Scientific writing workshop

An Overview of Study Design

F. Hosseinpanah
Obesity Research Center
Research Institute for Endocrine sciences
Shahid Beheshti University of Medical Sciences
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Tehran

Study Design

- Protocol for selecting persons to study and method in which data are collected

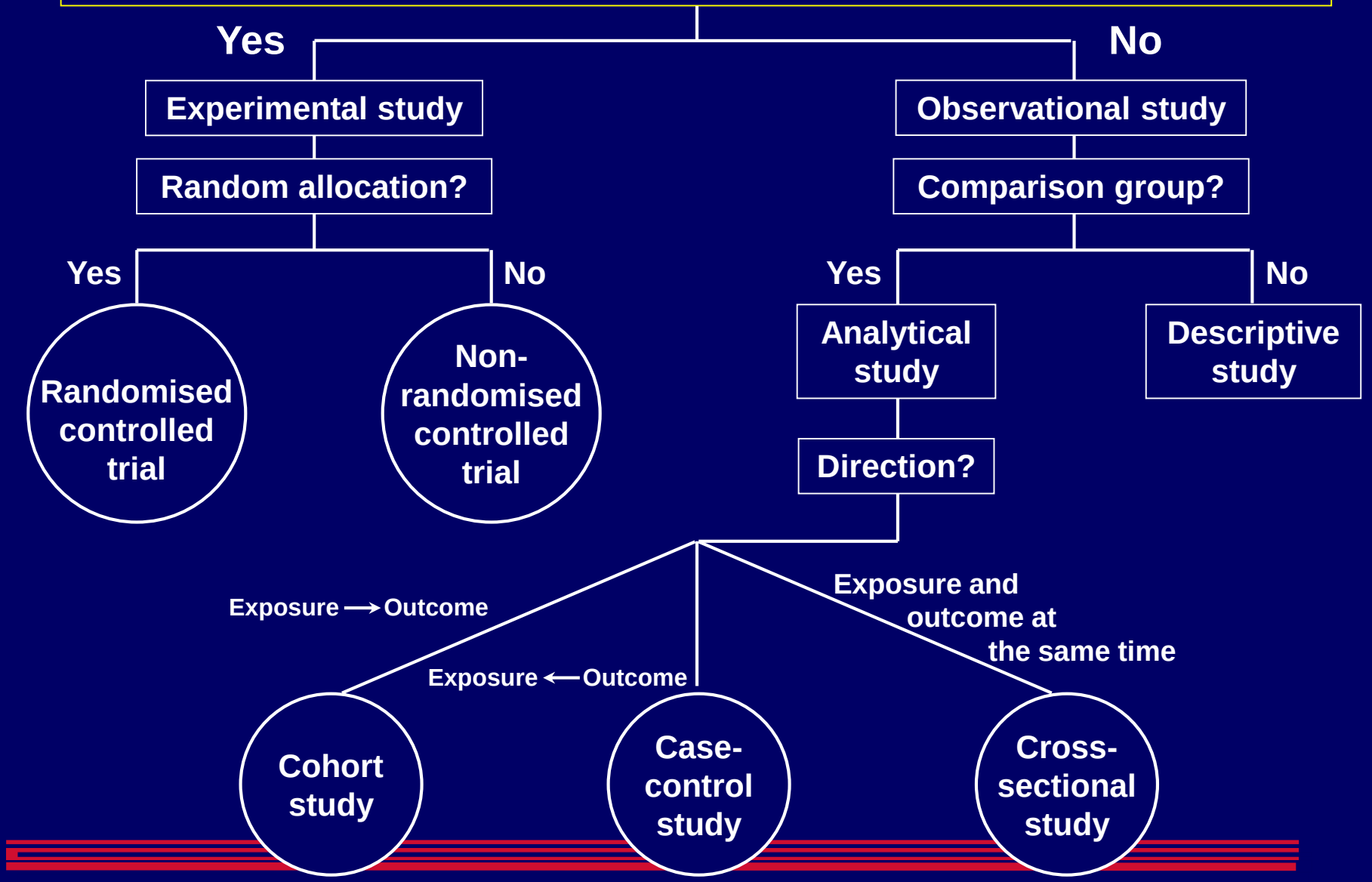
What can studies do?

