

Module 3 Hierarchy of Evidence:

Observational Studies

KEY POINTS

The Hierarchy of Evidence for Observational Studies

Analytic observational studies support a hypothesis:

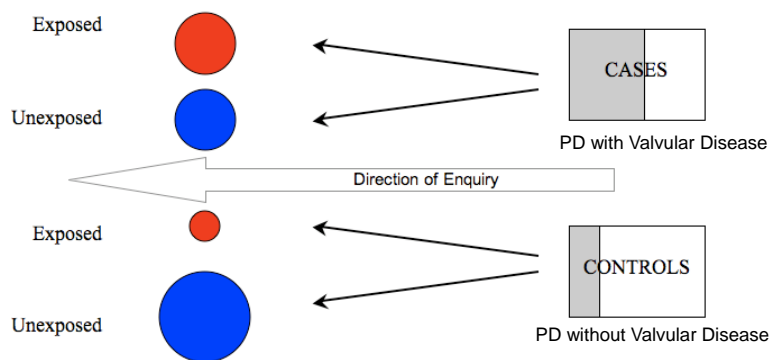
- **Case control studies**

- **Cohort studies**
 - **Retrospective**
 - **Prospective**

Why Do We Need Alternatives to Randomized Trials?

- Randomized trials may not be feasible
 - Unethical
 - Randomization to cigarette smoking
 - Impractical
 - Very expensive
 - Study results are delayed
- We need alternatives

Case-Control Study Design



Note the direction of enquiry: starting with outcome and asking about the frequency of exposure and non-exposure

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Quantitative Measures in Case-Control Studies

		Disease		
		↓	↓	
		Yes	No	
Exposure (dopamine agonist)	Yes	a	b	<u>Odds of disease</u> Exposed: a/b Not Exposed: c/d Odds Ratio $\frac{a/b}{c/d} = \frac{ad}{bc}$
	No	c	d	

Remember: if the frequency of the disease is low, the odds ratio is a good approximation of the relative risk

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Advantages of Case-Control Studies

- Efficient for the study of **rare diseases (outcomes)**
- Typically requires smaller sample sizes and is often less expensive than cohort studies
- Can evaluate multiple risk factors in one study
- Improved feasibility based on sample size and cost (often the only feasible study design for very rare diseases)

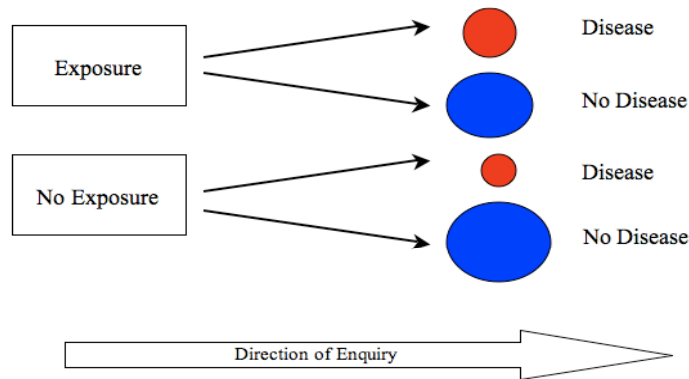
Disadvantages / Challenges

- Inefficient for rare **exposures**
- Temporal relationship of exposure and outcome may not be clear
- Selection bias common - frequency of exposure amongst the sample of cases or controls is not representative of the source population
- Recall bias common - systematic difference in recollections of exposure between cases and controls
- If multiple risk factors are evaluated, some associations may arise due to chance alone

Cohort Studies

- Definition of Cohort: A group of individuals that are all similar in some trait and **move forward together as a unit**
- Definition of a Cohort Study: The observation of a cohort, over time, to measure outcome(s)

Cohort Study Design



Quantitative Measures in Cohort Studies

		Disease		Risk of disease
		Yes	No	
Exposure	→ Yes	a	b	$\frac{a}{a+b}$
	→ No	c	d	$\frac{c}{c+d}$
				Relative risk
				$\frac{a}{a+b}$
				$\frac{c}{c+d}$

Follow **forward** to find new cases

Thus, you have incident data and calculate risk and risk ratios

Advantages

- Good for **rare** exposures
- Offers an opportunity for maximal investigator control over:
 - Exposure classification
 - Uniform follow-up
 - Case finding
- Can evaluate multiple outcomes in one study
- When prospective and done well, may come close (but not quite equal) to a clinical trial in providing reliable data and reliable evidence

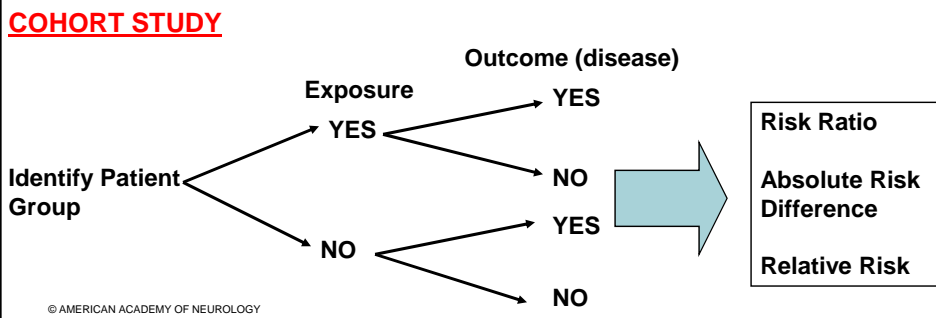
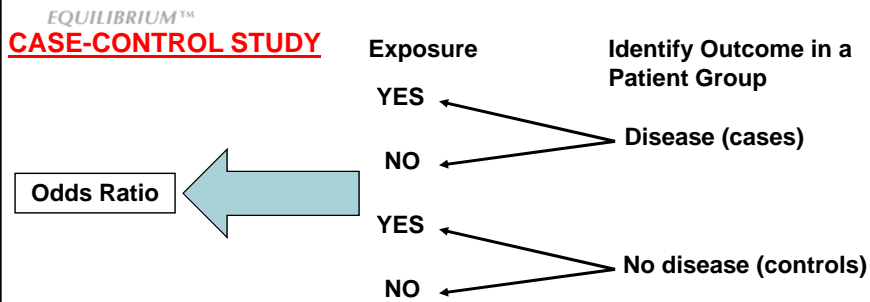
Disadvantages / Challenges

- Large
- Change in methods over time
- **Loss to follow-up is often problematic**
- When prospective, especially expensive and time consuming
- When retrospective, in general, the reliability is close to that of an ecologic association study – it may generate questions, but not answers
- If evaluating multiple outcomes, some may appear associated due to chance alone

Cohort vs. Randomized Clinical Trial

	Cohort	RCT
Randomization	NO	YES
Intervention	NO (just passage of time)	YES
Prospective	USUALLY	YES
Control of Initial Study Conditions	NO	YES

	Case Control	Cohort
Measure	Odds of disease in the exposure and non-exposed	Incidence of disease (outcome) in exposed and non-exposed
Risk Assessment	Odds ratio	Risk ratio (also Relative risk and Absolute risk)
Best When	Disease is rare , exposure frequent in disease	Exposure rare , disease frequent in exposure, multiple outcomes
Temporal Association	Not always clear	Established
Time	Short	Long
Cost	Low	High
Size	Small	Large
Challenges	Controls difficult to select well; recall bias a risk	Temporal changes in methods



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Final Words

- Observational studies are often the most practical way to answer research questions
- Bias is a major challenge
- Thus interventional (i.e., randomized, masked) studies are preferred to guide treatment decisions

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