Observational Study Designs

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Objectives

- To understand the difference between descriptive and analytic observational studies

- To identify the strengths and weakness of different designs and apply different study designs to the same research question

Descriptive vs. Analytic

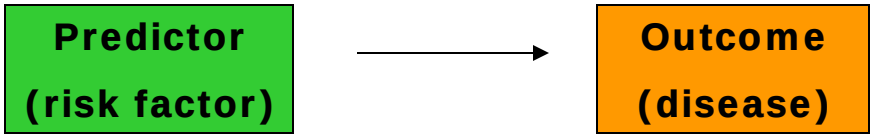
Descriptive Questions

- What proportion of patients in the DGIM have heart failure?
- What is the average age of patients with heart failure in the DGIM?

- **Analytic Questions**
- Is race/ethnicity associated with heart failure among DGIM patients?
- Is excessive consumption of sugar-sweetened beverages associated with heart failure among DGIM patients?

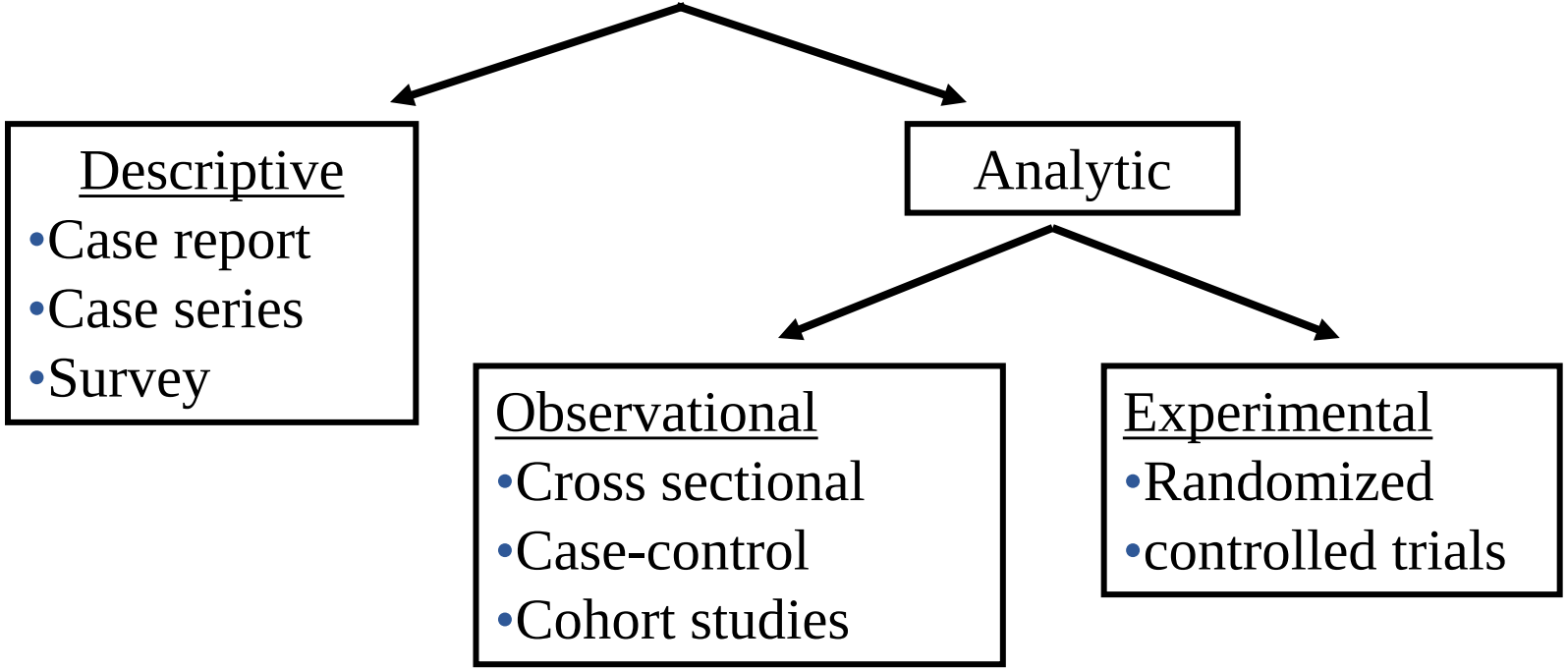
Analytic Studies

- Attempt to establish a causal link between a predictor/risk factor and an outcome.