Descriptive: Describe the situation

Analytical: Explain the situation

Experimental: Apply an intervention

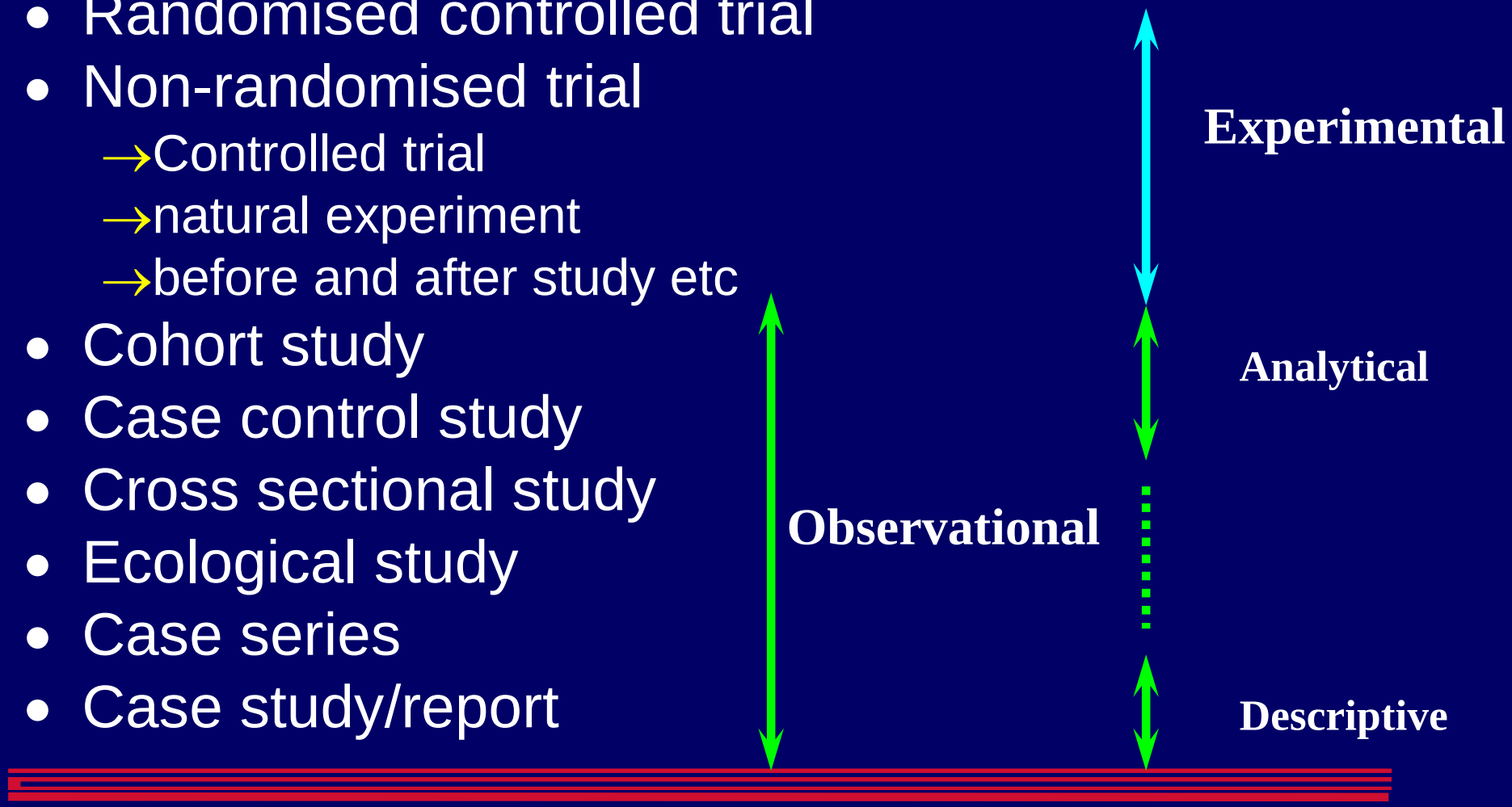
Did Investigator Assign Exposures?



