Articles of Harm

March 14, 2013

Jeff Kushinka, MD

Jamie Fox, MD
Objectives

✓ Study design
✓ Validity criteria for Harm studies
✓ Odds vs. Risk
  ▪ MATH!
  ▪ Stuck with odds
  ▪ Odds ≈ Risk

FUN!!

INTERACTION

VISUAL EXAMPLES

CLINICAL CASE
Evidence-based Medicine Cycle

The 5 A’s

THE PATIENT

ASSESS

ASK

ACQUIRE

APPLY

APPRAISE
Clinical scenario
Clinical scenario
What clinical questions can we pose?

P
I
C
O
(T)
STUDY DESIGN!

3 Volunteers, Please
Randomized, Controlled Trial

- Drug
- Placebo
- Cure
- No Cure

Measure Here

TIME
Exposure Present → Outcome Yes
Exposure Absent → Outcome No

Exposure Present → Outcome No
Exposure Absent → Outcome Yes

Measure Here

TIME
Randomized, Controlled Trial
Special Prospective Cohort

Drug

Placebo

Cure

No Cure

Measure Here
Retrospective Cohort Study
Retrospective Cohort Study

Exposure Present → Outcome Yes
Exposure Absent → Outcome No

TIME

Measure Here

PRESENT
Case-Control Study

Exposure Present

Exposure Absent

Outcome Yes (Cases)

Outcome No (Controls)

Measure Here

PRESENT

TIME
Hierarchy of Evidence

- Meta-analysis
- Systematic Reviews
- Randomized Controlled Trials
- Cohort studies
- Case-control studies
- Case series
Advantages of Case Control

- They are relatively **CHEAP**
- They are relatively **FAST**
  - You don’t have to wait for a rare event to happen
  - Database / Questionnaire-driven
- Common for studies on **HARM**
Disadvantages of Case Control

- You don’t get a true estimate of population RISK, because you are artificially defining your population

- Risk = (Harmful events) / (# of subjects)
  - You choose the number of harms to monitor
  - You choose the number of cases and controls

- Because YOU choose the controls, there are all kinds of biases that can be introduced
# Study Design Review

## Directions of Inquiry and Key Methodologic Strengths and Weaknesses for Different Study Designs

<table>
<thead>
<tr>
<th>Design</th>
<th>Starting Point</th>
<th>Assessment</th>
<th>Strengths</th>
<th>Weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized controlled trial</td>
<td>Exposure status</td>
<td>Outcome event status</td>
<td>Low susceptibility to bias</td>
<td>Feasibility and generalizability constraints</td>
</tr>
<tr>
<td>Cohort</td>
<td>Exposure status</td>
<td>Outcome event status</td>
<td>Feasible when randomization of exposure not possible, generalizability</td>
<td>Susceptible to bias</td>
</tr>
<tr>
<td>Case-control</td>
<td>Outcome event status</td>
<td>Exposure status</td>
<td>Overcomes temporal delays and the need for huge sample sizes to accumulate rare events</td>
<td>Susceptible to bias</td>
</tr>
</tbody>
</table>
How we doin’?
Clinical scenario
Study Designer for a Day
Clinical scenario,
CONTINUED.....
Clinical scenario, CONTINUED.....
Clinical scenario, CONTINUED.....
NEW QUERY

Are these two images related?
Searching ......
A Case-Control Study of Baldness in Relation to Myocardial Infarction in Men

Samuel M. Lesko, MD; Lynn Rosenberg, ScD; Samuel Shapiro, MB, FRCP(Edin)

Objective.—To examine the relationship between male pattern baldness and the risk of myocardial infarction in men under the age of 55 years.

Design and Participants.—A hospital-based, case-control study was conducted in eastern Massachusetts and Rhode Island. Cases were men admitted to a hospital for a first nonfatal myocardial infarction (n=665); controls were men admitted to the same hospitals with noncardiac diagnoses (n=772). Extent of baldness was assessed using the 12-point modified Hamilton Baldness Scale; other information was obtained by personal interview. Among the controls, the prevalence of any baldness was 34%, while the prevalence of baldness involving the vertex scalp was 23%.

