  
Limit impact of biases  
Rigorous quality appraisal of all included studies  
Clear eligibility criteria  
Conclusions which are most methodologically sound  
Engage stakeholders in shaping review questions

**Traditional Reviews**

Unclear Criteria for including/excluding studies  
Unspecified Search strategy  
Do not usually attempt to locate all relevant studies  
Do not consider differences in study quality  
Do not differentiate between methodologically sound and unsound studies  
Do not attempt to engage stakeholders
Figure. Hierarchy of Research Design

1. Randomized controlled trial and meta-analysis
2. Nonrandomized trial, concurrent and historical controls
3. Cohort study, prospective and retrospective
4. Case-control study
5. Cross-sectional study
6. Case study
7. Case report
**systematic reviews (SR’s)** - answers a defined research question by collecting and summarising all empirical evidence that fits pre-specified eligibility criteria

**meta-analysis** - use of statistical methods to summarise the results of these studies

Key elements in both evidence-based healthcare and evidence-based research

SR’s support clinicians in making well-informed decisions about health care and researchers in deciding which topics are the most relevant for new research
Meta-analysis

Meta analysis is a statistical method
Not a synonym to systematic reviews
Systematic reviews **may or may not** have meta analysis
What is so special about a Cochrane systematic review?

Rigorous methodology
- Systematic search, all languages, risk of bias assessment, GRADE-ing of evidence
- Evolving methodology

Very comprehensive manuscripts
- Electronic resource
- Some of them may have several hundred pages

Updates of previously published reviews
Which databases is necessary to search and how many?

• comprehensive literature search to identify all published studies relevant to the specific research question

• The Cochrane Collaborations Methodological Expectations of Cochrane Intervention Reviews (MECIR) guidelines state that searching MEDLINE, EMBASE and CENTRAL should be considered mandatory


Steps which lead to systematic review

1. **Framing the question** - clear, unambiguous and structured questions before beginning the review work

2. **Identifying relevant work** - To capture as many relevant citations as possible, a wide range of medical and scientific databases were searched to identify primary studies

3. **Assesing the quality of studies** - Selected studies should be subjected to a more refined quality assessment by use of general critical appraisal guides and design-based quality checklists

4. **Summarizing the evidence** - Data synthesis consists of tabulation of study characteristics, quality and effects as well as use of statistical methods for exploring differences between studies and combining their effects (meta-analysis). Exploration of heterogeneity and its sources should be planned in advance (Step 3). If an overall meta-analysis cannot be done, subgroup meta-analysis may be feasible

5. **Interpreting the findings** - The risk of publication bias and related biases should be explored. Exploration for heterogeneity should help determine whether the overall summary can be trusted, and, if not, the effects observed in high-quality studies should be used for generating inferences. Any recommendations should be graded by reference to the strengths and weaknesses of the evidence


| **P** Patient, Population or Problem | What are the users, patients or community being affected? What are their symptoms, age, gender etc. |
| **I** Intervention, Prognostic Factor, or Exposure | What is being done for the population e.g. screening, surgery, rehabilitation, services etc. |
| **C** Comparison | Is there a control group or comparison e.g. different treatment options, placebos etc. |
| **O** Outcome | What do you want to achieve via the study? What do you hope to change or measure? |
Practical case.....

In middle aged male amputees suffering phantom limb pain

is gabapentin,

compared with placebo,

effective in decreasing pain symptoms?
Now it is your turn…..

Are serotonin and noradrenaline reuptake inhibitors effective, tolerable, and safe for adults with fibromyalgia?

Based on the above title, what would be…?
Interpreting forest plots and meta-analysis statistics
Meta-analysis

- Meta analysis is a statistical method and
- Not a synonym to systematic reviews
- Systematic reviews **may or may not** have meta analysis

- useful guide to improve reporting of systematic reviews and meta-analyses is the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-analyses) statement

- the results of meta-analyses are often presented in a forest plot (each study is shown with its effect size and the corresponding 95% confidence interval)
Meta-analysis

- several methods have been developed to provide an assessment of publication bias - most commonly used is the funnel plot

- the classical meta-analysis compares two treatments while network meta-analysis (or multiple treatment meta-analysis) can provide estimates of treatment efficacy of multiple treatment regimens

- meta-analysis can also be used to summarize the performance of diagnostic and prognostic tests
Forest plot (blobbogram)

• graphical representation of a meta-analysis of the results of RCT’s
• accompanied by a table listing references (author and date) of the studies included in the meta-analysis → addressing one particular question
• the right-hand column is a plot of the measure of effect (e.g. an odds ratio) for each of these studies (often represented by a square) incorporating confidence intervals represented by horizontal lines
Interpretation of forestplots...

1. **To determine the effect size**: black diamond at the bottom of the graph shows the average effect size of the studies.

2. **Assess the heterogeneity (or difference) between studies**: - if heterogeneity is due to chance (or not) by interpreting the $I^2$ statistic (found at the bottom of the table in a forest plot).
   - $I^2$ statistic $> 50\%$ is considered high.