Grimes and Schulz, *Lancet*, 359:57-61, 2002.

Hierarchy of study design

- Randomised controlled trial
- Non-randomised trial
  - →Controlled trial
  - →natural experiment
  - →before and after study etc
- Cohort study
- Case control study
- Cross sectional study
- Ecological study
- Case series
- Case study/report



Descriptive study

- A descriptive study is “concerned with and designed only to describe the existing distribution of variables, without regard to causal or other hypotheses

The descriptive triad

When a statistic is being described or interpreted, we need to reference

Who (person) -- what population or subgroup

When(time)-- what time point or time period

Where (place)-- the geographical location

The descriptive triad—or pentad?
Five "W" questions

- "W"
- questions—who, what, why, when, and where—and an
- implicit sixth question, so what?

Who

- Who has the disease in question? Age and sex are universally described, but other characteristics might be important too, including race, occupation, or recreational activities.
- The risk of venous thromboembolism, for example, increases exponentially with age.
- Only 1% of breast cancers arise in men, but Klinefelter's syndrome or a family history of breast cancer increase their risk.
- Race affects the risk of leiomyomas of the uterus.

What

- What is the condition or disease being studied?
- Development of a clear, specific, and measurable case definition is an essential step in descriptive epidemiology.
- Without such a description, the reader cannot interpret the report.
- Some conditions, such as fractures, can be overt.
-
- Other diagnoses might be challenging: multiple sclerosis, systemic lupus erythematosus, and pelvic inflammatory disease (salpingitis).

Why?

- Why did the condition or disease arise?
- Descriptive studies often provide clues about cause that can be pursued with more sophisticated research designs.

When

- When is the condition common or rare? Time provides important clues about health events.
- Example: outbreak of gastroenteritis soon after ingestion of staphylococcal toxin.
- Some temporal relations can be long—eg, vaginal adenosis and clear cell carcinoma of the vagina appeared years after intrauterine exposure to diethylstilboestrol.
- Osteomalacia in winter

Where

- Where does or does not the disease or condition arise?
- Geography has had a huge effect on health.
- Latitude plays a part in both multiple sclerosis and vitamin D deficiency
- sunlight might decrease or increase cancer risk.

So What?

- So What? The implicit “W” relates to the public health effect. In view of the proliferation of descriptive reports, what is their importance?

Examples of early leads from descriptive studies

Clinical observation	Underlying association
Hepatocellular adenoma in young women	Exposure to high-dose oral contraceptives
Blindness in newborn infants	High ambient oxygen concentrations in incubators
Kaposi's sarcoma in young men	Infection with HIV-1
Angiosarcoma of the liver in employees	Industrial exposure to vinyl chloride
Cataracts, heart defects, and deafness in newborns	Maternal infection with rubella during pregnancy

Types of descriptive studies

- Case report
- Case series
- Prevalence studies
- Surveillance
- Ecological studies

What studies can and cannot do

- An important caveat (often forgotten or intentionally ignored) is that descriptive studies, which do not have a comparison group, do not allow assessment of associations.