- You are doing an analytic study if you have any of the following words in your research question:
  - *causes, leads to, compared with, more likely than, associated with, related to, similar to, correlated with, greater than, less than*

Hierarchy of Study Types?



Strength of evidence for causality between a risk factor and outcome

Key elements of study design

1. Timing of the study
   - Prospective
   - Historical
2. Timing of variable occurrence & measurement
   - When are predictors and outcomes measured?
3. How the subjects will be sample

Research Question

Among patients seen in General Medicine Clinic, who is at risk for heart failure?

Great idea, but how do you get started…

- Observations in clinical practice
  - Describing cases of heart failure in clinic
    - Case report or Case series
  - Describe characteristics of all heart failure patients (e.g. average age)
- Moving from descriptive to analytic studies
  - What are the risk factors associated with developing heart failure?

Measures of association

Risk Factor	Disease: Yes	Disease: No
Yes	A	B
No	C	D

Risk ratio (relative risk)

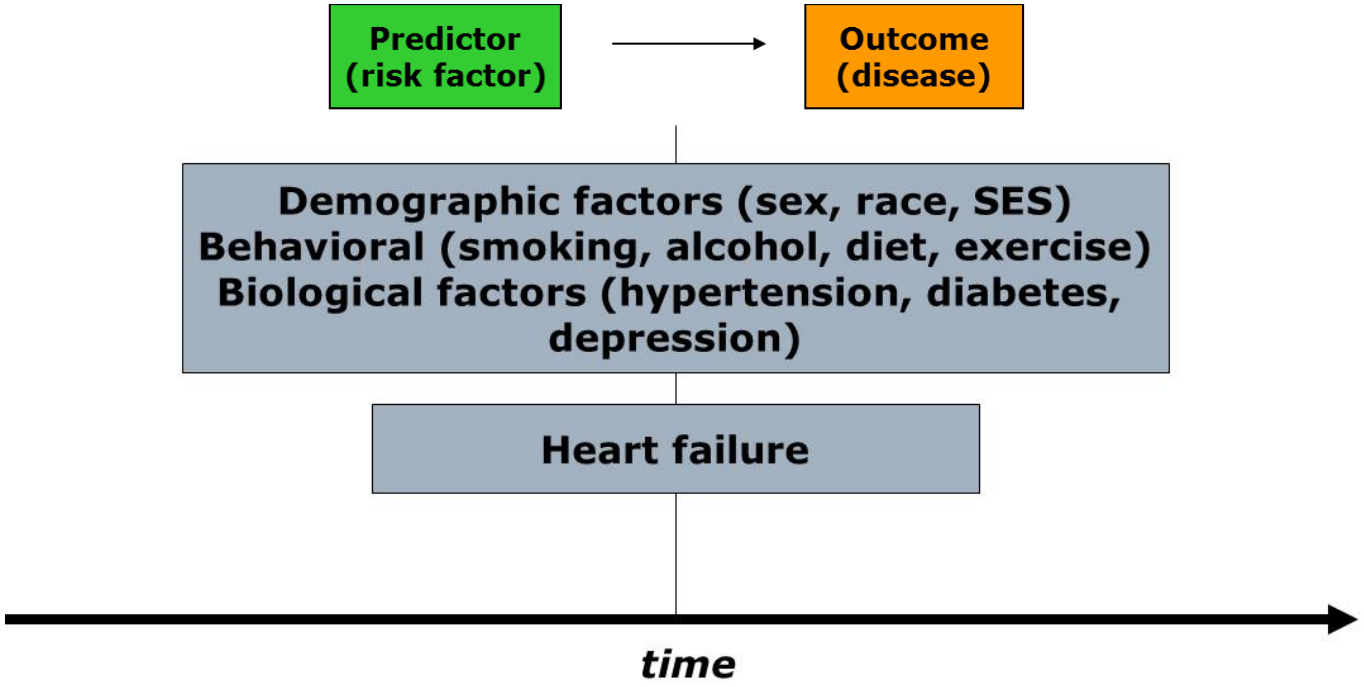
$$\frac{\frac{A}{A+B}}{\frac{C}{C+D}}$$

Study Design #1

Cross-sectional study

- National Health and Nutrition Exam Survey (NHANES)
- Outcome: “have you been told by a doctor that you have heart failure?”
- Multiple possible predictors (demographic, behavioral/lifestyle, other risk factors)
- Research question: Is hypertension associated with heart failure risk?

