Study design and Levels of Evidence

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**Research questions**

- **determine problem**
  - (case reports/case-series, ecological/cross-sectional studies)

- **implement activities**
  - (surveillance studies, meta-analyses)

- **find potential causes**
  - (case-control/cohort studies)

- **design interventions**
  - (randomized controlled trials)
Taxonomy of trial design

- **Epidemiological Studies**
  - Non-experimental (Observational)
    - Data from groups: Descriptive
      - Ecological study
    - Data from individuals: Analytic
      - Cross-sectional study
  - Experimental (Intervention)
    - Data from groups: Descriptive
      - Cohort study
    - Data from individuals: Analytic
      - Case-control study
Hierarchy of Evidence

- Systematic Reviews and Meta-analyses
- Randomized Controlled Double Blind Studies
- Cohort Studies
- Case Control Studies
- Case Series
- Case Reports
- Ideas, Editorials, Opinions
- Animal research
- In vitro ('test tube') research
<table>
<thead>
<tr>
<th>Level</th>
<th>Therapy</th>
<th>Prognosis</th>
<th>Diagnosis</th>
<th>Aetiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Systematic Review</td>
<td>Systematic Review</td>
<td>Systematic Review</td>
<td>Systematic Review</td>
</tr>
<tr>
<td>II</td>
<td>RCT</td>
<td>Inception cohort</td>
<td>Cross-sectional (consecutive)</td>
<td>Prospective cohort</td>
</tr>
<tr>
<td>III</td>
<td>Non-Randomised experimental</td>
<td>Untreated control patients in RCT</td>
<td>Cross-sectional (non-consecutive)</td>
<td>Retrospective cohort</td>
</tr>
<tr>
<td></td>
<td>Comparative with concurrent control group</td>
<td>Retrospective cohort</td>
<td>Diagnostic case-control</td>
<td>Case-control / Ecological</td>
</tr>
<tr>
<td>IV</td>
<td>Case series</td>
<td>Cohort patients different disease</td>
<td>Case series</td>
<td>Cross-sectional</td>
</tr>
</tbody>
</table>
Describe patients’ characteristics, and may generate ideas for future studies
Randomized Controlled Trial

- Typical RCT randomises two (or more) groups of patients to different treatments.

Diagram:

1. Population
2. Sample
3. Meet Inclusion Criteria?
4. Patients
5. Treatment Group
6. Control Group
7. Follow-up
8. Compare results
9. Baseline Assessment
10. Random assignment
11. Follow-up assessments
Observational Studies

- Ecological
- Cross-sectional
- Case-control
- Cohort or “follow-up” studies
Ecological study

- Focuses on the characteristics of population *groups* rather than their individual members.
- The group could be defined by
  - time (calendar period, birth cohort),
  - geography (country, city),
  - socio-demographic characteristics (ethnicity, religion).
- Used to examine the differential distribution of diseases among people with different risk profiles.
  - The kinds of comparisons usually take advantage of routinely collected data and are therefore inexpensive.
A cross-sectional study is a single “snapshot” in time.

- We can only study current risk factors and diseases (prevalence).
Case-control study

- Case-control studies examine the association of disease with past exposure (s).

Starting point: Past Exposure History

- Population of non-diseased individuals
- Sample of non-diseased individuals
- Sample of diseased individuals
- Group of interest (e.g. cancer patients)

Take histories

Comparison group (e.g. non-patients)

Draw conclusions

Compare histories
Selected group of disease-free people who are classified according to a specific exposure.

- Observed over time to see who develops the disease or outcomes (s) of interest.
- Can measure incidence (new cases of disease) and thus risk
Principles of Evidence Grading

1. Different research evidence for different types of clinical questions

2. Top level of evidence – Systematic Reviews (Irrespective of type of clinical question)

3. When SR not available, efficient strategies required to identifying relevant evidence

4. Study “Level” alone should not be used to grade evidence

5. Balanced assessments use different types of research
Bias in RCTs

Effect of study features on effect size in 229 trials

<table>
<thead>
<tr>
<th>Study Feature</th>
<th>Odds Ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment</td>
<td>0.70</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Random #</td>
<td>0.95</td>
<td>0.58</td>
</tr>
<tr>
<td>Inappropriate Exclusions</td>
<td>1.07</td>
<td>0.32</td>
</tr>
<tr>
<td>Double-blind</td>
<td>0.83</td>
<td>0.01</td>
</tr>
</tbody>
</table>

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Bias in Diagnostic Studies

Lijmer JG et al. JAMA 1999;282:1062-1067

- Case-control: 3.0 (2.0-4.5)
- Different reference tests: 2.2 (1.5-3.3)
- Partial verification: 1.0 (0.8-1.3)
- Not blinded: 1.3 (1.0-1.9)
- Non-consecutive: 0.9 (0.7-1.1)
- Retrospective: 1.0 (0.7-1.4)
- No description test: 1.7 (1.1-2.5)
- No description population: 1.4 (1.1-1.7)
- No description reference: 0.7 (0.6-0.9)