RESEARCH METHODS FOR CLINICAL INVESTIGATORS
Session 1:

Study Designs: Which design best fits my study question?

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Objectives

At the end of the presentation, the audience will be able to:

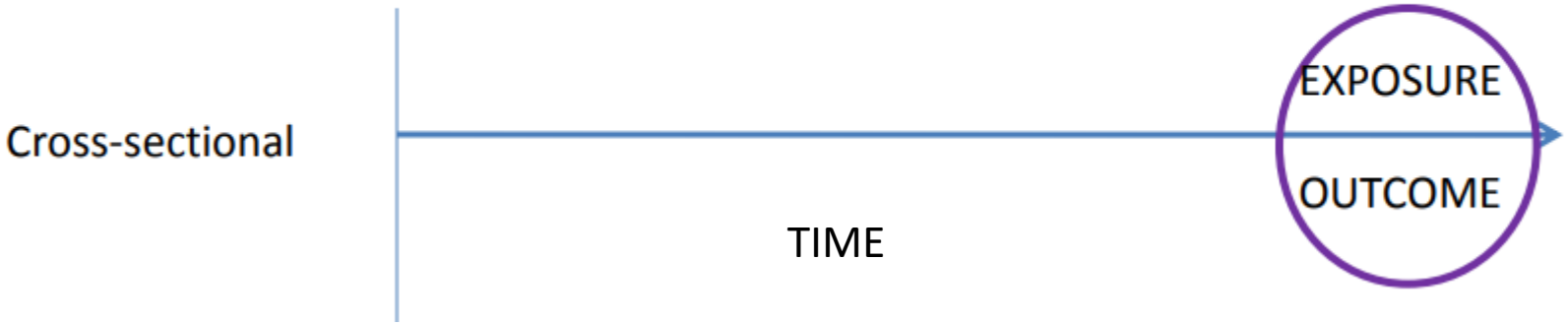
- Determine which study design answers the research question
- Define the differences between observational and experimental study designs
- Identify a study design by its description and measures of association

Overview of Study Designs

- **Observational studies**
  - Descriptive Studies: Cross-sectional surveys
  - Analytic Studies: Ecologic studies, Case-control studies, Cohort studies
- **Experimental studies**
  - Clinical Trials
  - Group Randomized Trials

Cross-Sectional Study

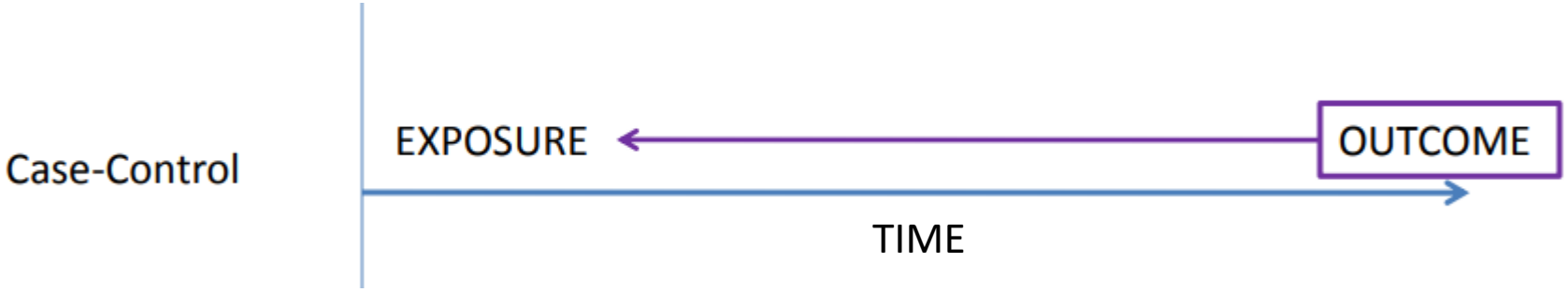
- Single period of observation
  Example: 1999
- Exposure and disease histories are collected simultaneously.
  Can tie to other existing data such as medical records
- Limitations: **a.)** Can't assess incidence **b.)** Difficult to study rare diseases



Gordis, Leon. (2018). *Epidemiology*. Saunders Elsevier.

Case-Control Study

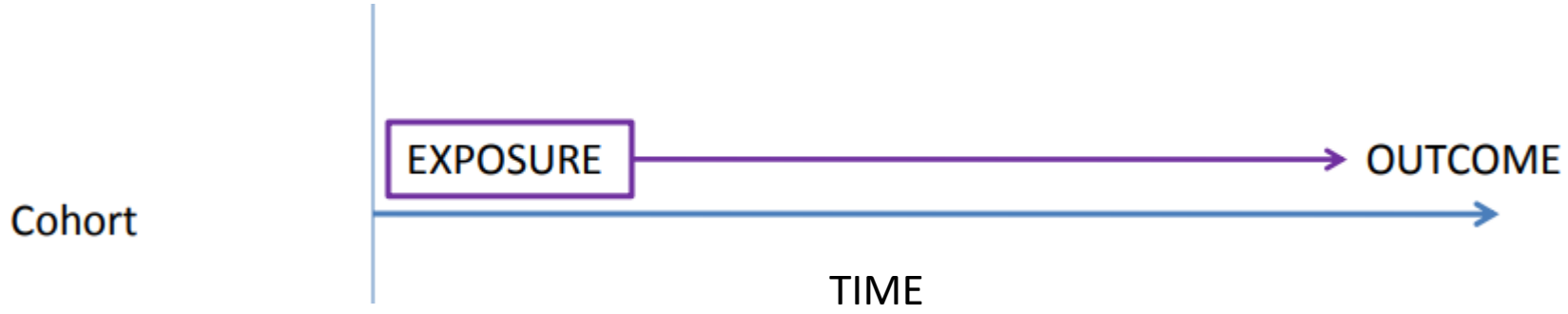
- Exposure is determined retrospectively
- Data collection typically involves a combination of both primary and secondary sources
- Limitations: **a.)** Bias and Confounding



Gordis, Leon. (2018). *Epidemiology*. Saunders Elsevier.