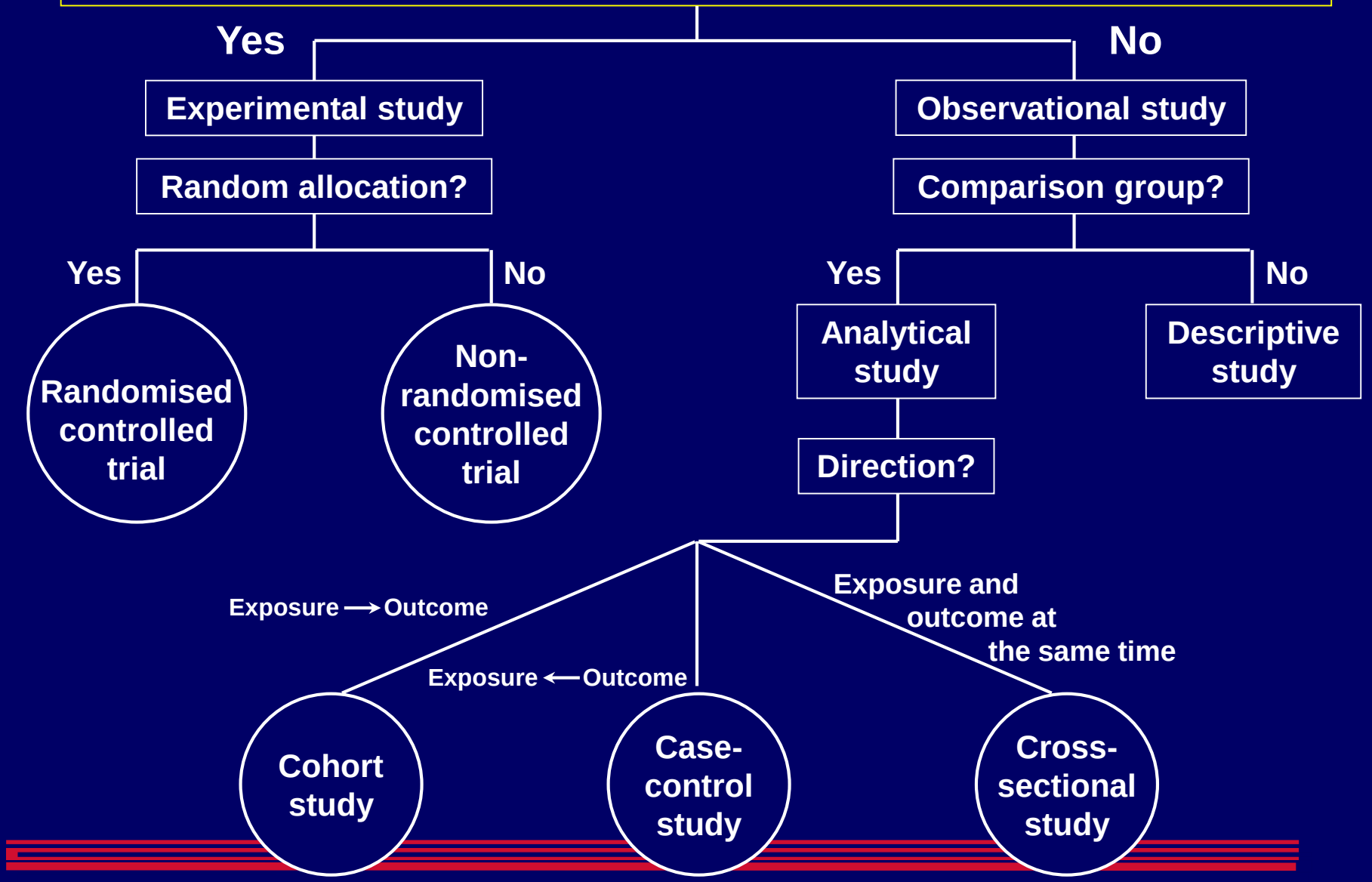
- Only comparative studies (both analytical and experimental) enable assessment of possible causal associations.

What studies can and cannot do?

- Starting at the bottom of the research hierarchy, descriptive studies are often the first foray into a new area of medicine. Investigators do descriptive studies to describe the frequency, natural history, and possible determinants of a condition.

- The results of these studies show how many people develop a disease or condition over time, describe the characteristics of the disease and those affected, and generate hypotheses about the cause of the disease.

Did Investigator Assign Exposures?



