

Critical Thinking

- In medical school, students are rewarded for your abilities to memorize.
- But memorization will only lead to a **good** physician. Good physicians do the right thing after other physicians tell them what is right.
- Memorization will not lead to a **great** physician. Great physicians make their own judgments to decide what is right.

The Basic Premise of Critical Thinking

- 50% of what is taught in medical school will be wrong in 2-10 years.
- More than 80% of articles in medical journals use improper methods. Most articles will not withstand the test of time.
- Most of a physician's postgraduate education will be sponsored by industry, which has a vested interest in having them prescribe new treatments it produces.

The Goals of Critical Thinking

- To teach physicians how to think.
- To teach physicians how to analyze.
- To teach physicians how to make judgments.
- To teach physicians how to reach conclusions.

How One Knows Something in Medicine

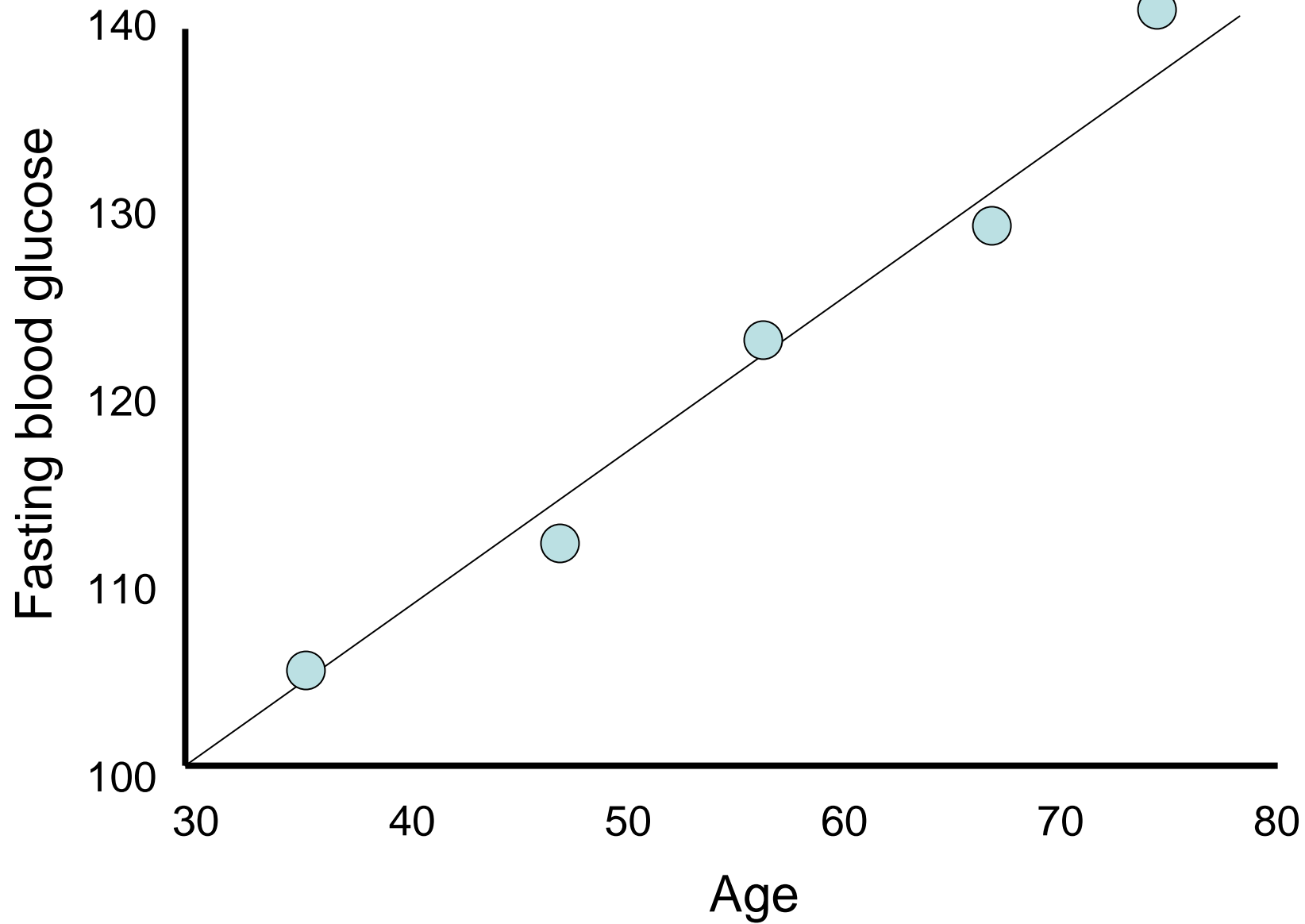
- Physicians reach conclusions by making observations.
- All observations yield data, but not all data are interpretable.
- The goal is to understand the limitations of observed data, so one can embrace those that are the most interpretable.

The First Step

Make a series of
observations.

You Decide to Make an Observation in the Next 5 Patients You See With Diabetes

- Three are men; 2 are women.
- Four have brown hair; one blond hair.
- All five have middle names beginning with S.
- Four of the 5 are receiving insulin.
- There was a close relation between their age and their blood sugar.



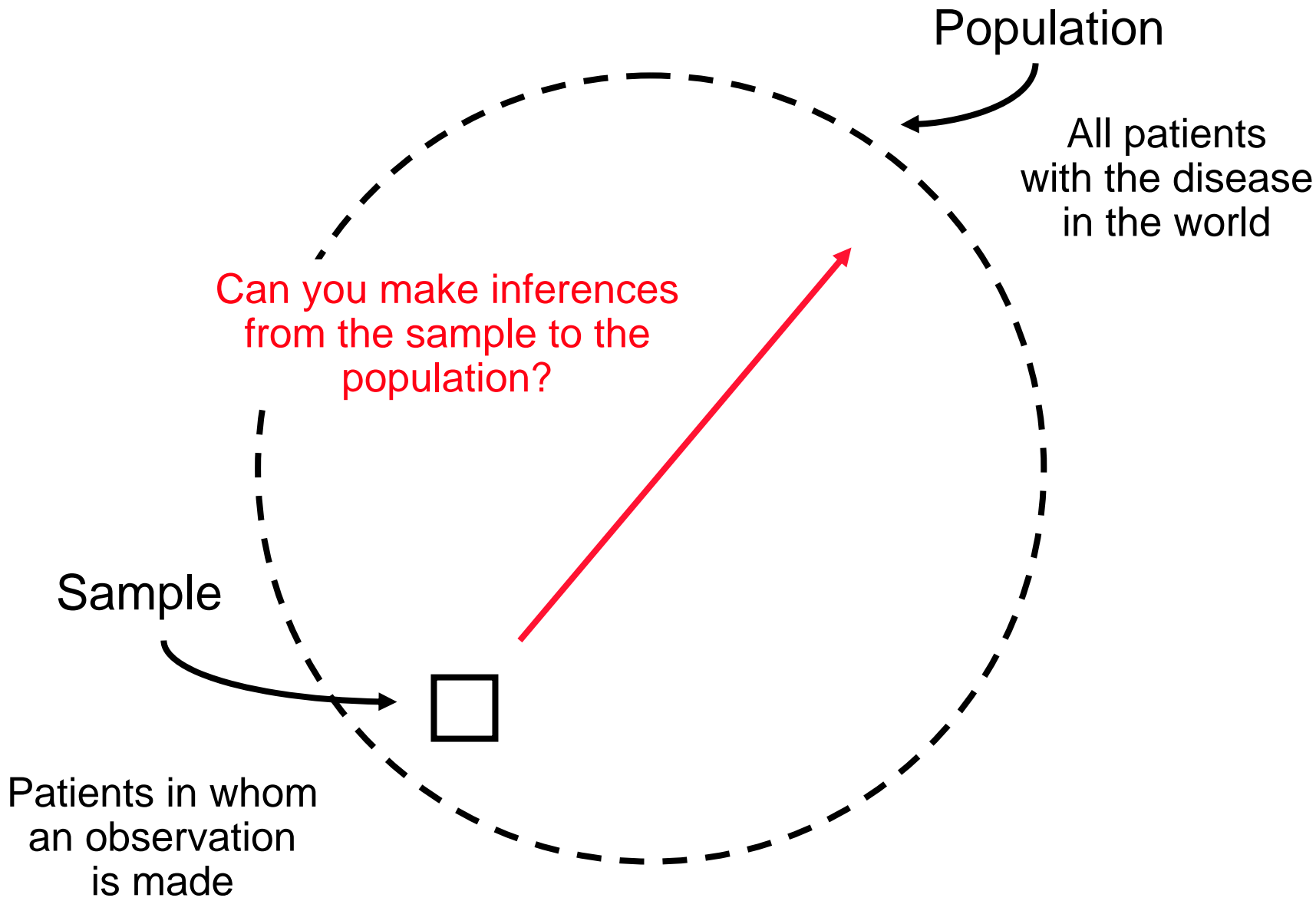
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- Four have brown hair; one blond hair.
- All five have middle names beginning with S.
- Four of the 5 are receiving insulin.
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What can you conclude?