Results.—After allowing for age, the relative risk estimate for frontal baldness compared with no hair loss was 0.9 (95% confidence interval, 0.6 to 1.3), for baldness involving the vertex scalp it was 1.4 (95% confidence interval, 1.2 to 1.9). Risk of myocardial infarction increased as the degree of vertex baldness increased (P<.01); for severe vertex baldness the relative risk was 3.4 (95% confidence interval, 1.7 to 7.0). The relationship between vertex baldness and myocardial infarction was consistent within strata defined by age and other risk factors for coronary artery disease.

Conclusion.—These data support the hypothesis that male pattern baldness involving the vertex scalp is associated with coronary artery disease in men under the age of 55 years.
Validity Criteria

1. Did the experimental and control groups **BEGIN** the study with a similar prognosis?
   a. Did the investigators demonstrate similarity with respect to all known important determinants of outcome? If differences existed, were adjustments made in the analysis?
   b. **CASE-CONTROL:** Were exposed patients equally likely to be identified among cases and controls?

2. Did experimental and control groups **RETAIN** a similar prognosis after the study started?
   a. Were exposures and outcomes measured in the same way in each comparison group?
   b. Was follow-up sufficiently long and complete?

3. Is there a reasonable temporal relationship between exposure and outcome?

4. Is there a dose-response gradient?

5. Do your patients match the characteristics of patients in this study?
Let’s talk about odds…

THE PROJECT HAS A 70% CHANCE OF MINOR SUCCESS AND A 30% CHANCE OF CORPORATE RUINATION.

I LIKE THOSE ODDS. WHEN CAN WE START?

START?

I WISH WE HAD TEN MORE PROJECTS LIKE THIS ONE.

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**Risk vs. Odds**

**Risk:** the number of times an event of interest occurs relative to the total possible number of events (i.e. batting average)

Risk = probability
Risk doesn’t necessarily mean “bad”

How often does an event occur?

\[
\text{Risk of Purple} = \frac{3}{3 + 1} = 0.75
\]
**Risk vs. Odds**

**Risk:** the proportion of times an event of interest occurs relative to the total number of events (i.e. batting average)

**Odds:** the number of times an event of interest occurs relative to the number of times it does not occur (i.e. gambling)

How often does an event occur … compared to how often is does not?

\[
\frac{3}{1} = 3
\]

Odds of Purple
**Risk vs. Odds**

**Risk:** the number of times an event of interest occurs relative to the total number of events (i.e. batting average)

What is the RISK of Green?

\[
\frac{1}{1 + 3} = 0.25
\]
Risk vs. Odds

**Odds:** the number of times an event of interest occurs relative to the number of times it does not occur (i.e. gambling)

What is the **ODDS** that Green occurs?

\[
\frac{1}{3} = 0.33
\]
2 Volunteers, Please.
<table>
<thead>
<tr>
<th>RISK</th>
<th>ODDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9</td>
<td>9</td>
</tr>
<tr>
<td>0.75</td>
<td>3</td>
</tr>
<tr>
<td>RISK</td>
<td>ODDS</td>
</tr>
<tr>
<td>-------</td>
<td>------</td>
</tr>
<tr>
<td>0.9</td>
<td>9</td>
</tr>
<tr>
<td>0.75</td>
<td>3</td>
</tr>
<tr>
<td>0.5</td>
<td>1</td>
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</table>

The pie chart shows a 50-50 split.
<table>
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<th>RISK</th>
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<tr>
<td>0.9</td>
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</tr>
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<td>0.5</td>
<td>1</td>
</tr>
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<td>0.33</td>
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</tr>
<tr>
<td>0.33</td>
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<tr>
<td>0.25</td>
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</tr>
<tr>
<td>0.33</td>
<td>0.5</td>
</tr>
<tr>
<td>0.25</td>
<td>0.33</td>
</tr>
<tr>
<td>0.1</td>
<td>0.11</td>
</tr>
</tbody>
</table>

The pie chart on the left indicates a risk level of 90, with a 10% slice highlighted.
Notice a trend?