Cross-sectional study: structure



Cross-sectional Study: Pluses

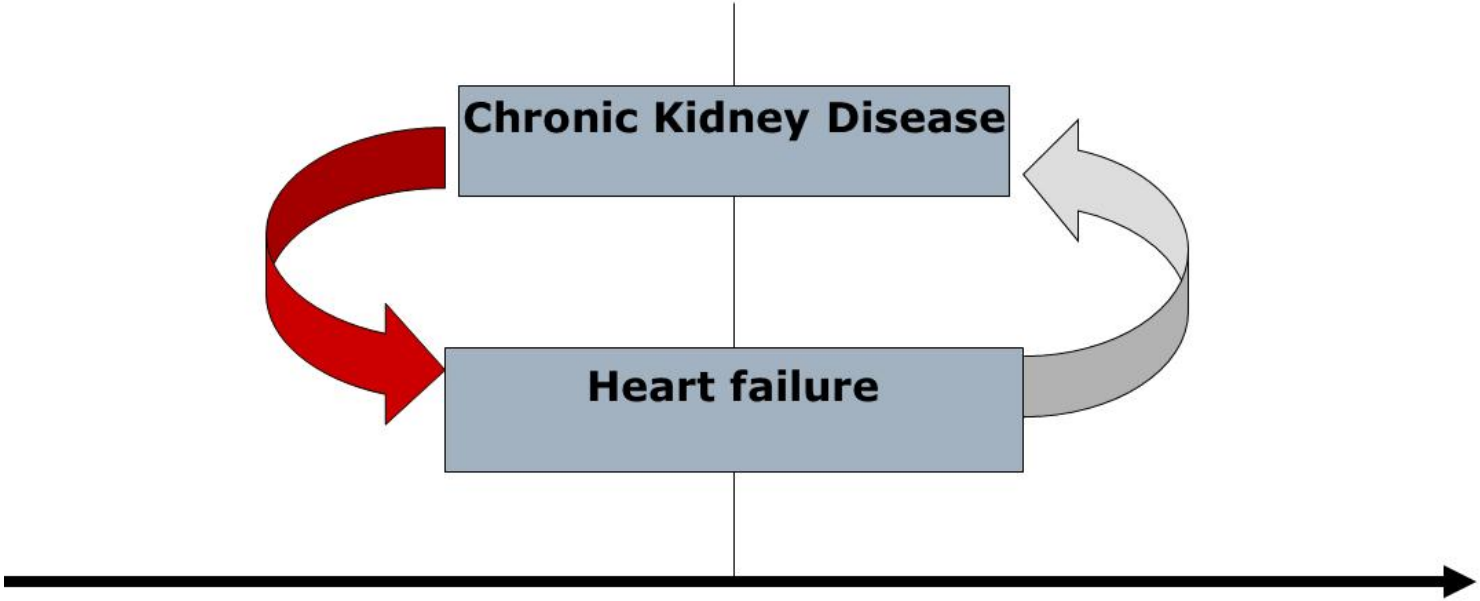
+ **Prevalence**
+ **Fast/Inexpensive - no waiting!**
+ **No loss to follow up**
+ **Associations can be studied**

Many well-known cross-sectional studies

- NHANES
- California Health Interview Survey (NHIS, CHIS)
- Behavioral Risk Factor Surveillance Survey (BRFSS)

Cross-sectional study: minuses

- **Cannot determine causality**



Cross-sectional study: minuses

- **Cannot determine incidence (new cases of disease)**
- **Cannot study rare outcomes**

What if you are interested in the rare outcome?

- Heart failure in adults before age 50
- Heart failure in adults before age 30
- Heart failure in children

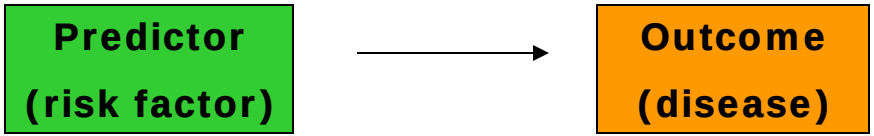
- **ANSWER: A Case-Control study**

Study Design #2

- **A case-control study**
- Cases: Adults with premature heart failure (18-50 years)
  - General medicine vs. cardiology/ UCSF vs. community practice
- Controls: Adults 18-50 without heart failure
  - Who are the appropriate controls?
- Potential predictors: Many – may be based on questionnaire
- Hypothesis: Hypertension early in adulthood are more likely to have premature heart failure.

