Health Studies 315

Clinical Epidemiology: Evidence of Risk and Harm

Patients encounter (possibly) risky exposures

- Alcohol during pregnancy (fetal risk)
- Electromagnetic fields (cancer risk)
- Vasectomy (prostate cancer risk)
- Oral contraceptives (thromboembolism risk)

To examine such risks

- **Evaluate validity of data**
- **Evaluate strength of association between risk and outcome**
- **Evaluate relevance to particular individuals**

Most studies of risk are observational studies

- These studies are nonrandomized
- Need:
  - Basic rules of evidence for nonrandomized studies
  - Pitfalls to which observational studies are prone

Types of observational studies

- Cohort studies
- Case-control studies
- In each case, we need
  - Well-defined outcome
  - Well-defined exposure
  - Clearly identified comparison groups
  - Similarity between groups wrt all other factors that might affect the outcome

Compare to randomized trial

- **Well-defined outcome: Primary endpoint**
- **Well-defined exposure: Active treatment**
- **Clearly identified comparison groups:**
  Control group for comparison
- **Similarity between groups wrt all other factors that might affect the outcome:**
  Randomization

Cohort studies

- **Prospective**
- **Useful when pts cannot be randomized to exposure**
- **Identify groups of exposed and non-exposed**
- **Follow forward to determine rate of outcome in each group**

Example of question for cohort study

- Do operating room personnel suffer higher rates of miscarriage than do others?
  - Outcome
  - Exposure
  - Clearly identified comparison groups
  - Similarity between groups re outcome

Problems with cohort studies

- Primary issue: self-selection to group
- Same factors that affect selection might also affect outcome
- Example: relationship of NSAIDs to GI bleeding
  - Increased age associated with increased use of NSAIDs
  - Increased age associated with increased GI bleeding
- Age here is a “confounding variable”
  - Document differences
  - Adjust for statistically (regression)

Relative strength of evidence: RCT & Cohort

- **Can never rule out the presence of unidentified confounders**
- **A good cohort study requires a great deal of investigator ingenuity**
  - **Identify possible biases**
  - **Document and/or adjust for potential biasing factors**
- **Thus, cohort studies are inherently less convincing than well-conducted clinical trials**

Case-control studies

- Retrospective
- Useful in assessing risks for very rare outcomes
- Useful when time between exposure and risk is long
  - in utero exposure to DES, clear-cell adenocarcinoma of the vagina
  - asbestos, mesothelioma
- Identify persons with the outcome of interest ("cases")
- Identify similar individuals ("controls") who
  - do not have outcome
  - are similar wrt all other factors associated with outcome
- Compare frequency of exposure between groups

Example of question for case-control study

- **What exposures predispose to lung cancer?**
  - **Outcome**
  - **Exposure**
  - **Clearly identified comparison groups**
  - **Similarity between groups re outcome**

Problems with case-control studies

- Susceptiblity to unmeasured confounders
- Outcome = identified with outcome of interest
  - Ascertainment bias
- Exposure = retrospective documentation of exposure
  - Recall bias
  - Interviewer bias
- Strength of C-C evidence is inherently more limited than cohort study

Second primary guide:

- **Were the exposures and outcomes measured in the same way in the groups being compared?**
  - **RCT, cohort: ascertainment of outcome**
  - **Case-control: ascertainment of exposure**

Secondary guides

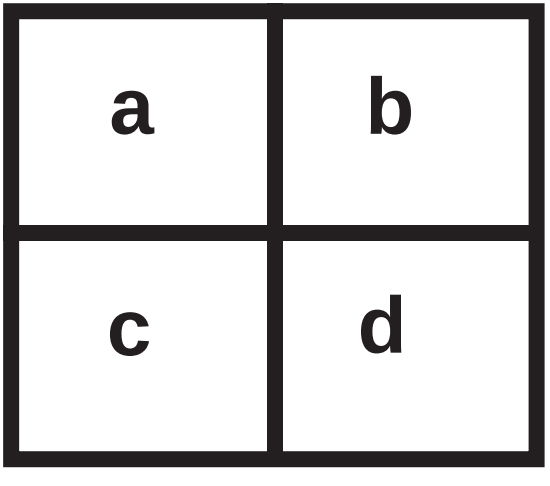
- **Is the temporal relationship correct?**
- **Is there a dose-response gradient?**

Measuring the association between exposure and outcome

- **Most common and useful: relative risk = p1/p2**
- **Exposure to encainide was associated with a 2.6-fold elevation in risk of death**
- **Can obtain relative risk from cohort studies or RCT (prospective)**

Case-control studies: No RR estimate

- CC studies cannot produce an estimate of the relative risk
- RR = a/(a+b) / c/(c+d)
- OR = a/b / c/d
  = ad / bc
- When outcome is rare,
  OR RR



Assessing applicability

- **Recall that the number needed to treat (NNT) depends on the absolute risk difference, not the relative risk**
- **Need to know something about the prevalence of the bad outcome**

Outcome: CC Adeno CA
Exposure: Maternal Smoking

	Case	Control
Exposed	7	21
Unexposed	1	11

OR= 3.7

p = 0.50

Outcome: CC Adeno CA
Exposure: Any prior pregnancy loss

	Case	Control
Exposed	6	5
Unexposed	2	27

OR= 16.2

p = 0.01

Outcome: CC Adeno CA
Exposure: In utero estrogen

	Case	Control
Exposed	7	0
Unexposed	1	32

OR 300-400

p < 0.0001