Conclusion

- There was a close relationship between age and fasting blood glucose *in the five patients with diabetes whom you studied.*



Conclusion

- There was a close relationship between age and fasting blood glucose *in the five patients with diabetes whom you studied.*
- You cannot say much as to whether age and glucose are related in the general population of patients with diabetes.

What Can't One Extrapolate?

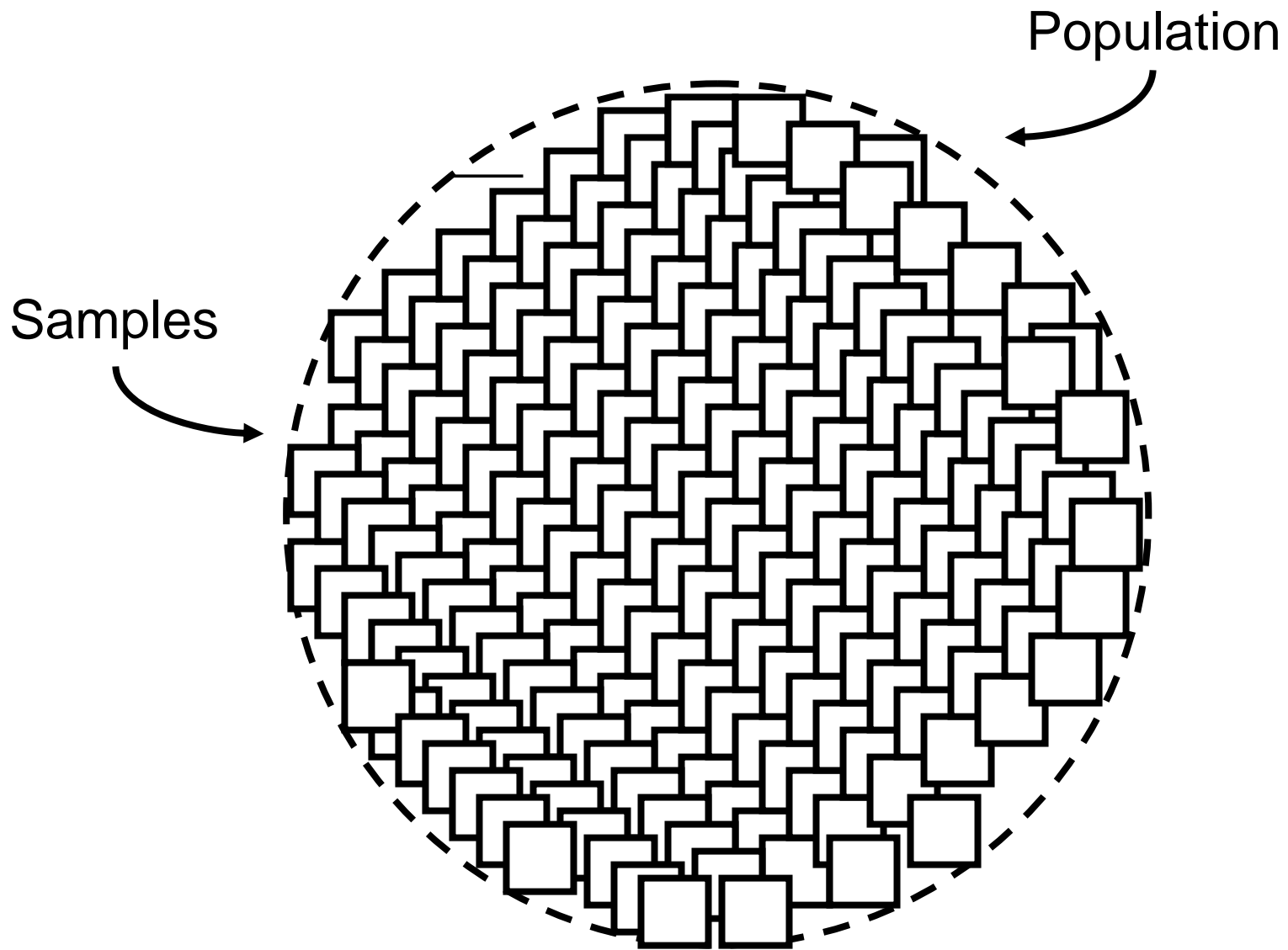
- There was no predefined *question*.
- There was no predefined *hypothesis*.
- There was no predefined *research plan*.
 - Which patients to study?
 - What variables to measure?
 - What comparisons to make?
- There was no predefined *analytical plan*.

Types of Clinical Research Studies

- Those that describe a characteristic or outcome in a sample of patients. [**Descriptive study**]
- Those that determine if a characteristic is associated with an outcome. [Observational study]
- Those that determine if a characteristic causes an outcome. [Experimental study]

Conclusions From a Descriptive Study?

- One can reach conclusions from the descriptions of a sample if the observations carried out in the sample are concordant with observations made on similar samples taken by many other investigators at many other times under many other conditions.



Are Descriptive Studies Worthwhile?

- The most basic level of scientific and medical evidence is the clinical description.
- Although subject to many types of error, clinical descriptions that are held in common by a large number of physicians carry enormous weight.
- Most of what physicians know about *patients* is based on observations in a single individual. Most of what physicians know about *medicine* is based on commonly held clinical observations.

What Can Descriptive Studies Do?

- Descriptive studies can fully characterize diseases and their treatments.
- Descriptive studies can generate hypotheses to be confirmed in observational or experimental studies.
- Descriptive studies can generate estimates critical to the design of confirmatory observational or experimental studies.

Question

- Can descriptive studies ever lead to a definitive conclusion about the importance of a risk factor or the efficacy of a new treatment without a confirmatory study ?

Study of Risk Factors for AIDS in the US (J Infect Dis 1983;148:339-45)

Characteristics of first 1000 patients with AIDS in the United States:

- 727 were homosexual or bisexual men
- 236 were injecting drug users.

*Do we understand the major risk
factors for AIDS?*

Study of a New Treatment for Advanced Metastatic Pancreatic Cancer

- In 2001, investigators treated 100 patients with advanced metastatic pancreatic cancer with polystatin. After 5 years, 63% survived.
- Prior to this study, the 5-year survival of patients with advanced pancreatic cancer was uniformly less than 20%.

Is polystatin effective?

Types of Study Designs

- **Descriptive study:** Useful when effect size is very large ($>100x$) and environment is highly predictable.

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Descriptive studies are inadequate if the environment is unpredictable.

I Have Developed a New Breakthrough Medicine Available For the First Time

It makes people who take a
single dose much smarter
and much sexier forever

I Have Developed a New Breakthrough Medicine Available For the First Time

- One year ago, I gave it to 2 people in this room, and they all got smarter and sexier.
- One year ago, I gave it to 10 people in this room, and they all got smarter and sexier.
- One year ago, I gave it everyone in this room, and they all got smarter and sexier.

Not convinced?

Why not?

Types of Study Designs

- **Descriptive study:** Useful when effect size is very large ($>100x$) and environment is highly predictable.

Descriptive studies are inadequate if the environment is unpredictable.

When the environment is unpredictable, you need a control group.

You need a control group,
but will any kind do?

Study of a New Treatment for Pneumonia

- In 2002, investigators treated 100 patients who presented to the hospital with pneumonia with neocillin. After 60 days, 92% survived.
- To identify a control group, the investigators identified 100 patients who presented to the hospital with pneumonia in the past who did not receive neocillin. After 60 days, 41% survived.

Is the treatment effective?