Cohort Study

- Retrospective & Prospective
  - Ex. Framingham Study[2]
- Can be thought of as going from cause to effect
- Limitations: **a.)** Loss to follow-up (Bias) **b.)** Expensive and time consuming **c.)** Difficult to study rare diseases



1. Gordis, Leon. (2018). *Epidemiology*. Saunders Elsevier.
2. https://www.nhlbi.nih.gov/science/framingham-heart-study-fhs

Clinical Trials

- Involves the administration of a test regimen to humans or animals to evaluate its EFFICACY and SAFETY
  - Ex. Systolic Blood Pressure Intervention Trial (SPRINT) Study[1]
- Individuals are randomly assigned to a study group
  - Intervention vs. Control (Placebo) **or** Attention Control[2]
  - Non-Inferiority Trials: New Rx vs Current Rx→ Tests whether New Rx in not worse than Current Rx
- Limitations: **a.)** May be harder to generalize findings if the study population isn't representative of the general population **b.)** Expensive and time consuming **c.)** Not always ethical if exposure is harmful

1. https://www.nhlbi.nih.gov/science/systolic-blood-pressure-intervention-trial-sprint-study
2. LaFave, S., et al. (2019). Attention control group activities and perceived benefit in a trial of a behavioral intervention for older adults. Johns Hopkins University. Doi: 10.1002/nur.21992

Study Designs

- **Method of data collection**
  - Survey: Questionnaire
  - Biomarkers: Blood draw
  - Interviews, i.e. Face-to-Face, Telephone

- **Measures of Association**
  - Odds Ratio (OR): Case-Control
  - Relative Risks (RR): Cohort
  - Hazard Ratio (HR): Randomized Clinical Trials

Study Designs cont'd

- **Measures of Association- OR**

  OR>1: The odds of exposure among cases are **greater** vs controls

  OR=1: The odds of exposure is the **same** for both study groups

  OR<1: The odds of exposure among cases are **less** vs controls

  Anticoagulation with heparin did not increase the likelihood of survival to hospital discharge or medical support for respiratory adverse events among patients diagnosed with COVID-19 vs those who received the standard thromboprophylaxis [1]

  (Adjusted OR: 0.83, 95% CI 0.67-1.03)

1. Bradbury, C., McVerry, B., et al. (2021). Therapeutic Anticoagulation with Heparin in Critically Ill Patients with COVID-19. *N England J Med*. 385(9): 777-789. doi: 10.1056/NEJMoa2103417

Study Designs cont'd

- **Measures of Association- RR**

  RR>1: The risk in exposed group is **greater** than the risk in non-exposed group

  RR=1: The risk in exposed group is **=** to the risk in non-exposed group

  RR<1: The risk in exposed group is **less** than the risk in non-exposed group

  - Shift work and insufficient sleep increased risk of coronary heart disease [1]

    (RR: 1.23, 95% CI 1.15-1.31)

1. Kecklund, G., Axelsson, J. (2016). Health consequences of shift work and insufficient sleep. *BMJ*. 355. doi.org/10.1136/bmj.i5210

Study Designs cont'd

- **Measures of Association- HR**

  HR>1: The hazard in exposed group is greater than the non-exposed group

  HR=1: The hazard in exposed group is the same in non-exposed group

  HR<1: The hazard in exposed group is less than the non-exposed group

  - Cardiovascular Rx reduces risk of major cardiovascular events in patients w/ Type II diabetes and previous myocardial infarction[1] (HR: 0.84, 95% CI 0.72-0.99)

1. Furtado, R., Bonaca, M., et al. (2019). Dapagliflozin and Cardiovascular Outcomes in Patients With Type 2 Diabetes Mellitus and Previous Myocardial Infarction. *Circulation*. 139(22): 2516-2527. doi: 10.1161/CIRCULATIONAHA.119.039996.

Study Designs cont'd

- **Hypothesis Testing:** Reject/Accept (Null=H_0 vs. Alternate=H_A)
  - P-values: Probability of obtaining test results at least as extreme as the result actually observed, under the assumption that the null hypothesis is correct[1,2]

p-value > 0.05= Accept the H_0 and reject H_A, No difference in groups

p-value ≤ 0.05= Reject the H_0 and accept H_A, Difference in groups

  - Confidence Intervals: Range of values that includes a population value, i.e. means, with a certain degree of confidence (95% CI)[2]
    - Population mean lies between an upper and lower interval

1. Dahiru.T., et al. (2008). P-value, A true test of statistical significance; A cautionary note. *Ann Ib Postgrad Med*. 6(1): 21-26. doi: 10.4314/aipm.v6i1.64038
2. Gordis, Leon. (2018). *Epidemiology*. Saunders Elsevier

Summary cont'd

- **Study Designs: Experimental vs. Observational**

- **Measures of Association and Hypothesis testing**
  - Ex. Statistical significance will/won't support the hypothesis that A predicts B

Research Question → Study Design → Data Collection → Analysis → Publication Support