Meta-analysis

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Meta-analysis

(Customarily now refers only to analysis of randomized trials)
(Systematic review = analysis of all available publications)

- The process of using statistical methods to combine results of randomized trials, which individually may not demonstrate statistically significant differences between study groups, to derive more clear trends.
  [critically dependent on quality of collected studies & bias control]
The Cochrane Collaboration is an international non-profit organization that aims to help people make well-informed decisions about healthcare by preparing, maintaining and promoting the accessibility of "systematic reviews" of the effects of healthcare interventions.

What does the Cochrane Collaboration do?

- Prepare and maintain systematic reviews
- Educate investigators in performing reviews
- Contribute to Cochrane's CENTRAL database of controlled trials (~350,000)
- Build trials registers (eg, eyes and vision)
- Encourage use of Cochrane reviews

Cochrane Eyes and Vision Group

- 1 of 49 disease-specific review groups
- Editorial base at Moorfields Eye Hospital, London
- Prepare and maintain reviews of all interventions used to prevent or treat eye diseases and/or visual impairment which have been evaluated by controlled trials
How to do a Cochrane systematic review?

- Select a topic and formulate a focused question
- Register the title
- Perform a comprehensive literature search
- Identify a co-reviewer (minimize bias)
- Prepare the protocol (peer review)
- Publish on The Cochrane Library
- Prepare the review (peer review)
- Publish on The Cochrane Library
- Respond to comments/criticism
- Keep the review up-to-date
- Submit for publication in journals

Protocol

- Title
- Background
- Objectives
- Criteria for including studies
- Search strategy
- Methods of the review

Literature Search

- Electronic data-bases:
  - MEDLINE
  - EMBASE
  - Cochrane Library
  - LILACS
  - Personal
- Hand Search
- Companies; manufacturers
- Published & unpublished
The Review = The protocol +...
- Description of studies
- Methodological quality
- Results
- Discussion
- Reviewers' conclusions...
  - Implications for practice and research

Principal Methodological Issues (Biases) considered across collected publications
- Selection Bias (concealment of allocation)
- Performance Bias (masking of providers?)
- Detection Bias (evaluators masked?)
- Attrition Bias (follow-up & compliance similar in control & study groups?)

After protocol....
- Assess search results
- Assess quality of studies
- Extract data
- Contacting trialists
- Data entry (RevMan)
- Summarize results
- Sensitivity analyses
- Final report
### Wormald et al: Failure at 12 months

**Failure Rate at 12 months**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Gender</th>
<th>Preoperative</th>
<th>Postoperative</th>
<th>Duration</th>
<th>Success Rate</th>
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<td>3</td>
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<tr>
<td>4</td>
<td>45</td>
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<td>15</td>
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### Wormald et al: IOP at 12 months

**IOP at 12 months**

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<th>Postoperative</th>
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<th>IOP Difference</th>
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### Aqueous Shunts in Glaucoma

**Draft Forest Plot**

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean (SD)</th>
<th>Effect Size</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>Test A</td>
<td>0.5 (0.1)</td>
<td>-0.2</td>
<td>-0.8 to 0.4</td>
</tr>
<tr>
<td>Test B</td>
<td>0.3 (0.2)</td>
<td>0.1</td>
<td>-0.3 to 0.5</td>
</tr>
<tr>
<td>Test C</td>
<td>0.7 (0.3)</td>
<td>0.5</td>
<td>0.1 to 1.9</td>
</tr>
</tbody>
</table>

Note: Draft Forest Plot
Aqueous Shunts in Glaucoma

Example: Comparing baseline and final IOP values

Double-plate Molteno vs. Schocket

How to pool data?

Aqueous Shunts in Glaucoma
(Ahmed vs Trabeculectomy)

Aqueous Shunts in Glaucoma
(Ahmed vs Trabeculectomy)

Meta-analysis

- **Advantage**
  - Increased statistical power across small studies

- **Disadvantages**
  - Publication bias (published/unpublished)
  - Variations in quality of available/selected studies
  - Important individual issues may be masked by synthesis of data
  - Lack of uniform standards (terminology, methodology, data-analysis)

Lack of Standard Terminology/concepts Re:
Aqueous Shunt RCTs (and all other glaucoma topics)

- Definitions of Success/Failure
- Small numbers of cases (without sample size/power statements)
- Variable randomization methods; random number tables best; quasi-randomization; alternating assignments; coin toss
- Unclear statements about "ITT" vs. "as treated" analysis; variable accounting for loss to follow-up
- Variable follow-up intervals (12 weeks - years); lack of individual-specific IOP data in favor of summary graphs; survival curves, data plots
- Group analyses less useful than individual-specific data for meta-analysis
- Incomplete (inconsistent) Demographics