Scores for Baseball Teams in August 2004

- On August 7, 2004, the Texas Rangers scored 5 runs. Did the Rangers win?
- On August 7, 2004, the Texas Rangers scored 5 runs. On August 6, 2004, the Yankees scored 3 runs. Are the Rangers the better team?

Scores for Baseball Teams in August, 2004

On August 6, 2004

Rangers 2

Yankees 3

On August 7, 2004

Rangers 5

Yankees 7

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Scores for Baseball Teams on Aug 7, 2004

In Arlington TX

| | |
|---------|---|
| Rangers | 5 |
| Red Sox | 8 |

In New York NY

| | |
|---------|---|
| Yankees | 3 |
| Orioles | 1 |

Study of a New Treatment for Pneumonia

- In 2002, investigators treated 100 patients who presented to the hospital with pneumonia with neocillin. After 60 days, 92% survived.
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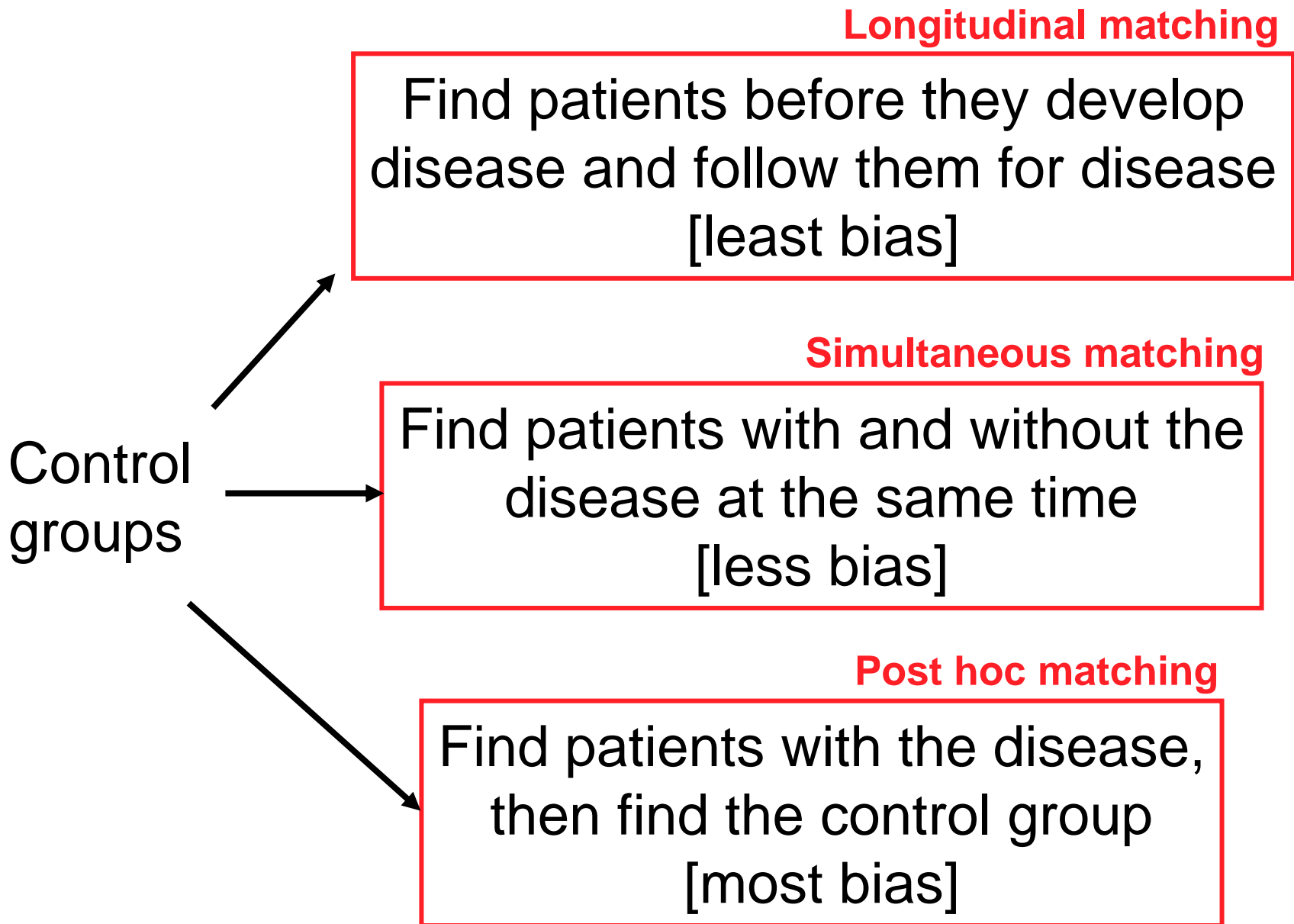
Is the treatment effective?

Treatment Groups for Pneumonia Study

Group #1 was selected from white patients with no risk factors presenting to a private hospital in Newport Beach, Rhode Island.

Group #2 was selected from black patients with AIDS presenting to a county hospital in Dallas, Texas.

A key element of interpretable research is to identify an appropriate control group.



Control
groups

Find patients before they develop
disease and follow them for disease
[add dimension of time]

Find patients with and without the
disease at the same time
[add unbiased sampling]

Find patients with the disease,
then find the control group
[add control group]

Control
groups

Find patients before they develop
disease and follow them for disease

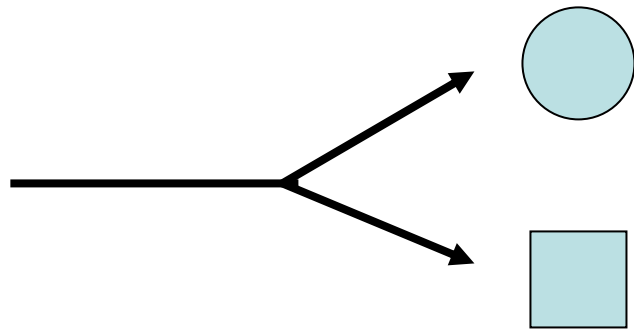
Cohort study

Find patients with and without the
disease at the same time

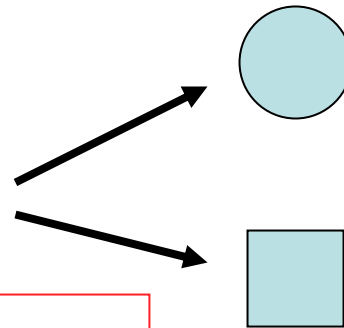
Cross-sectional study

Find patients with the disease,
then find the control group

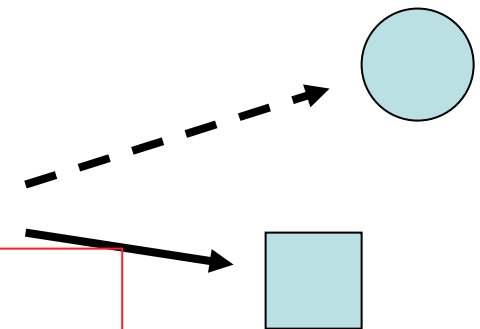
Case-control group



Cohort
(prospective identification)



Cross-sectional
(simultaneous identification)



