Foundations for Evaluating Clinical Literature
Outline

• Definitions
• Study Design
• Sampling
• Bias
• Reliability and validity
Research Areas

• Clinical Research (humans)
  – Diagnosis
  – Frequency (prevalence/incidence)
  – Risk factors
  – Prognosis
  – Treatment
  – Prevention

• Laboratory Research (basic)
  – Typically animal models
  – Human and animal cell cultures and biologic samples
  – Genetic material

• Translational Research
  – New area (relatively)
Classification of Studies

Descriptive
- Populations
- Prevalence/incidence
- Distribution (disease, risks, demographics, etc.)

Observational
- Individuals
- Test cause-effect hypotheses
- Uncontrolled assignment to study groups (naturalistic)

Experimental
- Individuals
- Test cause-effect hypotheses
- Controlled assignment to study groups
Causes and Effects

X
Independent variable
“cause”
Examples?

Y
Dependent variable
“effect”
Examples?

Probabilistic causality
Study Design

• Laboratory experiment
  – Causality: chemical X \( \rightarrow \) cancer
  – Method: 100 mice randomized to exposed and unexposed groups (e.g. 50 each)
  – Follow up for some time
  – Measure cancer incidence rate in the two groups
  – Proof of causation
Study Design

• Experimental
  – Randomization --> independent variable (drug X) --> Dependent variable (outcome/endpoint Y)

• Analytic/observational
  – Independent Variable (risk factor) --> Dependent Variable (outcome)
Sampling

Target Sample

Intended Sample

Actual Sample

Potential bias
(e.g. non-responder)

Study hypothesis testing

Inference/generalization
Measurement

- Two types of issues to expect:
  - Random (instrument sensitivity)
  - Systematic (instrument bias)
Reliability vs. Variability

Observer

Instrument

Subject
# Observer Reliability

Observer 1

<table>
<thead>
<tr>
<th></th>
<th>Positive</th>
<th>Negative</th>
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<tbody>
<tr>
<td>Positive</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>Negative</td>
<td>c</td>
<td>d</td>
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</tbody>
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Observer 2 (or 1 but diff time)

Percent agreement = \((a+d)/N\)

Kappa = \((\text{Observed } \% \text{ agr} - \text{Expected } \% \text{ agr}) / (100\%-\text{Expected } \% \text{ agreement})\)
Validity/Accuracy

Outcome condition (disease)

<table>
<thead>
<tr>
<th>Test</th>
<th>Present</th>
<th>Absent</th>
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<tbody>
<tr>
<td>Positive</td>
<td>a (TP)</td>
<td>b (FP)</td>
</tr>
<tr>
<td>Negative</td>
<td>c (FN)</td>
<td>d (TN)</td>
</tr>
</tbody>
</table>

Sensitivity = TP/(TP+FN)  
PPV = TP/(TP+FP)  
Specificity = TN/(FP+TN)  
NPV = TN/(TN+FN)
Summary

- Things to keep an eye out for when designing or evaluating studies:
  - Hypothesis
  - Sample (size and sampling strategy)
  - Bias (sampling or measurement)
  - Instruments (reliability and validity)