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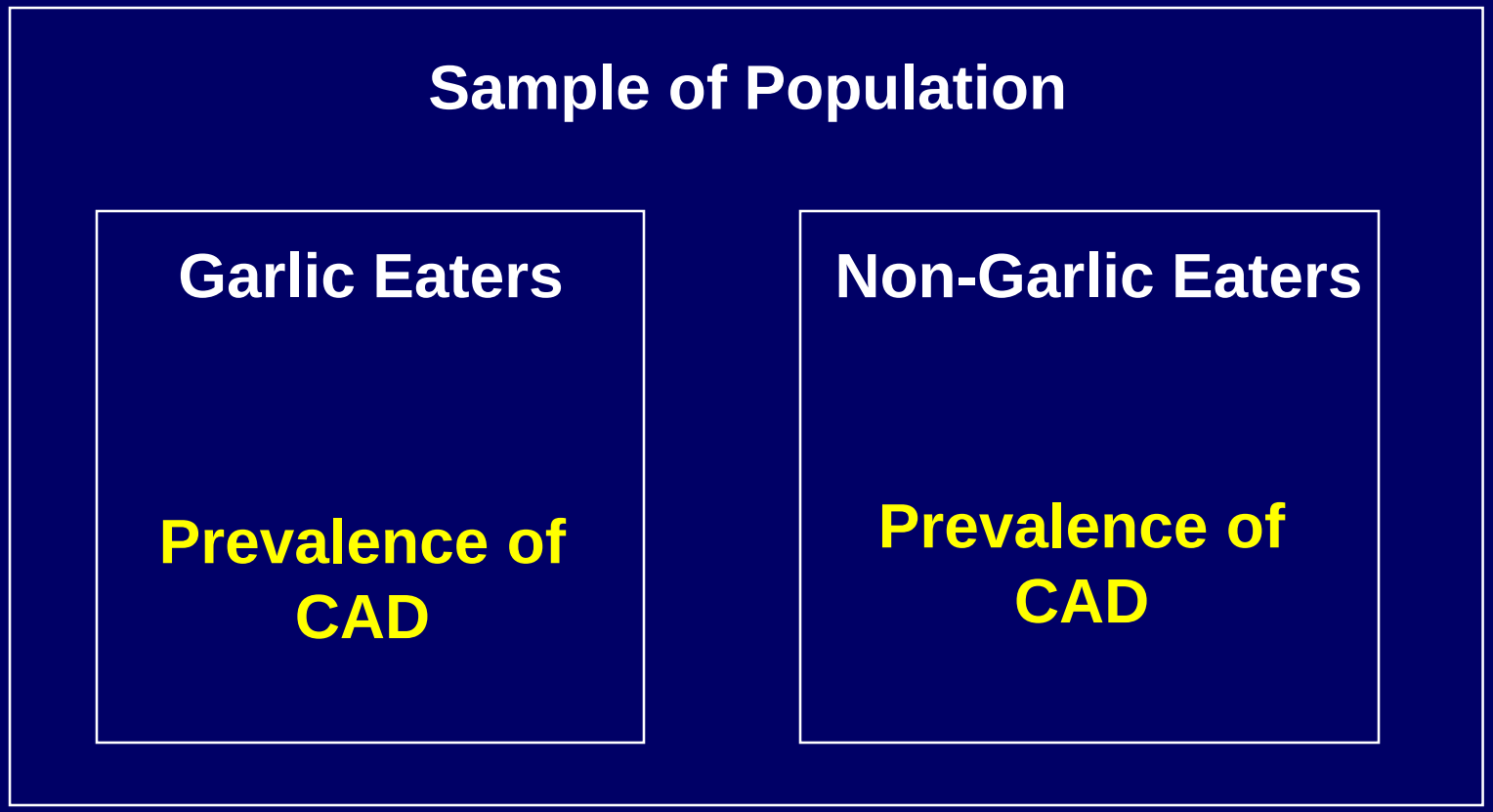
Example of a Cross-Sectional Study

Association between garlic consumption

and CAD in the Family Practice Clinic

Cross-sectional Study



Time Frame = Present

Cross-sectional Study

CAD	Garlic Consumption +	Garlic Consumption -
+	10	90
-	90	10

Research Question :

- What is the prevalence of chlamydia infection in women attending STD clinics ?