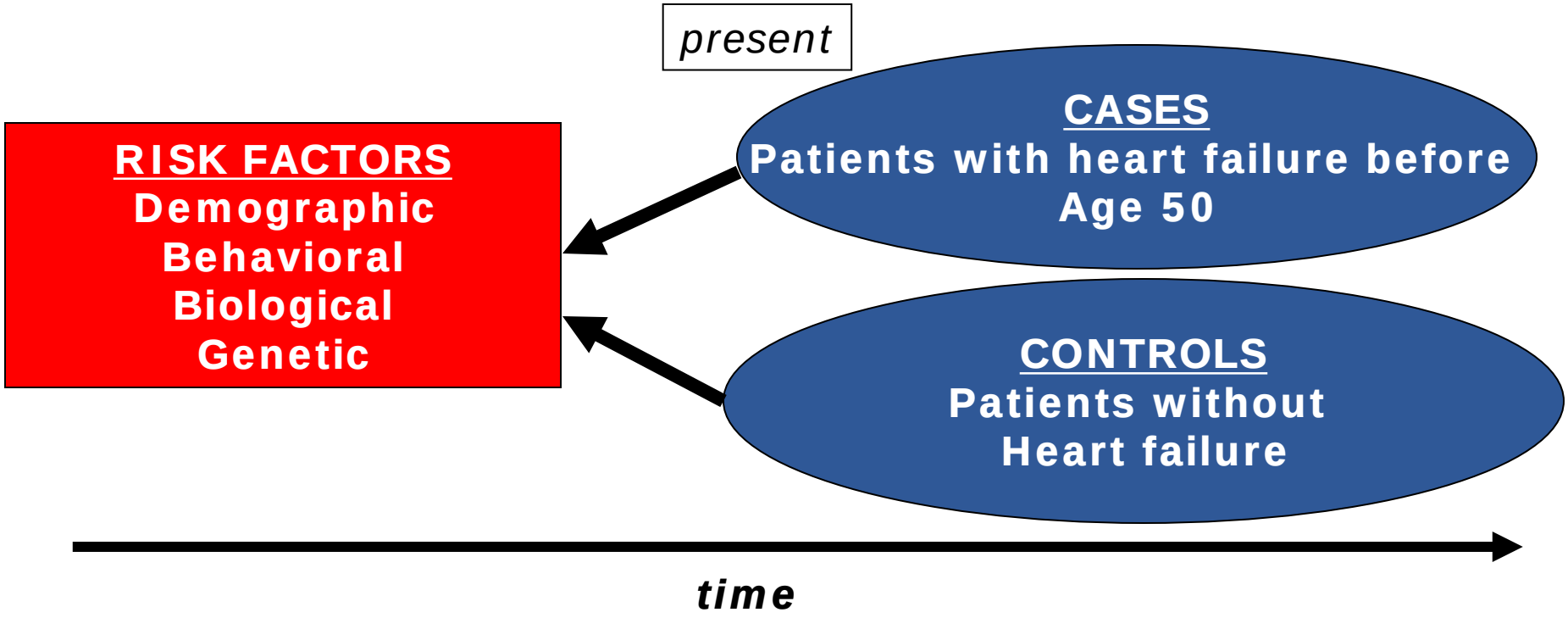
Case control studies

- **Investigator works “backward” (from outcome to predictor)**



- **Sample chosen on the basis of outcome (cases), plus comparison group (controls)**