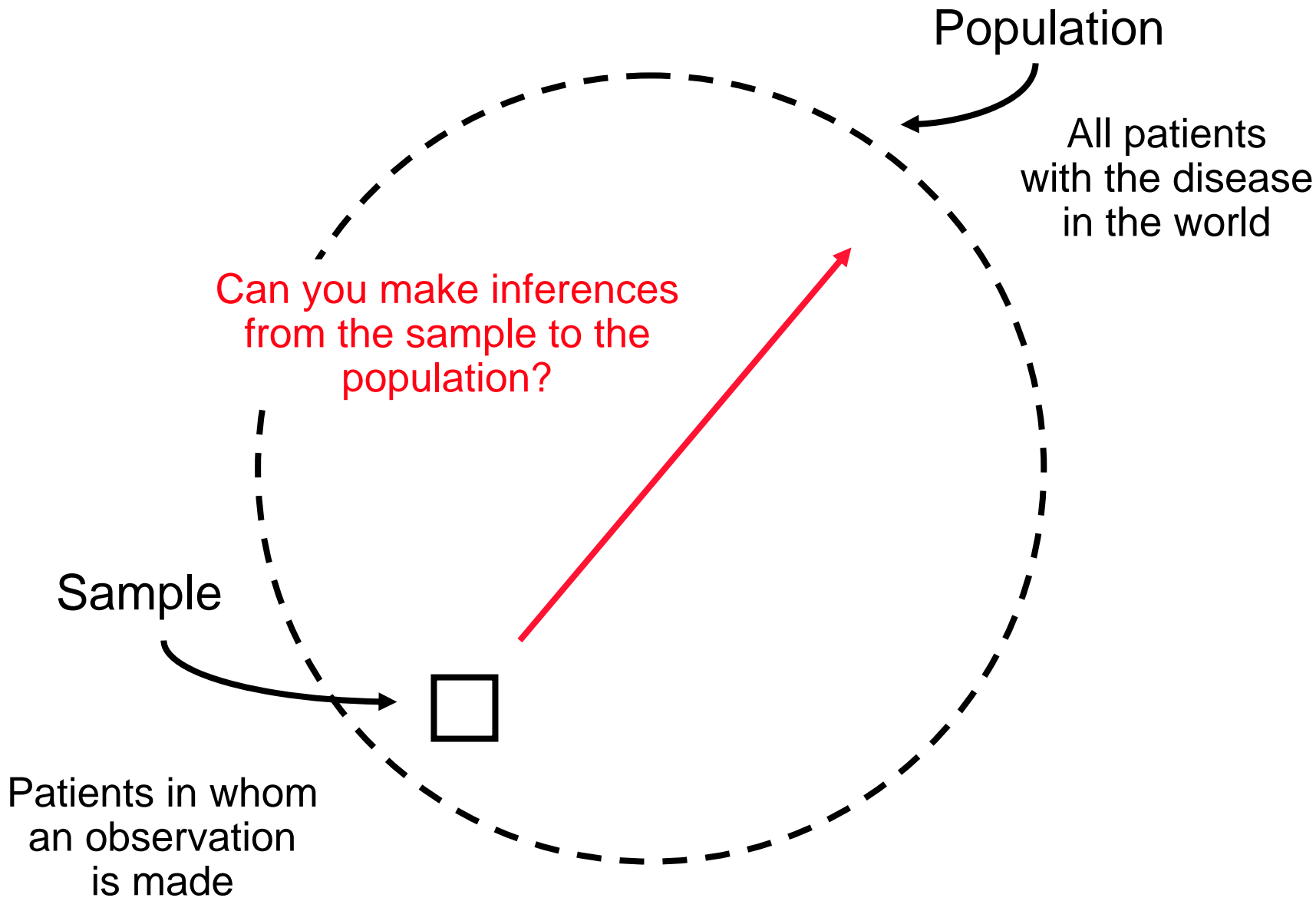
Case-control
(post hoc identification)

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Conclusions From Observational Studies

- Identification of risk factors for causation of disease (e.g., cancer and heart disease).
- Understanding the genetic basis of disease and most mechanisms underlying diseases.
- Development of many new treatments (especially vaccines, antibiotics, anticancer agents).



In all of these cases,
the results are interpretable
only if there were a
predefined hypothesis.

The Fortune Teller

You go to a fortune teller. She says:

- You are going to fall in love and be successful.

The Fortune Teller

You go to a fortune teller. She says:

- You are going to fall in love and be successful.
- You will meet your future spouse within the next several years and be promoted.

The Fortune Teller

You go to a fortune teller. She says:

- You are going to fall in love and be successful.
- You will meet your future spouse within the next several years and be promoted.
- You will meet your future spouse on December 17, 2006 and be promoted to Associate Professor by March 1, 2007.

In all of these cases,
the results are interpretable
only if there were a
predefined and specific
hypothesis.

Observational Studies Have . . .

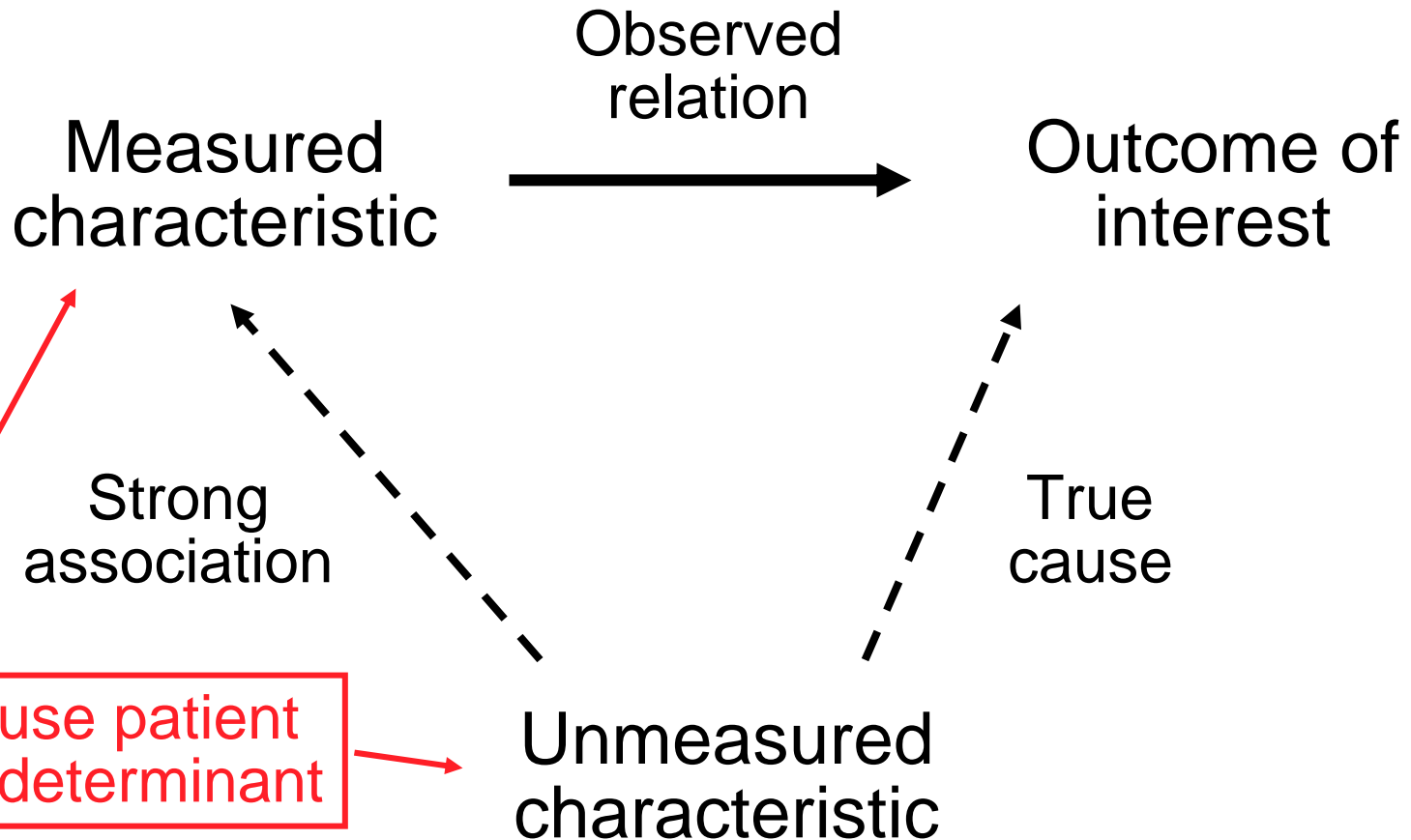
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- A predefined and specific *hypothesis*.
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Types of Study Designs

- **Descriptive study:** Useful when effect size is very large ($>100x$) and environment is highly predictable.
- **Observational study:** Useful when effect size is large (3-100x) and environment is unpredictable but can be fully evaluated.