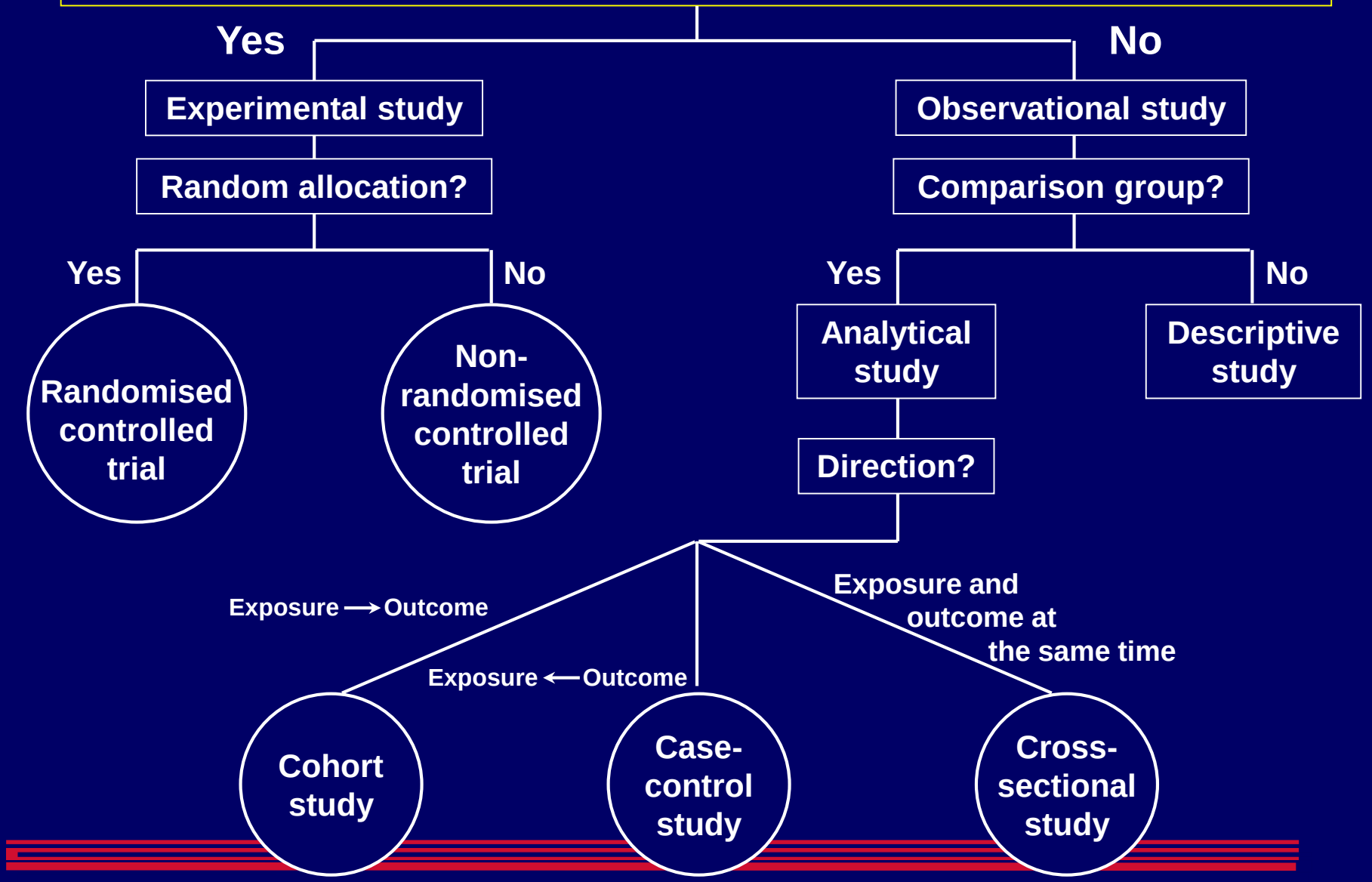
- Is it associated with use of OCP ?

Example :

Predictor	Chlamydia +	Chlamydia -	total
OCP +	4	16	20
OCP -	8	72	80
Total	12	88	100

$$\text{Relative prevalence} = \frac{4/20}{8/80} = 2.0$$

Did Investigator Assign Exposures?