Case-control study structure

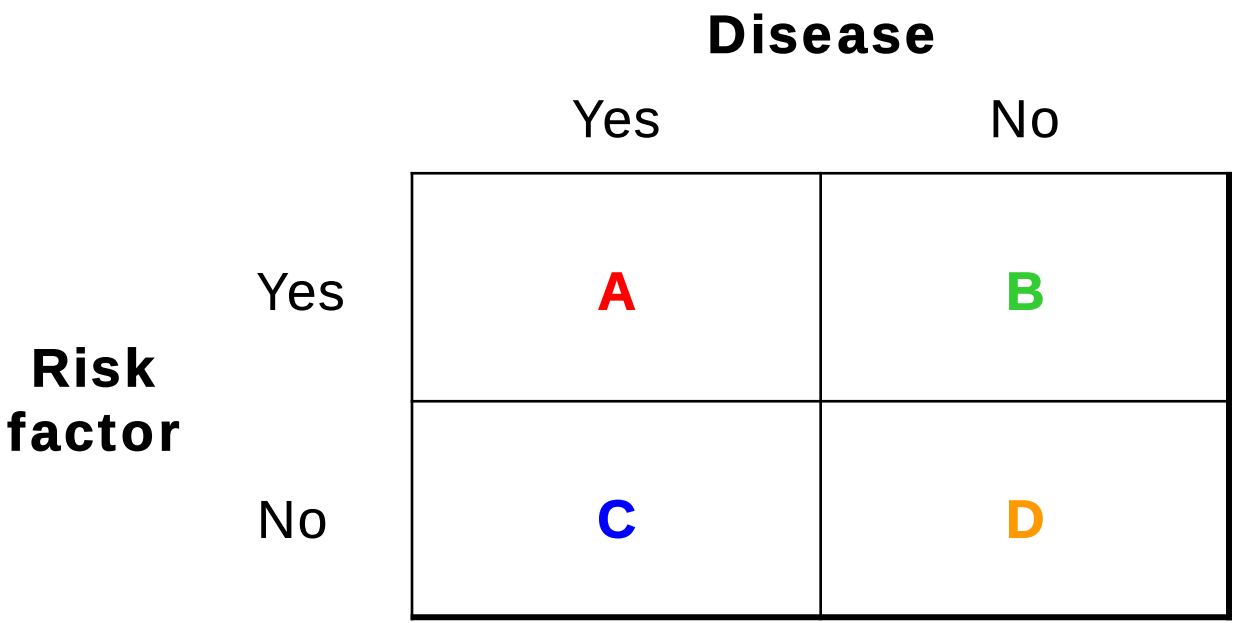


Case control studies

- **Cannot yield estimates of incidence or prevalence of disease in the population (why?)**

- **Odds Ratio is statistics**

Measures of association



Odds ratio

$$\frac{A}{B}$$

$$\frac{C}{D}$$

Also…

$$\frac{A\ D}{C\ B}$$

Case-control Study: pluses

+ **Rare outcome/Long latent period**
+ **Inexpensive and efficient: may be only feasible option**
+ **Establishes association (Odds ratio)**
+ **Useful for generating hypotheses (multiple risk factors can be explored)**

Case-control study-minuses

- **Causality still difficult to establish**
  - **Selection bias (appropriate controls)**
    - **Caffeine and Pancreatic cancer in the GI clinic**
  - **Recall bias: sampling (retrospective)**
    - **Abortion and risk of breast cancer in Sweden**

Case-control study--minuses

- Incidence
  - New cases of an outcome that occur
  - Can measure in a cohort study
- Prevalence
  - Cases that exist at a given time
  - Can measure in a cross-sectional study
- Neither can be measured in a case-control study

Case-control - “the house red wine”

- Rely tampons and toxic shock syndrome:
  - High rates of toxic shock syndrome in menstruating women
  - Suspected OCPs or meds for PMS
  - Cases: 180 women with TSS in 6 geographic areas
  - Controls: 180 female friends of these patients and 180 females in the same telephone code
  - Tampon associated with TSS (OR = 29!)
  - Super absorbency associated with TSS (OR 1.34 per gm increase in absorbency)
  - Led to “RELY” brand tampons being taken off the market.

Where are we?

- Cross-sectional studies and case-control studies are important for generating hypotheses about risk factors for heart failure.
- What's missing? - strengthening evidence for a causal link between risk factors and heart failure.
- Use results from our previous studies to apply for funding for a prospective cohort study!

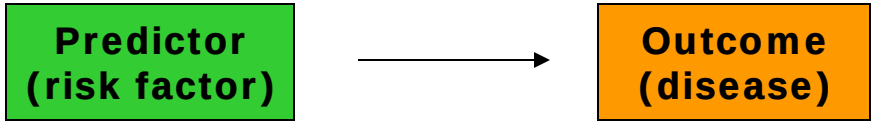
Study design #3

- **Prospective cohort study**

- CARDIA study:
  - Prospective cohort study
  - 5000 (M/W, black/white, low/high SES)
  - Age 18-30 at enrollment
  - Followed 20 years
  - Exam visits years 0, 2, 5, 7, 10, 15, 20