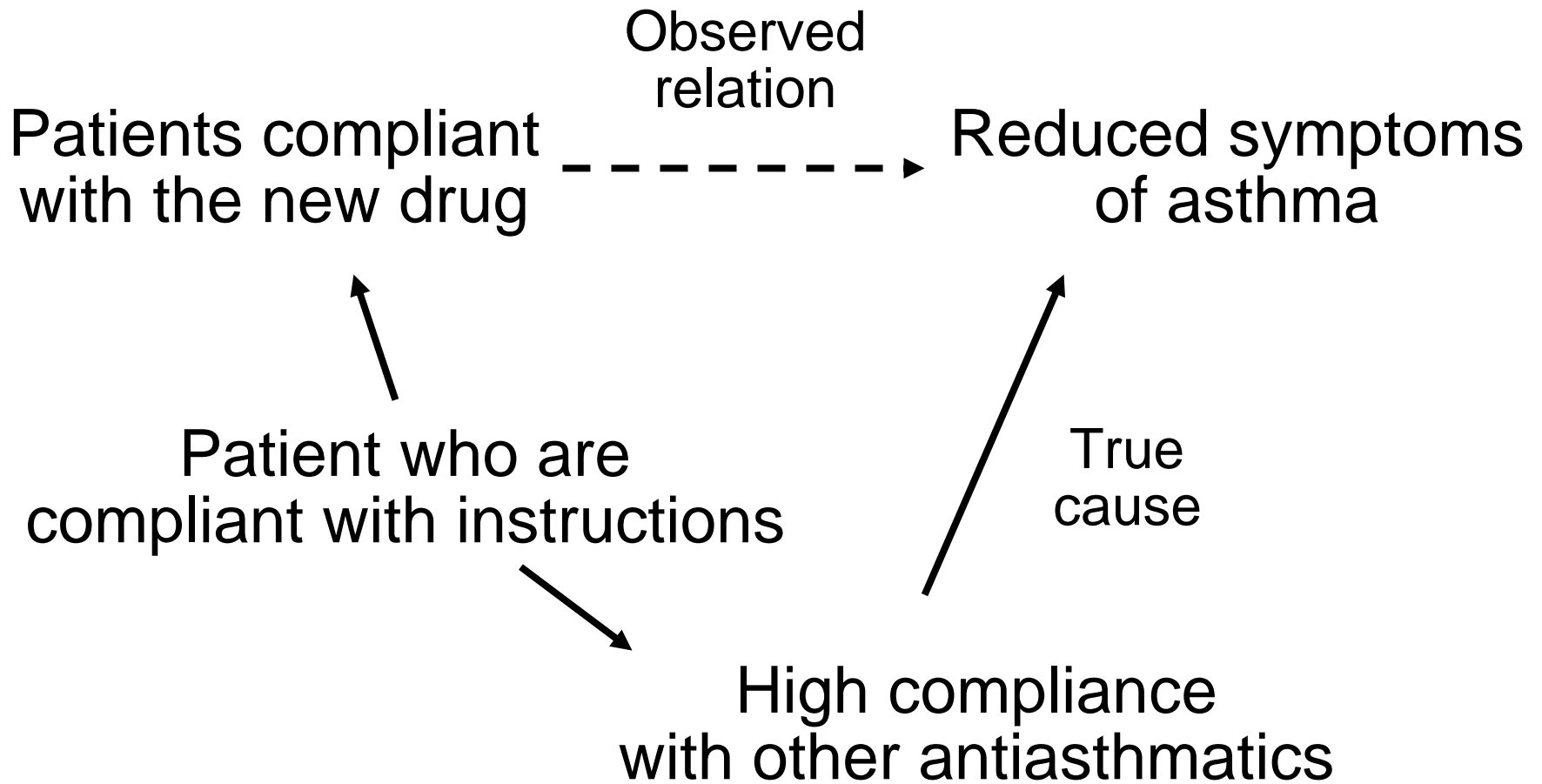
Observational studies are inadequate if the effect size is small or if intent is to demonstrate cause-and-effect relation.

Studies of Association Are Always Hard to Interpret Because of Confounding



New Treatment for Asthma

- 1000 patients with asthma are offered treatment with a new drug to determine if it is effective.
- At the end of 6 months, 35% are taking 80-100% of the recommended doses, whereas 35% are taking 0-20% of the recommended doses.
- Patients taking 80-100% of the recommended doses have substantially fewer episodes of asthma than patients taking 0-20% of recommended doses.
- The new drug is an effective treatment for asthma.



Types of Clinical Research Studies

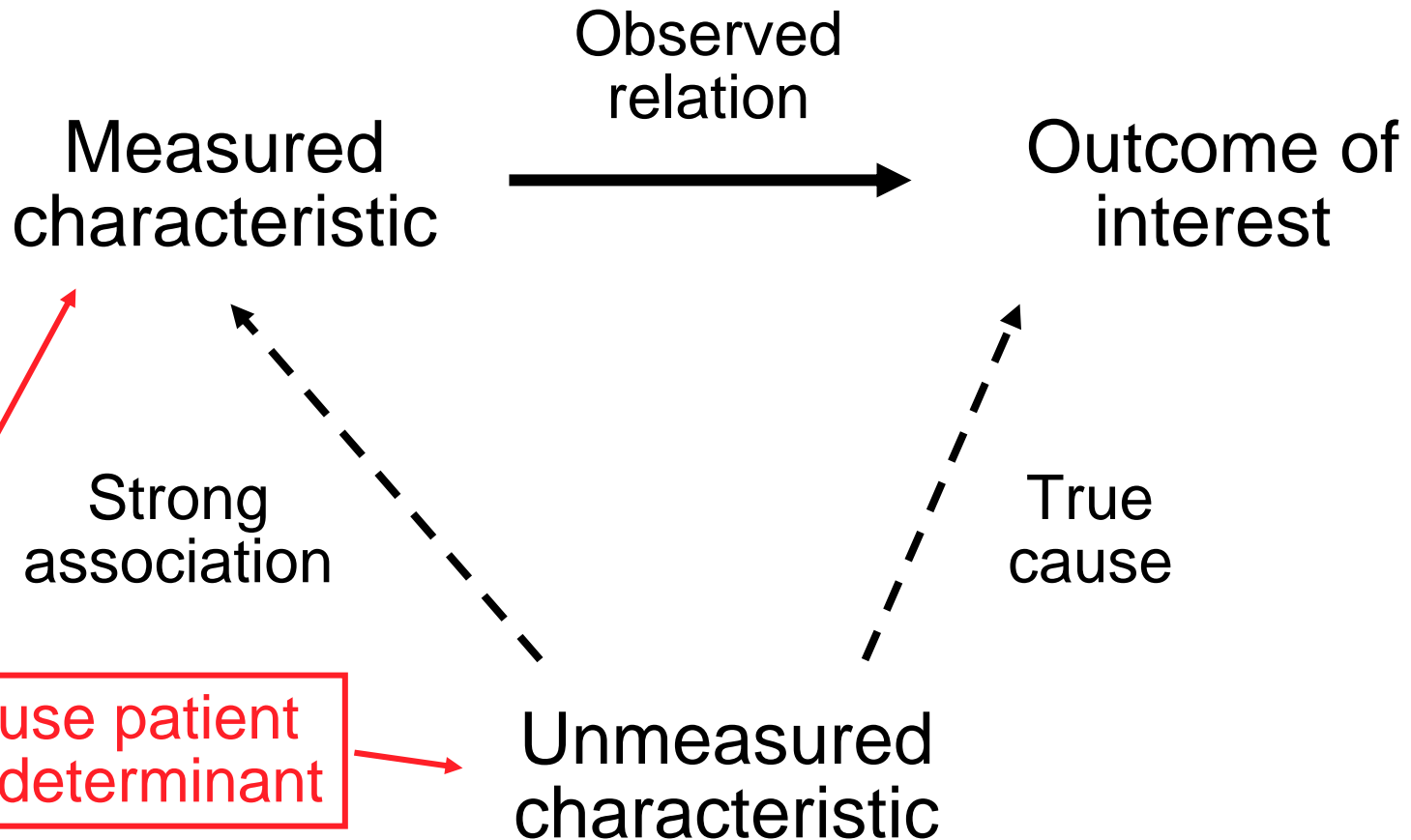
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Observational \Rightarrow Experimental Studies

A Key Distinction

- In an *observational* study, the patient (and thus a patient characteristic [measured or unmeasured]) determines the predictive variable \Rightarrow the outcome variable.
- In an *experimental* study, the study (actually the investigator) determines the predictive variable \Rightarrow the outcome variable.