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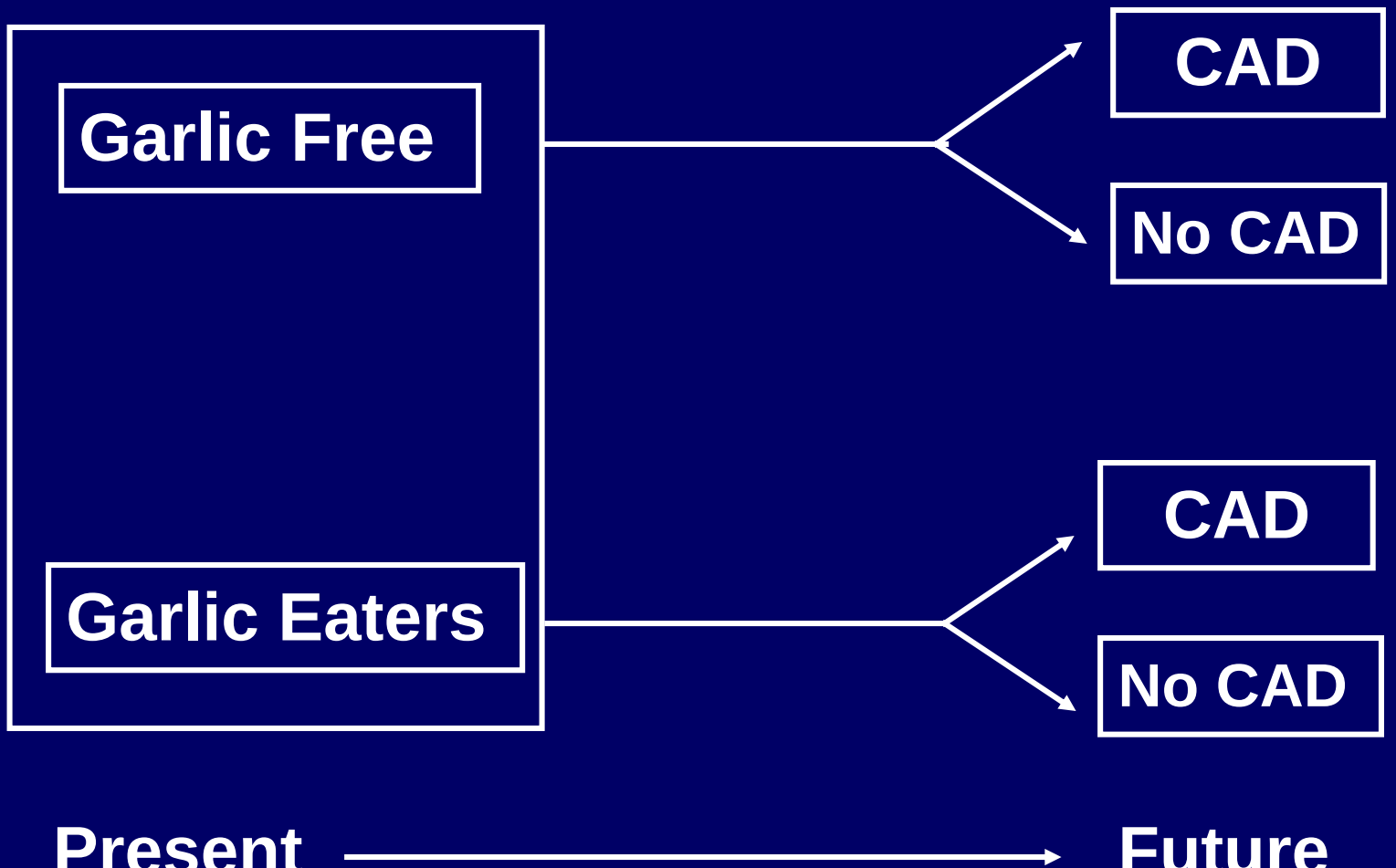
Cohort Study

- Begin with disease-free patients
- Classify patients as exposed/unexposed
- Record outcomes in both groups
- Compare outcomes using relative risk