- Outcome: Incident heart failure

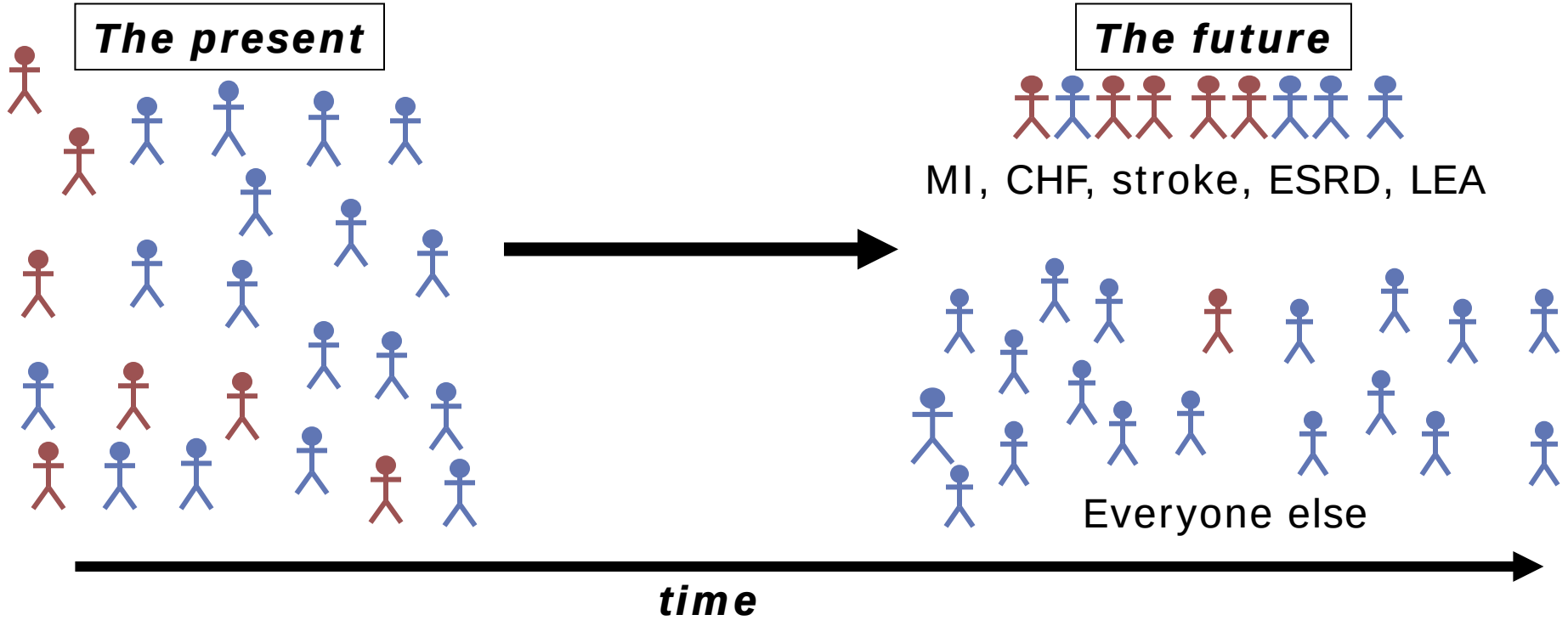
Elements of a cohort study



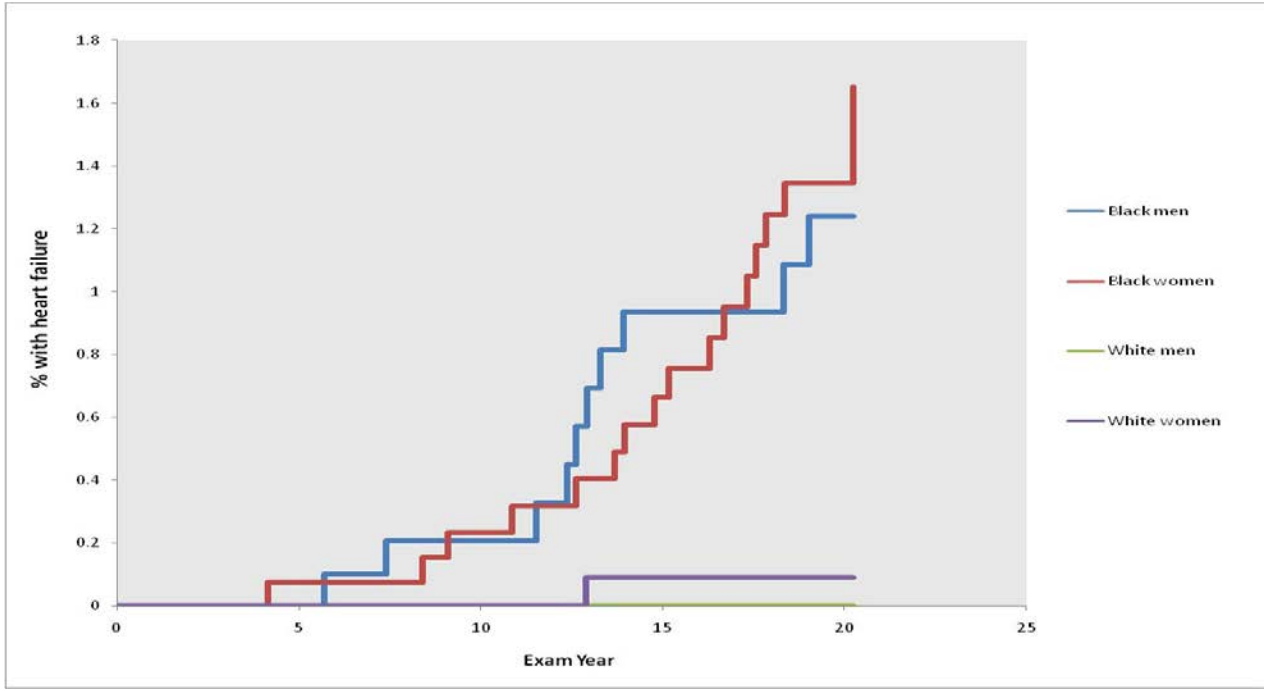
- Selection of sample from population
- Measures predictor variables in sample
- Follow population for period of time
- Measure outcome variable

- Famous cohort studies
  - Framingham