<table>
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</tr>
<tr>
<td>0.1</td>
<td>0.11</td>
</tr>
<tr>
<td>0.01</td>
<td>0.01</td>
</tr>
</tbody>
</table>
Risk RATIO
Odds RATIO

RATIO is a
RATIO is a
RATIO is a
__________!
Risk Ratio = Relative Risk (Cohort study)

Risk of outcome in exposed group

Risk of outcome in unexposed group
Risk Ratio = Relative Risk
(Cohort study)

% of balding males who have MI

% of males with hair who have MI
Odds Ratio
(Case-control study)

ODDS of exposure when outcome occurs

ODDS of exposure when outcome does NOT occur
Odds Ratio
(Case-control study)

\[
\text{Odds Ratio} = \frac{\text{ODDS of EXPOSURE in diseased group (cases)}}{\text{ODDS of EXPOSURE in healthy group (controls)}}
\]
Odds Ratio
(Case-control study)

ODDS of balding in patients with MI

ODDS of balding in patients without MI
The 2x2 Table!!

<p>| | |</p>
<table>
<thead>
<tr>
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The Angels in Heaven know your Fate

Exposure

<table>
<thead>
<tr>
<th>+</th>
<th>Outcome present in exposed pt</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>Outcome absent in exposed pt</td>
</tr>
<tr>
<td>C</td>
<td>Outcome present in unexposed pt</td>
</tr>
<tr>
<td>D</td>
<td>Outcome absent in unexposed pt</td>
</tr>
</tbody>
</table>
Cohort Study

Exposure Present

Exposure Absent

Outcome Yes

Outcome No

Measure Here
What is the RISK Ratio?

COHORT STUDY

+ 50 200 + 100 1800
-
What is the ODDS Ratio?

COHORT STUDY

<table>
<thead>
<tr>
<th></th>
<th>+</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>50</td>
<td>200</td>
</tr>
<tr>
<td>-</td>
<td>100</td>
<td>1800</td>
</tr>
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Case-Control Study

Measure Here

Exposure Present

Exposure Absent

Outcome Yes (Cases)

Outcome No (Controls)

TIME
### CASE-CONTROL STUDY

<table>
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**ODDS RATIO**

PIC OF JEFF'S HEAD
WHY BOTHER?

- Cohort study: prefer RR or OR?
- Can’t escape OR
When the outcome is rare, OR and RR are very similar.
Properties of a Ratio

OR = 0.01
Less Likely

OR = 0.1
Less Likely

OR = 0.2
Less Likely

OR = 5
More Likely

OR = 10
More Likely

OR = 100
More Likely

0
Exposure less likely among Cases

∞
Exposure more likely among Cases

RATIO = 1
Exposure is NOT ASSOCIATED with outcome
A Case-Control Study of Baldness in Relation to Myocardial Infarction in Men

Samuel M. Lesko, MD; Lynn Rosenberg, ScD; Samuel Shapiro, MB, FRCP(Edin)
Now...which one is Jeff?

None

Frontal Only

Mild Vertex

Moderate Vertex

Severe Vertex
Mild or Moderate or Severe?
What are the Results?

1. How strong is the association between exposure and outcome?
2. How precise is the estimate of risk?
Case resolution

How can I apply the results to my patient?

1. Were the study patients similar to my patient?

2. Was the duration of follow-up adequate?

3. Should I attempt to stop the exposure?
What should we tell Jeff?
How would you counsel these folks?
Strength of Association

- Temporal relationship
- Dose-response
- Consistency with other studies
- Biological plausibility
- Epidemiological plausibility
- Reversibility
- Specificity of association
What did you learn today?
Summary

1. Case-control studies are INEXPENSIVE, FAST, measure ASSOCIATIONS

2. Odds and Risk approximate each other when outcomes are RARE

3. A Ratio is a Ratio is a ________?
Thank You!