

Study Design

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Lecture Topics

- Randomized/controlled study design
- Methods of randomization
- Natural experiments
- Observational studies
- Case/control studies

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Section A

Making the Case for Randomized Controlled Studies

Clofibrate Trial

- A study was performed to look at the effect of a drug, Clofibrate, on mortality rates for individuals with heart disease
 - Individuals were followed for five years after administration of the drug

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Results: Clofibrate Group

- Coronary heart disease
 - Results from group randomized to take Clofibrate

		Five Year Mortality	
Clofibrate Group (p < .01)	Compliers		.15
	Non-compliers		.25

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Results: Clofibrate Group

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		Five Year Mortality	
Clofibrate Group (p < .01)	Compliers		.15
	Non-compliers		.25

- Question: Do these results strongly demonstrate the efficacy of Clofibrate in reducing the mortality in subjects with CHD?

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Results: Placebo Group

- Coronary heart disease
 - Results from group randomized to take placebo

Placebo Group (p < .01)	Five Year Mortality	
	Compliers	.15
Non-compliers	.25	

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The Dangers of Self-Selection

- Overall mortality in each of the groups in this randomized trial

	Five Year Mortality	
	Clofibrate	n = 1,103
Placebo	n = 2,789	0.21 (21%)

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The Dangers of Self-Selection

- Randomized trial
 - No significant difference (p > .20) between the treatment and placebo groups!
- No difference between TX groups
 - The compliers and non-compliers were similar with respect to other variables (age, etc.)
 - There were no apparent harsh side effects of Clofibrate relative to placebo that may have resulted in differential compliance between the Clofibrate and placebo groups

Source: Coronary drug research group (1980), NEJM, 1038-1041.

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A Randomized Control Group

- Important for accounting for many kinds of biases
- Randomization, done correctly on a large number of subjects nearly ensures that the only systematic difference in the groups being compared is the exposure(s) of interest

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Note

- A very famous randomized trial (once again)
 - 200,745 vaccinated for polio
 - ≈ 400,000 school children randomized
 - 201,229 given a placebo

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1954 Salk Polio Vaccine Trial

- At the end of the follow-up period there were 82 cases in the vaccine group and 162 in the placebo group
- Subsequently analyses report slightly different numbers because some false positives were discovered in each of the two groups

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1954 Salk Polio Vaccine Trial

- Results

	Vaccine	Placebo	Total
Polio	82	162	
No Polio	200,663	201,067	

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Results in 2x2 Table Format

- How to test for an association between vaccine and polio? (Flashback to 611!)
 - $H_0: P_{\text{vaccine}} = P_{\text{placebo}}$
 - $H_A: P_{\text{vaccine}} \neq P_{\text{placebo}}$
- Where P_{vaccine} is the percentage of children with polio in vaccine group, P_{placebo} is the percentage in the placebo group
- How to test for an association between vaccine and polio? (Flashback to 611!)
 - You can use either Fisher's Exact test or Chi-Squared test (Why?)
- With FET, $p < .001$

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Randomized Study Design

- Prospective cohort studies
 - Choose a fixed number with and without exposure
 - Follow subjects for set time period and determine who has disease/outcome of interest
- Measures of association
 - Difference in proportions
 - Relative risk (ratio of proportions)
 - Odds ratio

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Benefits of Randomization

- Randomization helps protect against self selection biases
 - Examples:
 - Males are more likely to volunteer for placebo than females
 - Smokers are less likely to be in the exposed group
 - Healthier persons sign up for the intervention
- The goal of randomization is to eliminate any systematic differences in characteristics of subjects in each of the exposure groups under study, save for the exposure itself

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Randomized Study Design

- Many epidemiological studies are concerned with estimating an association between two dichotomous (binary) variables
 - Example: exposure-disease association
- Randomized study design with control group is a type of **prospective cohort study**

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