  - Nurses' Health Study
  - Physicians' Health Study

Prospective cohort study structure

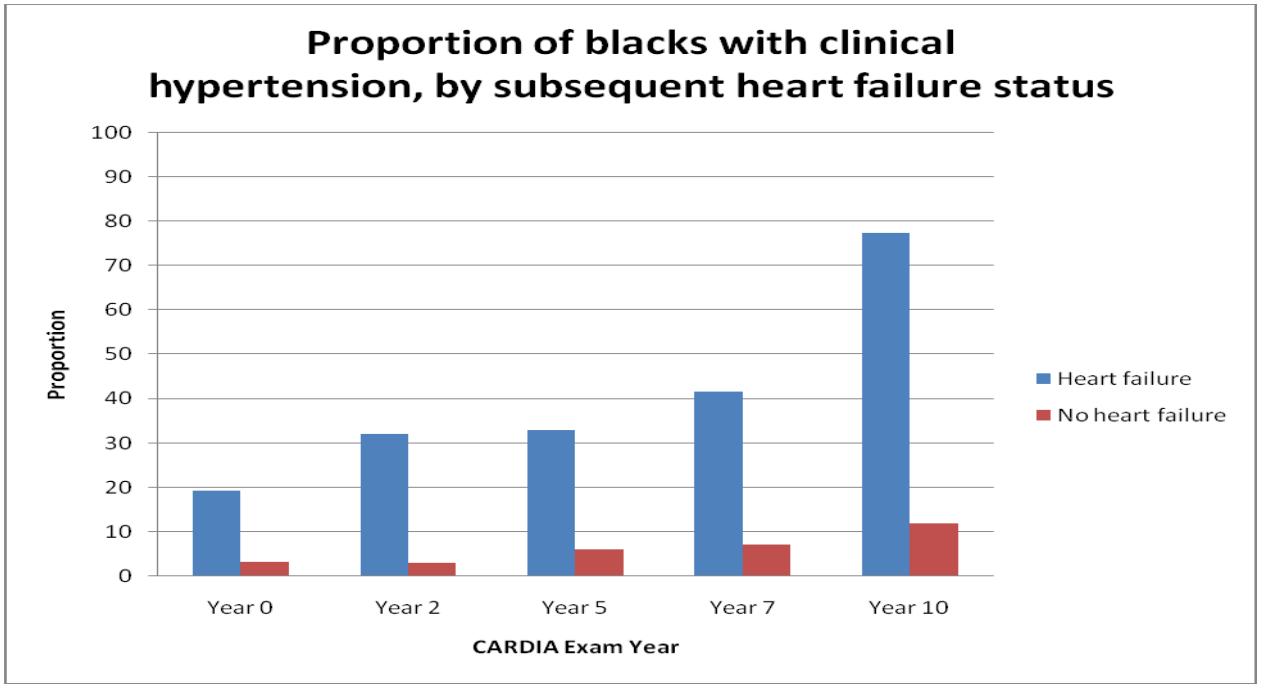


Incidence of heart failure before age 50 in black and white adults



•Bibbins-Domingo et al. N Engl J Med 2009; 360:1179-1190

Hypertension early in life is a risk factor for heart failure before age 50 among blacks