Observational Studies and Confounding



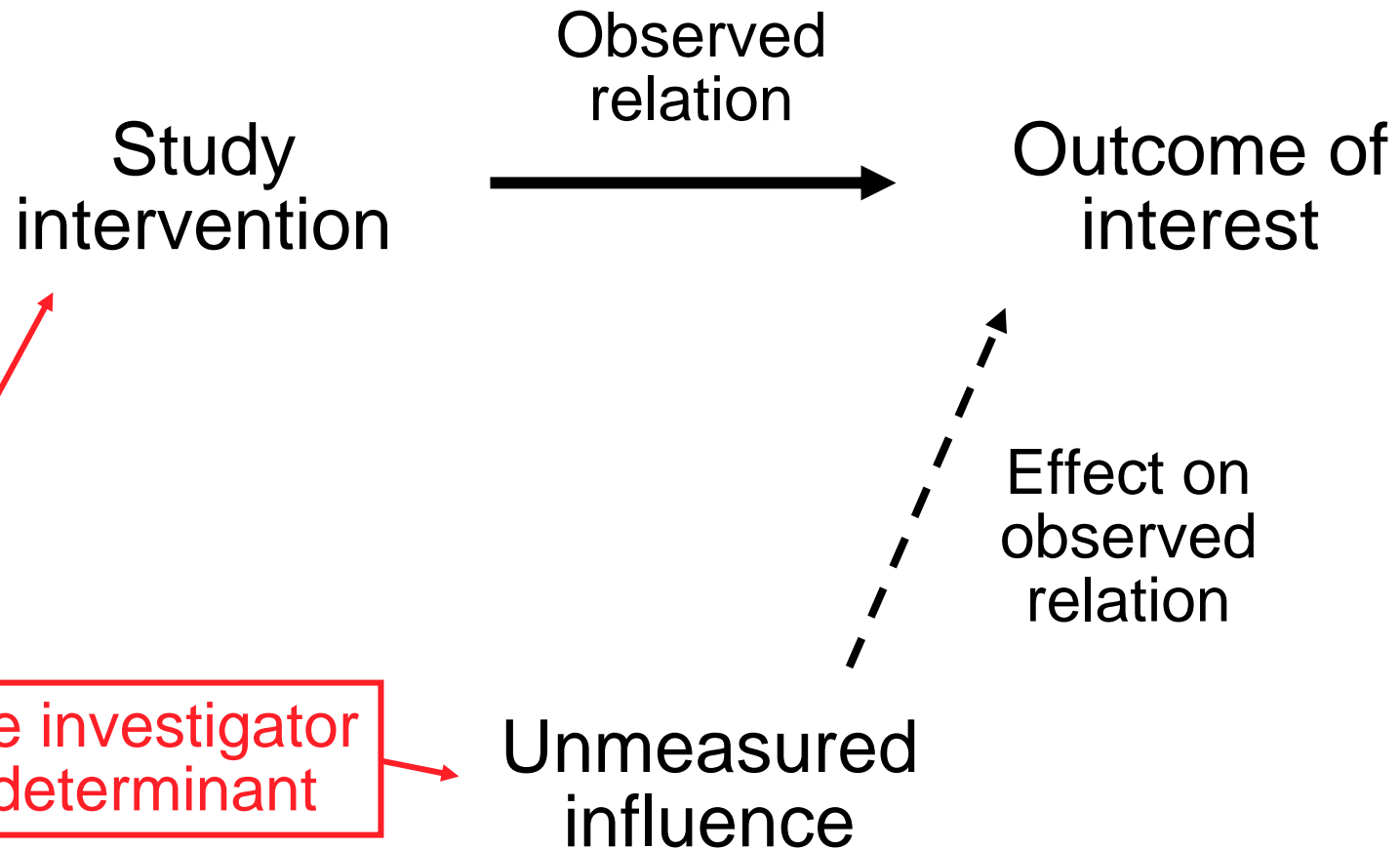
Experimental Studies



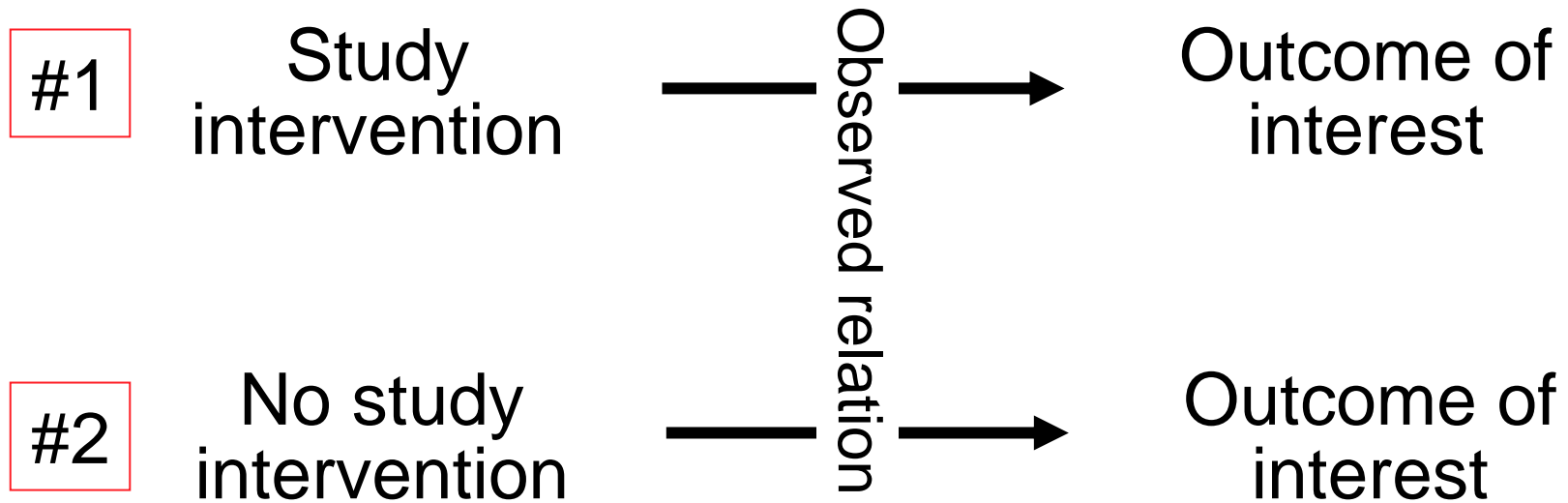
Because investigator is the determinant

~~Unmeasured characteristic~~

Experimental Studies

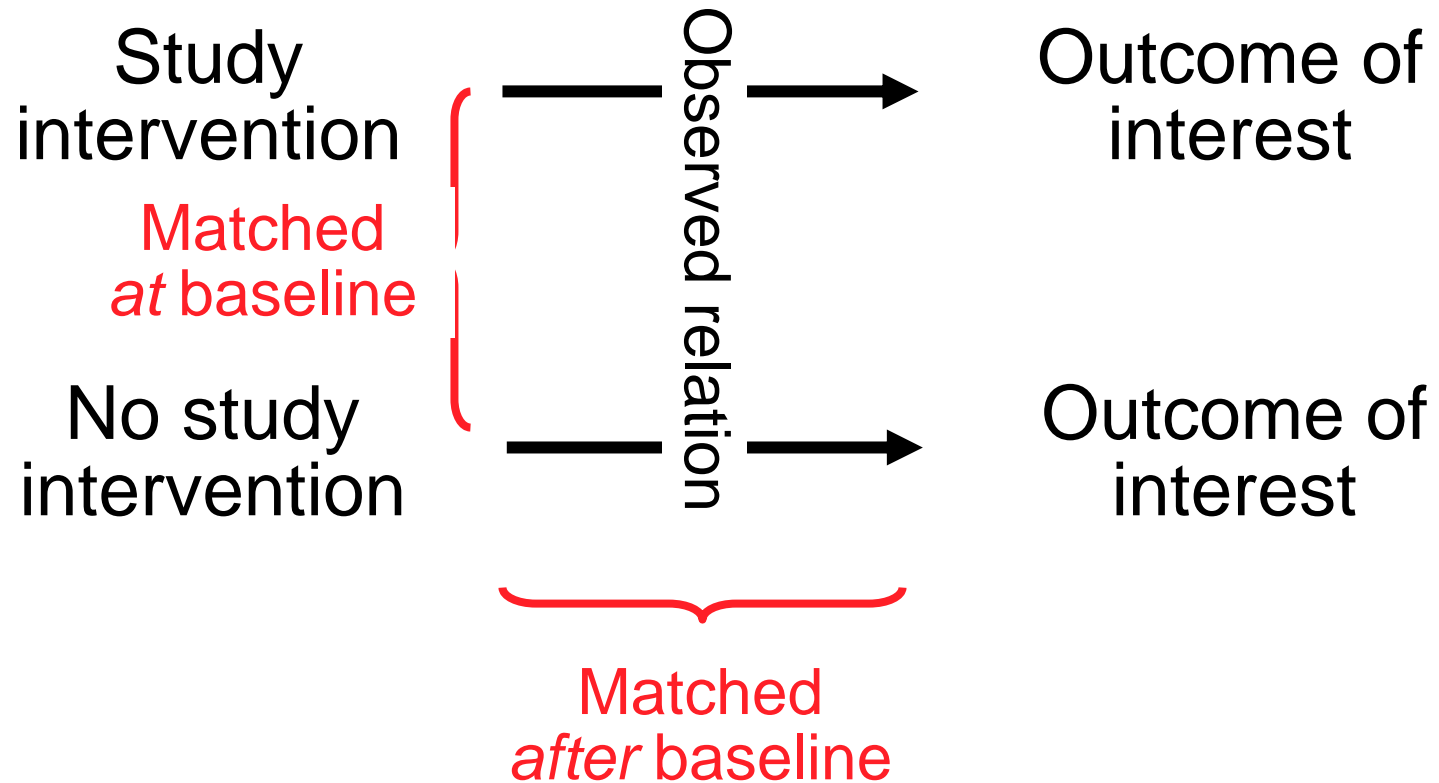


Experimental Studies



Effect of study intervention is the effect in the first group minus effect in second group

Experimental Studies



Importance of Randomization and Blinding

Randomization

- Randomization addresses confounding by *pre*-intervention variables.

Blinding

- Blinding addresses confounding by *post*-intervention variables.

Accommodating Confounders

An Important Principle

- *Observational* studies attempt to control for confounding variables by trying to identify, control and adjust for them. They can not accommodate for unmeasured confounders.
- *Experimental* studies does not try to identify or measure confounding variables. They control for measured or unmeasured confounding variables by randomization and blinding.

Types of Study Designs

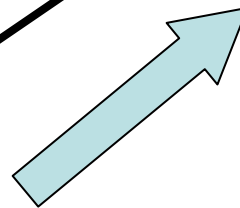
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- **Observational study:** Useful when effect size is large (3-100x) and environment is unpredictable but can be fully evaluated.
- **Experimental study:** Useful when effect size is small or moderate ($< 2x$) and environment is unpredictable and cannot be fully assessed.

