Study Designs

- Experimental studies
- Observational studies
  - Analytic studies
  - Descriptive studies
- Randomized Controlled trials
- Case control
- Cohort
- Cross sectional

Two by Two table

<table>
<thead>
<tr>
<th>COHORT</th>
<th>CASE CONTROL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure</td>
<td>Outcome</td>
</tr>
<tr>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Total a+c b+d N

Calculate: Row percentages
- Risk of outcome in exposed = a/(a+b)
- Risk of outcome in nonexposed = c/(c+d)
- Odds of exposure in cases = a/c
- Odds of exposure in controls = b/d
- Exposure odds ratio = (a/c) / (b/d) = ad/bc

Case Control Study: 2 x 2 table

Start with OUTCOME — Go backwards — Check for EXPOSURE

Case Control Study

- Sample of people who have outcome
  - Exposed
  - Not Exposed
- Sample of people who do not have outcome
  - Exposed
  - Not Exposed

Two by Two table

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**Case Control Study: 2 x 2 table**

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Outcome</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>a</td>
<td>b</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>c</td>
<td>d</td>
<td></td>
</tr>
</tbody>
</table>

Exposure odds ratio = \( \frac{a/c}{b/d} = ad/bc \)

Outcome odds ratio = \( \frac{a/b}{c/d} = ad/bc \)

Odds Ratio (OR) = \( \frac{ad}{bc} \)

**Case Control Study: Example 1**

Assess the association between artificial sweetener (AS) and Bladder Cancer (BC)

<table>
<thead>
<tr>
<th></th>
<th>BC</th>
<th>No BC</th>
</tr>
</thead>
<tbody>
<tr>
<td>As</td>
<td>66</td>
<td>66</td>
</tr>
<tr>
<td>No As</td>
<td>22</td>
<td>134</td>
</tr>
</tbody>
</table>

- Odds of BC among As = 66/66
- Odds of BC among no As = 22/134
- Odds of As among BC = 66/22
- Odds of As among no BC = 66/134
- Odds Ratio (OR) = \( \frac{66 \times 134}{66 \times 22} = 6.37 \)

**Case Control Study: Example 2**

Tea drinkers (TD) & renal cancer (RC)

<table>
<thead>
<tr>
<th>RC</th>
<th>No RC</th>
</tr>
</thead>
<tbody>
<tr>
<td>TD</td>
<td>400</td>
</tr>
<tr>
<td>No TD</td>
<td>100</td>
</tr>
</tbody>
</table>

- Odds of RC among TD = 400/333
- Odds of RC among no TD = 100/167
- Odds of TD among RC = 400/100
- Odds of TD among no RC = 333/167

OR = \( \frac{400 \times 167}{333 \times 100} = 2 \)

**Why odds ratio not relative risk?**

- RR varies according to the sample size of cases & controls.
- OR is fixed regardless of the sample size of cases & controls.

**Scenario 1**

<table>
<thead>
<tr>
<th>Exposed</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>80</td>
<td>90</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

OR = 2.25
RR = 1.4

**Scenario 2**

<table>
<thead>
<tr>
<th>Exposed</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>200</td>
<td>800</td>
<td>90</td>
</tr>
<tr>
<td>Total</td>
<td>1000</td>
<td>100</td>
</tr>
</tbody>
</table>

OR = 2.25
RR = 1.05

**Characteristic of Odds Ratio**

- If the outcome is **RARE**, the OR (in a case control study) is an estimate of the RR if one was to do a cohort study.

\[ RR = \frac{a/b}{c/d} \]

- If \( a \) is small with respect to \( b \); and \( c \) is small with respect to \( d \); then \[ RR = \frac{a/b}{c/d} = \frac{ad}{bc} \]
**Selection of cases**

- All or a sample of cases in a defined community
- All or a sample of cases listed in a defined hospital/physician based setting

**Selection of controls**

Does smoking cause lung cancer?
Consider 2 control groups; one myocardial infarction & another injured patients.

<table>
<thead>
<tr>
<th></th>
<th>Lung Cancer</th>
<th>Myocardial infarction</th>
<th>Lung Cancer</th>
<th>Injured Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>70</td>
<td>65</td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>35</td>
<td>30</td>
<td>70</td>
</tr>
</tbody>
</table>

**OR = 1.2**  **OR = 5.4**

**Selection of controls**

- General population of a defined area
- Hospital controls
- Neighbors
- Relatives or associates (spouse, sibling, classmate, partner)
- Others (visitors, trauma victims)

Phone: random digit dialing; walk: door to door; letters

**Case Control Study**

**Advantages**

- Require short time when outcomes are delayed.
- Cheap.
- Practical for study of rare diseases.
- Can test many hypotheses (but with respect to one outcome).

**Disadvantages**

- Information bias (Recall bias) of the exposure.
- Indirect estimate of the Relative Risk.
**Case Control Study**

**Hypothesis**

Is Hockey associated with Asthma?

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**Case Control Study: Abstract 1**

**OBJECTIVE:** Determine associations between passive smoking and the use of non-cigarette tobacco products with pancreatic cancer.

**METHODS:** The authors collected information on passive smoking and the use of non-cigarette tobacco products in 808 patients with pancreatic adenocarcinoma and 808 healthy controls by personal interview.

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**Issues to consider in a cohort study:**

- Is a case control design appropriate for the question asked or would another study design be more appropriate or cost-efficient?
- Have case and control groups been selected independent of the exposure of interest?
- Are incident versus prevalent cases considered?
- Do the cases reflect a range of disease severity (cases from a single hospital/ambulatory care clinic represented)?
- Were appropriate controls selected?

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**Analytic studies**

**Case control study**

- Was the study adequately powered?
- Has categorization of exposure been categorized into appropriate dose categories?
- Were the individuals involved in data collection blinded to the study question and case/control status?
- Are appropriate odds ratios and confidence intervals presented?
- Have potentially confounding variables been adequately considered and controlled for in the analysis?

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**Case Control Study: Abstract 1**

**RESULTS:** Passive smoking showed a non-significantly elevated risk for pancreatic cancer in the entire study population (OR, 1.3; 95% CI, 0.9-1.7). The AOR was 1.7 (95% CI, 1.4-2.2) for regular smokers, 1.8 (95% CI, 1.4-2.4) for long-term smokers, and 3.1 (95% CI, 2.2-4.3) for former smokers.
Case Control Study: Abstract 2

OBJECTIVE: Evaluate the relationships between coffee, tea and caffeine and ovarian cancer risk.

METHODS: Women with epithelial ovarian cancer (EOC) (n = 696) and control women selected from the Electoral Roll (n = 786) provided comprehensive reproductive and lifestyle data and completed a food frequency questionnaire.

RESULTS: Increasing coffee consumption was associated with a decreased risk of invasive EOC (p trend = 0.009) with an odds ratio (OR) of 0.51 (95% confidence interval (CI) 0.32-0.80) for consumption of >/=4 cups of coffee per day compared to non-drinkers. An inverse relationship was also seen between caffeine intake and EOC. Tea consumption was not related to EOC (OR: 1.10 95% CI: 0.76-1.61 for >/=4 cups/day versus none).