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Strengths of cohort studies

- Know that predictor variable was present before outcome variable occurred (some evidence of causality)
- Directly measure *incidence* of a disease outcome
- Can study multiple outcomes of a single exposure (RR is measure of association)

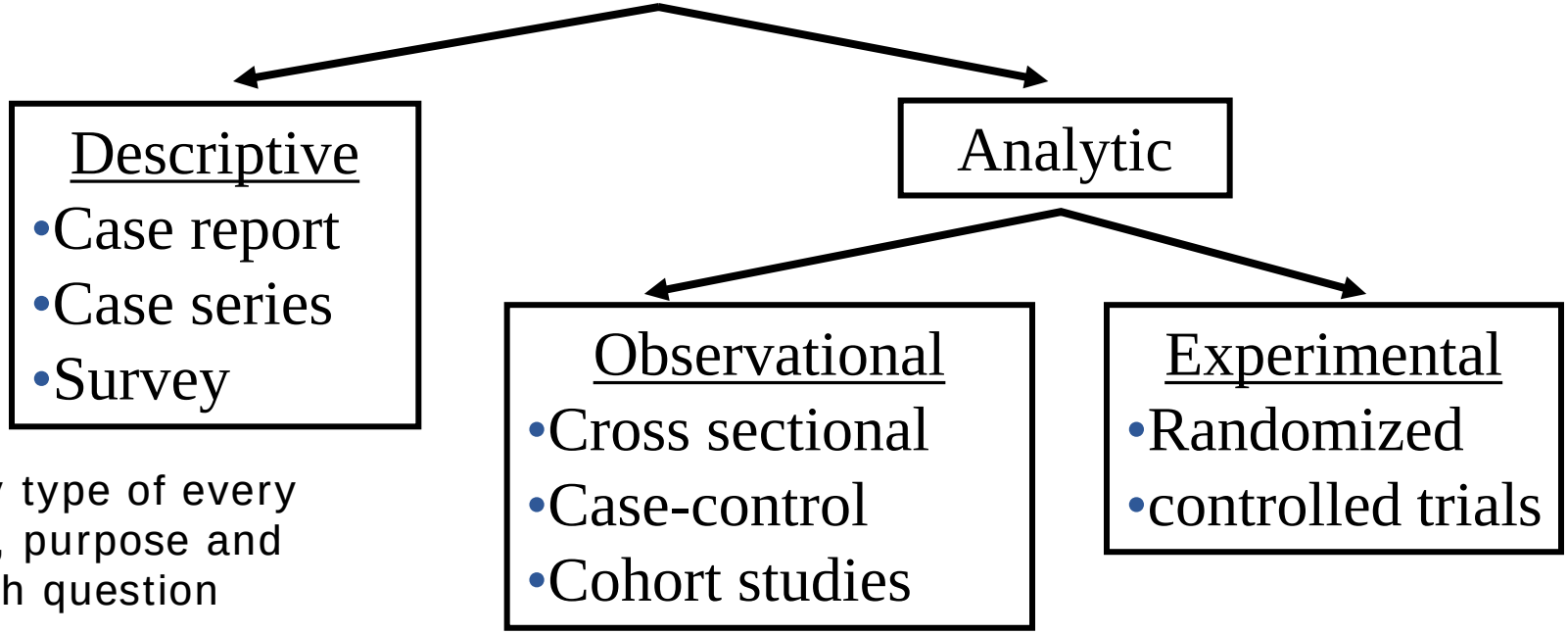
Weaknesses of cohort studies

- Expensive and inefficient for studying rare outcomes
  - HERS vs. WHI
- Often need long follow-up period or a very large population
  - CARDIA
- Loss to follow-up can affect validity of findings
  - Framingham

Other types of cohort studies

- Retrospective cohort
  - Identification of cohort, measurement of predictor variables, follow-up and measurement of outcomes have all occurred in the past
  - Much less costly than prospective cohorts
  - Investigator has minimal control over study design

A study type for every budget, purpose, and research question



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