Description

Descriptive Study

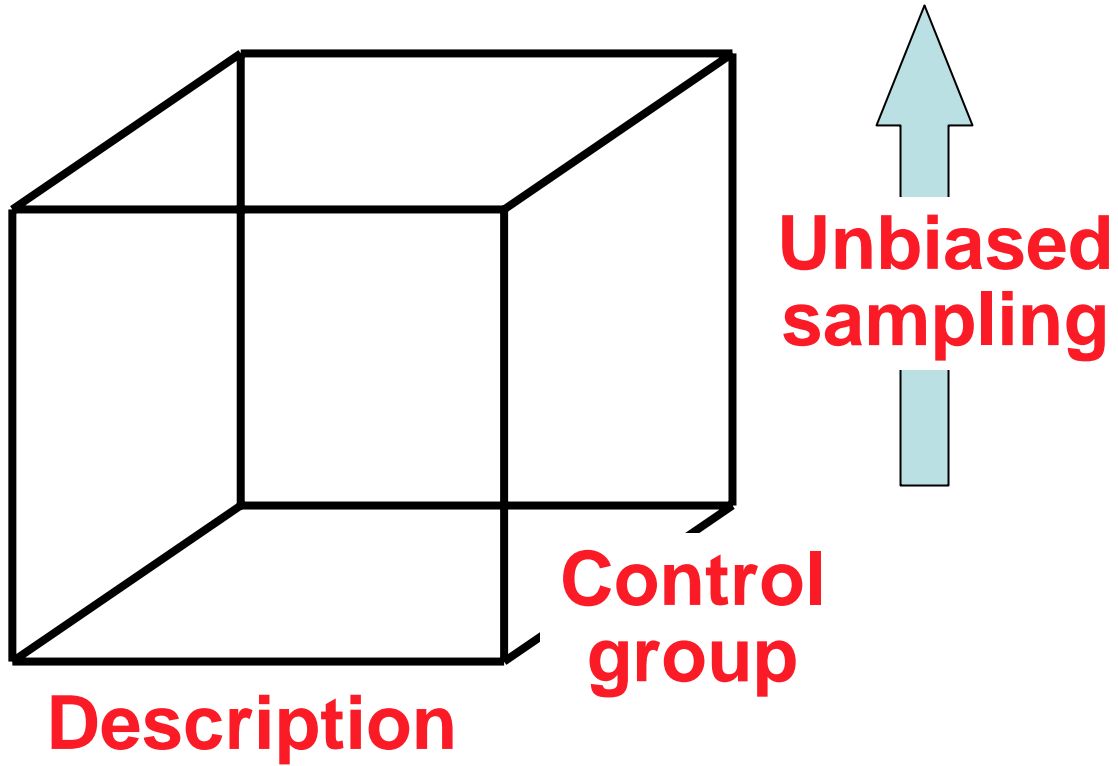


Description

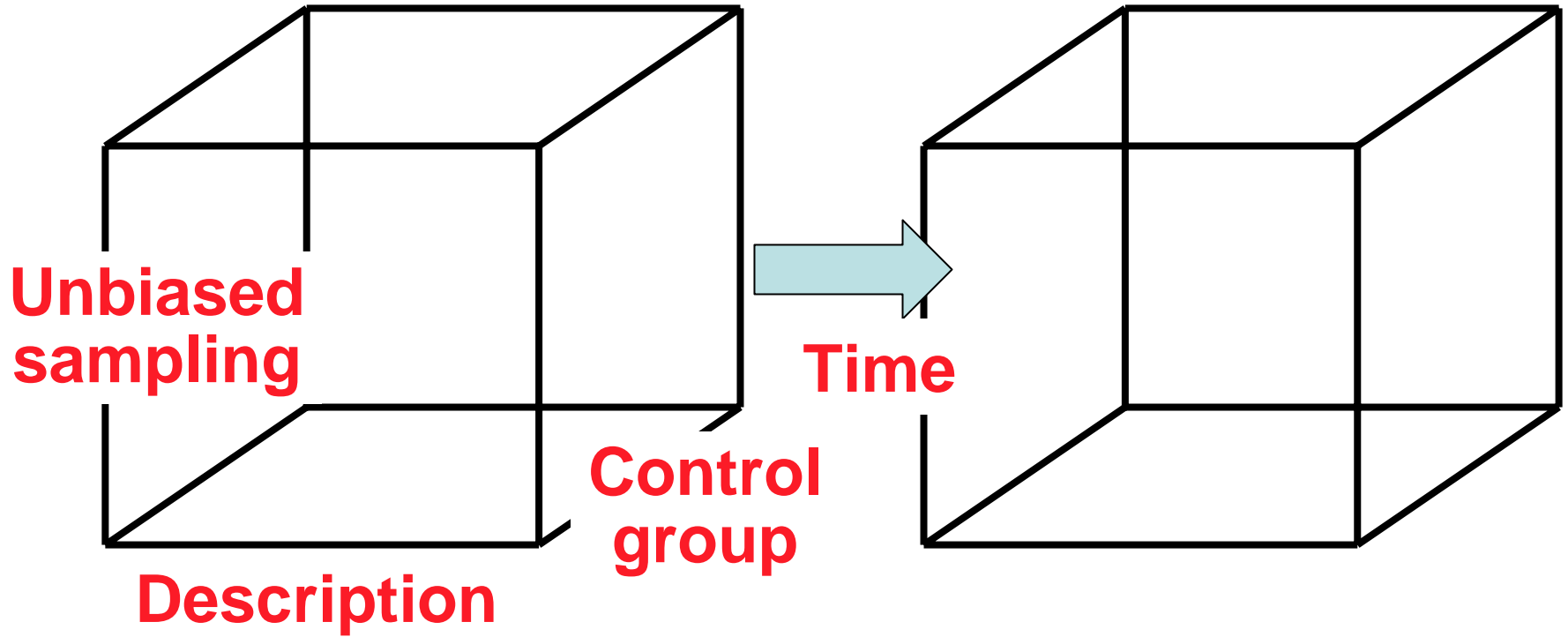


**Control
group**

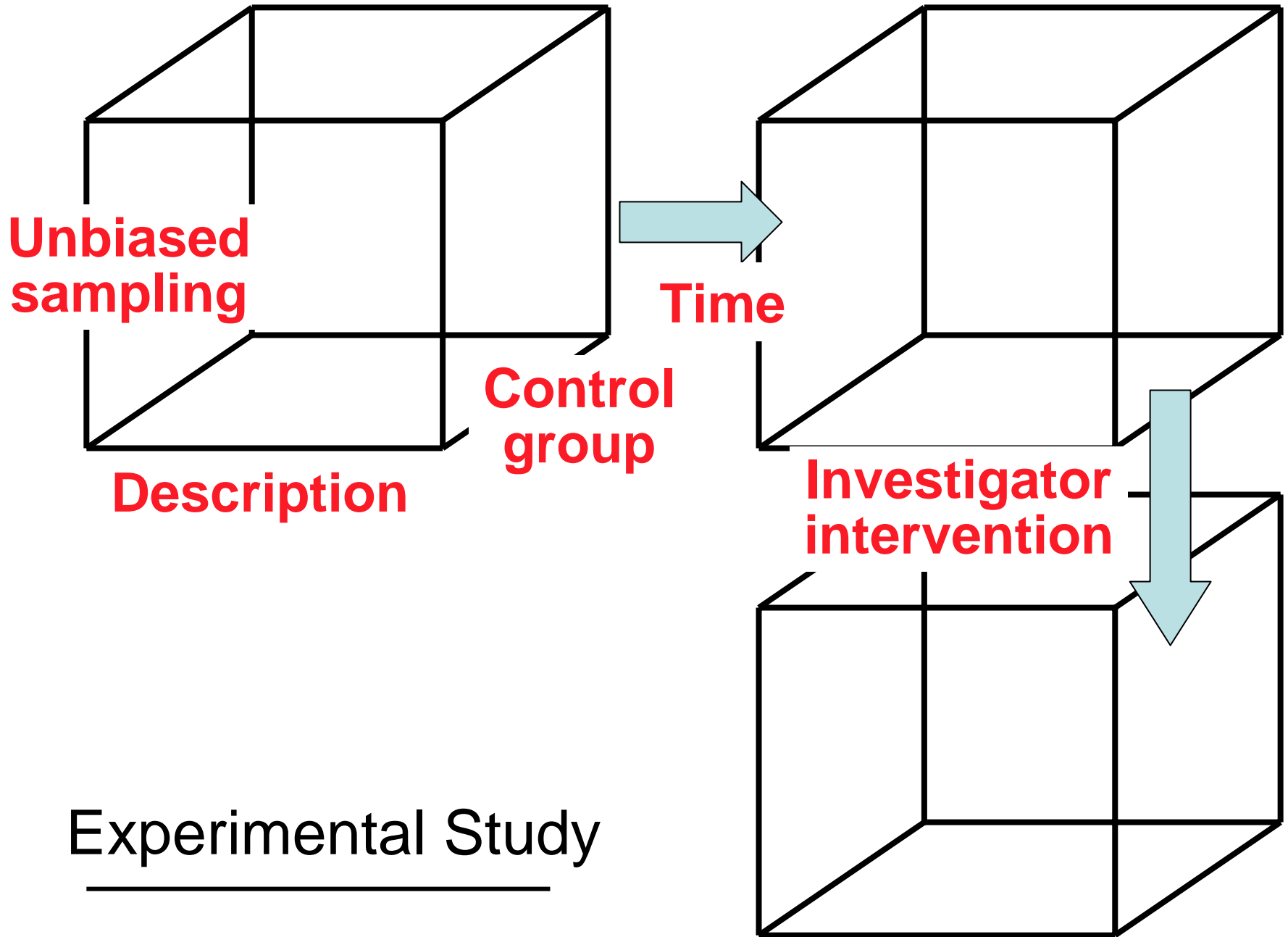
Case-Cohort Study

