



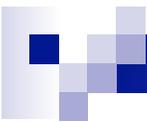
# Overview of Study Designs:

- A. Descriptive Epidemiology

- 1. Often Ecologic (Correlational)
- 2. Often Cross-sectional

- B. Analytic Epidemiology

- 1. cohort studies
- 2. case-control studies
- 3. randomized clinical trials



# Experiments → ' Ceteris

## Paribus'

- Experiment: investigator assigns (randomizes) study factor
  - Lab
  - Intervention e.g. vaccine studies
  - weaknesses – ethics, cost, time
  - Strength- “with a large enough sample, a well-designed experiment can be expected to control for nearly all distorting effects from extraneous risk factors, *including those that are unmeasured*” (KKM)
- Quasi-Experiment
  - Less control, e.g. seat belt laws
  - E.g. natural experiments of John Snow



# Randomized Clinical Trials

- “gold standard” – closest to experiment
- Study factor most often therapeutic intervention
- Sometimes not necessary
  - PCN ↓ pneumonia mortality 95% → 15%
- Sometimes efficacy immediately evident (AZT)
- Sometimes reveals no efficacy
  - CASS- 5 yrs, 780 MI/Angina pts
  - Lumpectomy vs. radical mastectomy (Halstead)
- Sometimes reveals harm (Portocaval Shunt)
- Classic RCT → Polio Vaccine
  - 1950' s, 200,000 children randomized



# Conduct of an RCT

- Select Study Population (reference, experimental, actual)



## Random Allocation

- equal (pre-determined) chance of assignment
- Placebo (inert) or 'usual' treatment
- Eliminates selection bias
- Groups comparable in both known and unknown factors
- More valid statistical treatment
- Works best in the aggregate (the more the better)
- Blinding (single, double, triple)



# RCT Weaknesses

- Expensive
  - \$3,000 - \$15,000 per patient
- Ethics
  - sufficient question of efficacy
  - May not withhold known effective treatments
  - IRB oversight

# Basic Analysis

- Compare disease rates of treated to untreated
- $RR = A/A+B / C/C+D$
- Must account for drop outs, loss to f/u, non-compliance, death from other D (Kaplan-Meier, Cox Proportional Hazards, Life Tables)

	D	d
E	A	B
e	C	D



# Take home message

- A well-conducted, double-blinded, placebo controlled RCT with adequate numbers is considered the gold standard of epidemiologic research



# Observational Studies

- Cohort, Case Control, Cross-Sectional
- Much of Epidemiology
- Participants Self-Assign Exposure
  - Ceteris paribus?
- Greater design and analytic complexity
- Greater generalizability?



# Design Options in Observational Studies

- 1. Subject Selection
- 2. Directionality
- 3. Timing
- 4. Definition of Disease Status
- 5. Units of Observation



# Subject Selection

## ■ Restriction

- Include only those with factors NOT associated with disease under study
- Most often age, sex, other diseases
- Improves comparability of the groups

## ■ Random Sampling

- Each person in population has equal chance of participating
- Not same as randomization

## ■ Statistical Control – during analysis

- But need to have collected the data



# Other Considerations

- Directionality – relationship of E to D
  - Forward ( $E \rightarrow D$ )
  - Backward ( $D \rightarrow E$ )
- Timing – relationship of study to D
  - Prospective (D not yet occurred)
  - Retrospective (D has occurred)
    - Can have forward directionality (retrospective cohort)
- Definition of Disease Status
  - Incident vs. prevalent
- Units of Observation
  - Individual vs. ecologic



# Cohort Studies

- Group shares common factor
  - Employment, geography, year of birth
  - Fixed vs Dynamic
  - Must be Disease Free at Start
- Observational Analog of Experiment
  - If well chosen, differences in disease rates ascribed to exposure
- Strengths
  - incidence rates
- Weaknesses
  - expensive
  - loss to follow up –differential ?



# Analysis of Cohort Studies

- **1) Relative Risk (Cumulative *Incidence* Ratio or CIR)**

- the cumulative incidence in the exposed, divided by the cumulative incidence in the unexposed

- **$RR = (A/A+B) / (C/C+D)$**

- **2) Incidence *Rate* Ratio (IRR)**

- Incidence Density Ratio (IDR) Relative Rate (RR)

- incidence *rate* in the exposed divided by the incidence *rate* in the unexposed

- **3) Odds Ratio**

# Anatomy of a Cohort Study