3. .....finally: **Evidence-based interventions or programmes are those which have been proven effective in multiple, high-quality randomised controlled trials (RCTs)**.
Behavioural physical activity interventions in participants with lower-limb osteoarthritis: a systematic review with meta-analysis

Wilby Williamson, Stefan Kluzek, Nia Roberts, Justin Richards, Nigel Arden, Paul Leeson, Julia Newton, Charlie Foster

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>IV, Random, 95% CI</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brosseau 2012</td>
<td>19.08</td>
<td>17.45</td>
<td>76</td>
<td>24.18</td>
<td>25.59</td>
<td>33</td>
<td>14.7%</td>
<td>-0.25 [-0.66, 0.16]</td>
<td></td>
</tr>
<tr>
<td>Hughes 2006</td>
<td>210.5</td>
<td>153.2</td>
<td>58</td>
<td>115.7</td>
<td>122.7</td>
<td>32</td>
<td>14.2%</td>
<td>0.66 [0.21, 1.10]</td>
<td></td>
</tr>
<tr>
<td>Lorig 2008</td>
<td>22.6</td>
<td>100.6</td>
<td>134</td>
<td>0.316</td>
<td>100.3</td>
<td>158</td>
<td>17.2%</td>
<td>0.22 [-0.01, 0.45]</td>
<td></td>
</tr>
<tr>
<td>Murphy 2008</td>
<td>3218</td>
<td>2539</td>
<td>25</td>
<td>2590</td>
<td>1778</td>
<td>26</td>
<td>18.0%</td>
<td>0.28 [-0.27, 0.84]</td>
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</tr>
<tr>
<td>Rosemann 2007</td>
<td>132.5</td>
<td>10.65</td>
<td>537</td>
<td>125.2</td>
<td>10.9</td>
<td>258</td>
<td>18.0%</td>
<td>0.68 [0.53, 0.83]</td>
<td></td>
</tr>
<tr>
<td>Schienk 2005</td>
<td>141.3</td>
<td>131.4</td>
<td>11</td>
<td>96.4</td>
<td>152</td>
<td>10</td>
<td>8.5%</td>
<td>0.30 [-0.56, 1.17]</td>
<td></td>
</tr>
<tr>
<td>Svege 2013</td>
<td>120</td>
<td>46.8</td>
<td>53</td>
<td>139</td>
<td>59.2</td>
<td>49</td>
<td>15.0%</td>
<td>-0.36 [-0.75, 0.04]</td>
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</tr>
<tr>
<td>Total (95% CI)</td>
<td>894</td>
<td></td>
<td></td>
<td>566</td>
<td></td>
<td>100.0%</td>
<td>0.22 [-0.11, 0.56]</td>
<td></td>
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</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.16$; Chi$^2 = 40.69$, df = 6 ($P < 0.00001$); $I^2 = 85$

Test for overall effect: $Z = 1.30$ ($P = 0.19$)

Figure 2 Forest plot for meta-analysis of self-reported physical activity outcomes following exercise intervention.
Effect sizes versus p-values: difference
Effect size

• quantitative measure of the difference between two groups

• effect sizes are calculated based on the ‘standardised mean difference’ (SMD) between two groups in a trial

• this is the difference between the average score of participants in the intervention group and the average score of participants in the control group

• Effect sizes are usually reported using the label ‘d=’, and in the form of a fraction, such as d=0.2 or d=0.5.

• interpreting effect sizes: < 0.2 = small effect size; 0.5 = medium effect size; > 0.8 and above = large effect size.

• Cohen’s suggestions are generally accepted and are a good basis for interpreting the results of trials and in reading systematic reviews and meta-analyses
What’s the difference between an effect size and statistical significance?

- **Statistical significance** → pointing you if an intervention had an effect that was unlikely to have happened by chance
- Not as useful for comparing effect sizes of multiple studies as done in SR’s
- Because statistical significance does not take into account sample size (i.e. the number of participants in a study)
- If two studies are identical except that one has a larger sample size, we would usually consider the study with the larger sample size to be more reliable, but statistical significance does not give more weight to a study with more participants – all studies are treated equally.

- **Effect sizes are ‘weighted’ according to the number of participants in a study**
- For instance, a study with 10 participants might have had a big effect size (such as 0.8); while another study of the same intervention may have had 1000 participants but a small effect size (such as 0.2).
- If all other things are equal (e.g. both studies had a low risk of bias), then both studies may have shown that the intervention had a statistically significant effect, but the overall effect size would be small, because the larger of the two studies would be given more ‘weight’.
GRADE

- Grades of Recommendation, Assessment, Development and Evaluation
- System for grading the quality of evidence
- Adopted by many different organizations (WHO, BMJ Clinical evidence, Cochrane Collaboration,....)

- Offers a transparent and structured process for developing and presenting evidence summaries for systematic reviews and guidelines and for carrying out the steps involved in developing recommendations
What authors DO

1. Identify the issue and determine the question
2. Write a plan for the review (protocol)
3. Search for studies
4. Sift and select studies
5. Extract data from the studies
6. Assess the quality of the studies
7. Combine the data (synthesis or meta-analysis)
8. Discuss and conclude overall findings

Systematic Review

Dissemination
Take home messages....

- systematic reviews often have to summarise findings from large and complex fields of research

- *Cochrane Library* provides a collection of full-text systematic reviews developed using rigorous reporting standards and methods

- each review has a plain language summary and a structured abstract, which includes a section for the authors’ conclusions
THE END
thank you all!