RATES AND RISK

Daniel E. Ford, MD, MPH
Johns Hopkins School of Medicine
Introduction to Clinical Research
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RATES

• Cornerstone of comparison in clinical research studies
• Used to quantitate risk
• Used to compare events when sample size differs between treatment or exposure arms (usually the case)

CHARACTERISTICS OF RATES

• Rates must have numerator, denominator and a time interval
• Time interval differentiates rates from proportions
• Everyone in the denominator must be at risk to be in the numerator
• Some “rates” are not really rates, e.g., crude birth rate, no. live births/total population/year. Only half the population can give birth!
DISEASE SURVEILLANCE IN A POPULATION OF 100 PERSONS

TYPES OF RATES

- Many types of rates
- **Prevalence**—proportion of individuals in a group with a specified condition during a defined period of time
  - Period vs. point prevalence
  - Prevalence of depression (in last week, last month, lifetime)
- **Incidence**—proportion of individuals in a group who develop a new condition during a defined period of time

INCIDENCE AND PREVALENCE COMPARISON

<table>
<thead>
<tr>
<th>Rate</th>
<th>Numerator</th>
<th>Denominator</th>
<th>Time Frame</th>
<th>Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>New cases</td>
<td>Disease-free at beginning of study</td>
<td>Duration of follow up</td>
<td>Prospective (incidence) study</td>
</tr>
<tr>
<td>Prevalence</td>
<td>All cases</td>
<td>Everyone examined</td>
<td>Usually one point in time (point)</td>
<td>Cross sectional (prevalence) study</td>
</tr>
</tbody>
</table>
RELATIVE RISK

- Incidence rate is a measure of risk
- In clinical research often want to assess whether exposure to a risk factor or treatment (exposure) increases or decreases risk of disease
- Relative risk is the ratio of morbidity, mortality, or any outcome in those persons WITH the factor compared to those WITHOUT the factor

2 x 2 TABLE

<table>
<thead>
<tr>
<th>Disease Status (Outcome)</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk Factor (Treatment, Exposure)</td>
<td>Yes</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>C</td>
<td>D</td>
</tr>
<tr>
<td>Total</td>
<td>A+C</td>
<td>B+D</td>
<td></td>
</tr>
</tbody>
</table>

Relative Risk = \( \frac{A}{A+B} \)

Odds Ratio = \( \frac{AD}{BC} \)

SMOKING AND RISK OF LUNG CANCER

<table>
<thead>
<tr>
<th>Lung Cancer (Outcome)</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking (Exposure)</td>
<td>Yes</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>2</td>
<td>98</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>178</td>
<td></td>
</tr>
</tbody>
</table>

Relative Risk = \( \frac{(20/100)}{(2/100)} = 10 \)
ATTRIBUTABLE RISK

• Difference in incidence between those treated or exposed compared to the untreated or unexposed group
• Population attributable risk is the product of the AR and prevalence of the risk factor

SMOKING AND RISK OF LUNG CANCER

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Relative Risk = \( \frac{A/A+B}{C/C+D} = \frac{20/100}{2/100} = 10 \)

Attributable risk = \( \frac{A/A+B-(C/C+D)} = 0.2-0.02 \approx 0.198 \)

Population Attributable Risk

• The number (or proportion) of cases that would not occur if the factor were eliminated. The attributable risk in a population depends on the prevalence of the risk factor and the strength of its association (relative risk) with the disease. The formula is

\[ PAR = \frac{Pe \times (RR-1)}{1 + Pe \times (RR-1)} \]

- \( PAR = \frac{0.5 \times (10-1)}{1 + 0.5 \times (10-1)} = 0.82 \)
RELATIVE RISK (RR) vs. ATTRIBUTABLE RISK (AR)

- RR of CVD associated with high (195 mmHg) versus low (105 mmHg) systolic blood pressure:
  - No risk factors: 150/75 per 1,000 per 8 yrs = 2
  - Smoking, chol, DM: 500/250 per 1,000 per 8 yrs = 2
- AR of CVD associated with high (195 mmHg) versus low (105 mmHg) systolic blood pressure:
  - No risk factors: 150-75 = 75 per 1,000 per 8 yrs
  - Smoking, chol, DM: 500-250 = 250 per 1,000 per 8 yrs
- Which group has the biggest change in risk?

RELATIVE VS. ATTRIBUTABLE RISK

- Relative risk assesses strength of the association, gauges magnitude of increased risk for an exposed group
- Attributable risk estimates burden of disease associated with risk factor
- PAR measures excess risk associated with a risk factor in the community, product of AR and risk factor prevalence
COMPARISON OF RATES

- **Crude rates**—may not be fair to compare crude rates between 2 groups, eg, death rates at Johns Hopkins Hospital vs community hospital
- **Variable specific rates**—age, gender, race specific rates
  - Ex, death rates for 65-74 year old white women.
    - Allow fairer comparisons
    - Akin to matching
    - Can be cumbersome with multiple strata,
      - ex, 6 age, 2 gender, 3 race groups

ADJUSTED RATES

- **Adjusted rates**—used to compare rates between groups or in the same population over time
- Most common methods of adjustment are: direct, indirect and multivariate analysis
- Multivariate is easiest and yields same results as direct adjustment
- Allows “fair” comparisons—holds adjustment variables constant
  - Ex, if age is the adjustment variable, differences in adjusted rates are not due to age
INCIDENT COUNTS AND ADJUSTED RATES, BY AGE

INCIDENT COUNTS AND ADJUSTED RATES, BY GENDER

INCIDENT COUNTS AND ADJUSTED RATES, BY RACE
How should we present data on efficacy of treatments?

- Events in control: 10/100
- Events in treated: 5/100

- Relative Risk Reduction = 50% reduction
- Absolute Risk Reduction = 5% reduction
- Number needed to treat = 20
  \[
  \frac{1}{(P_c - P_t)} = \frac{1}{(.10 - .05)} = 20
  \]