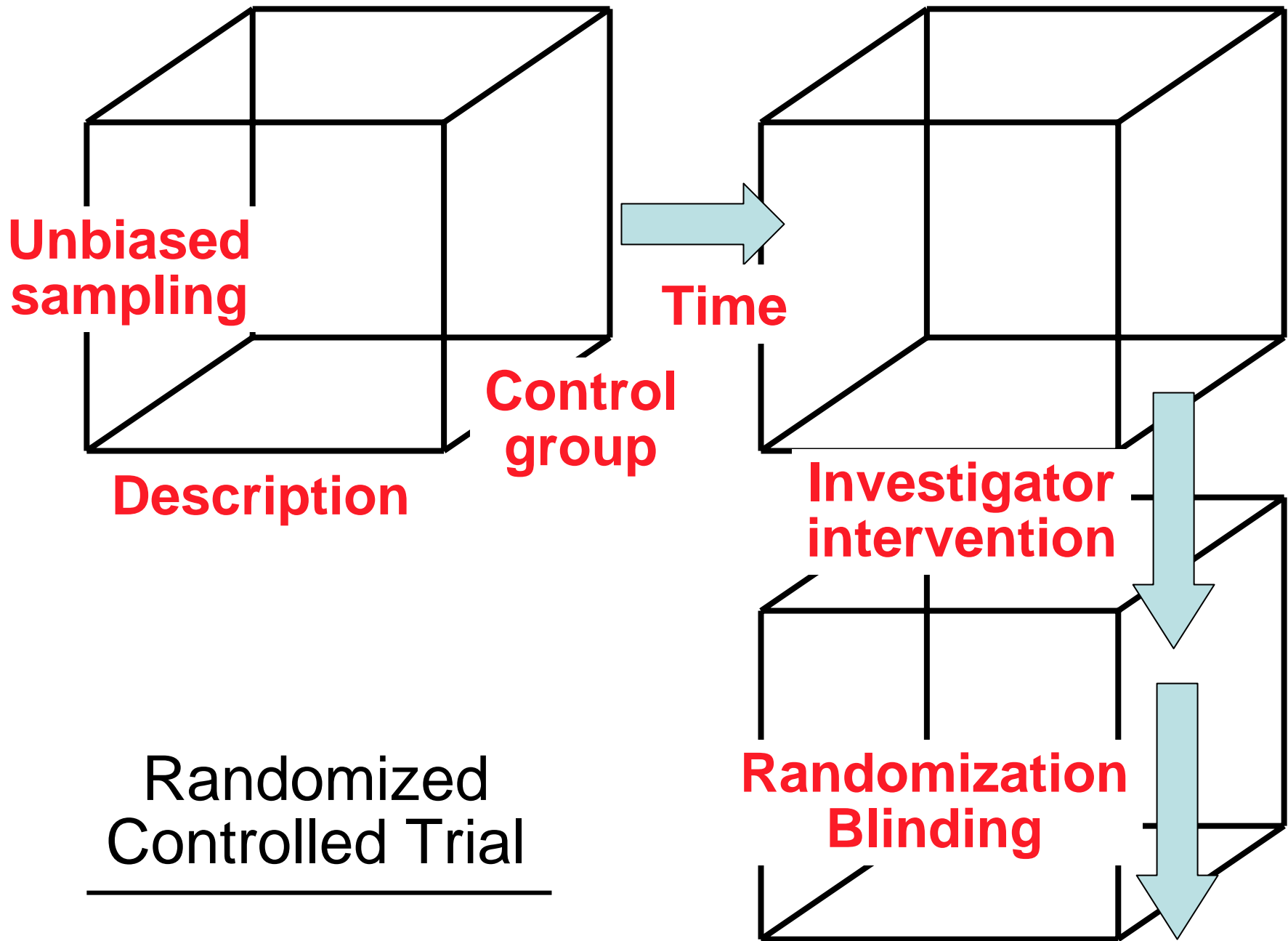


Cross-Sectional Study



Cohort Study





The Goals of Critical Thinking

- To teach physicians how to think.
- To teach physicians how to analyze.
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