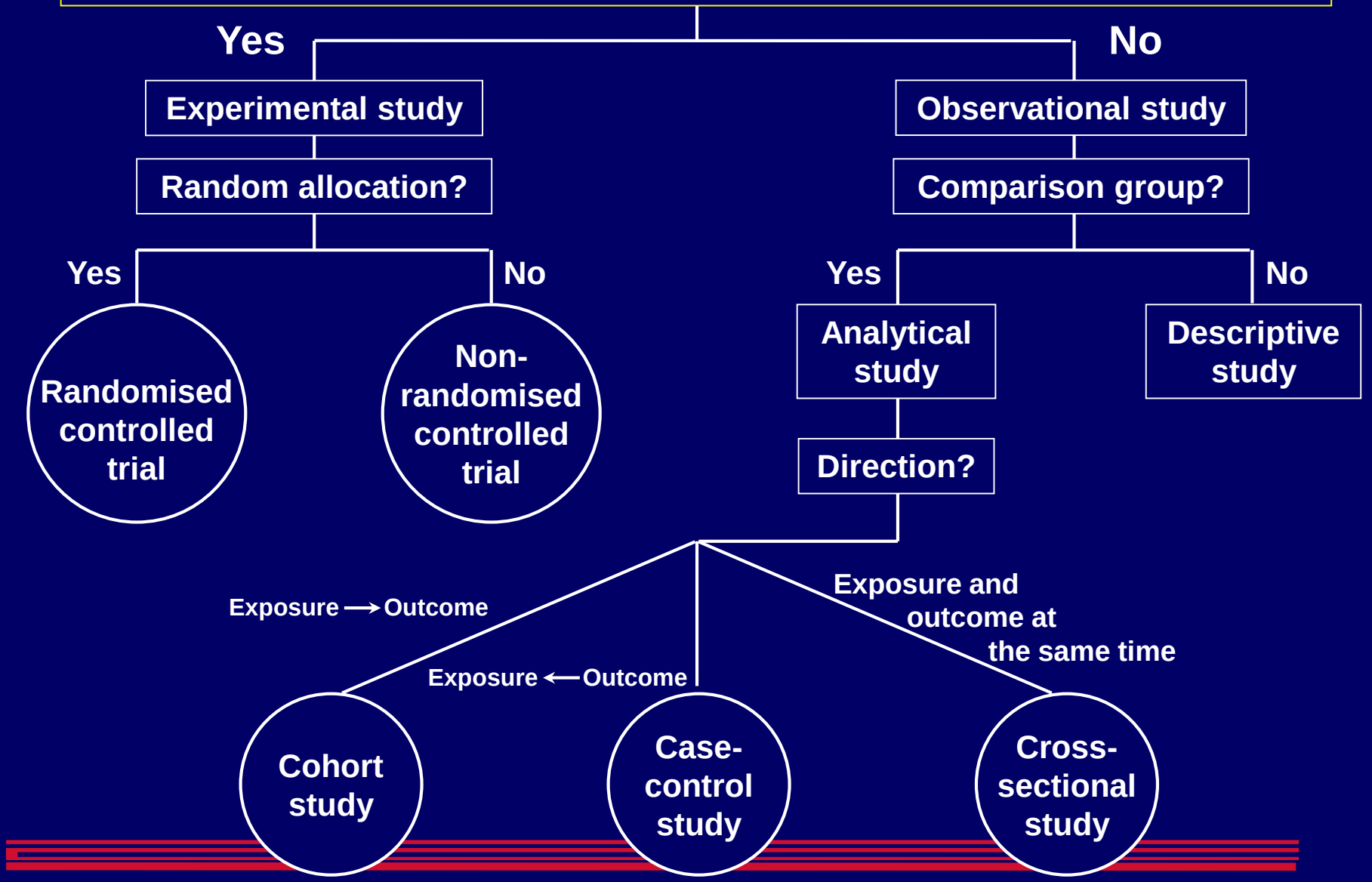
Example of a Cohort Study

To see the effects of garlic use on CAD mortality in a population

Prospective Cohort Study



Did Investigator Assign Exposures?



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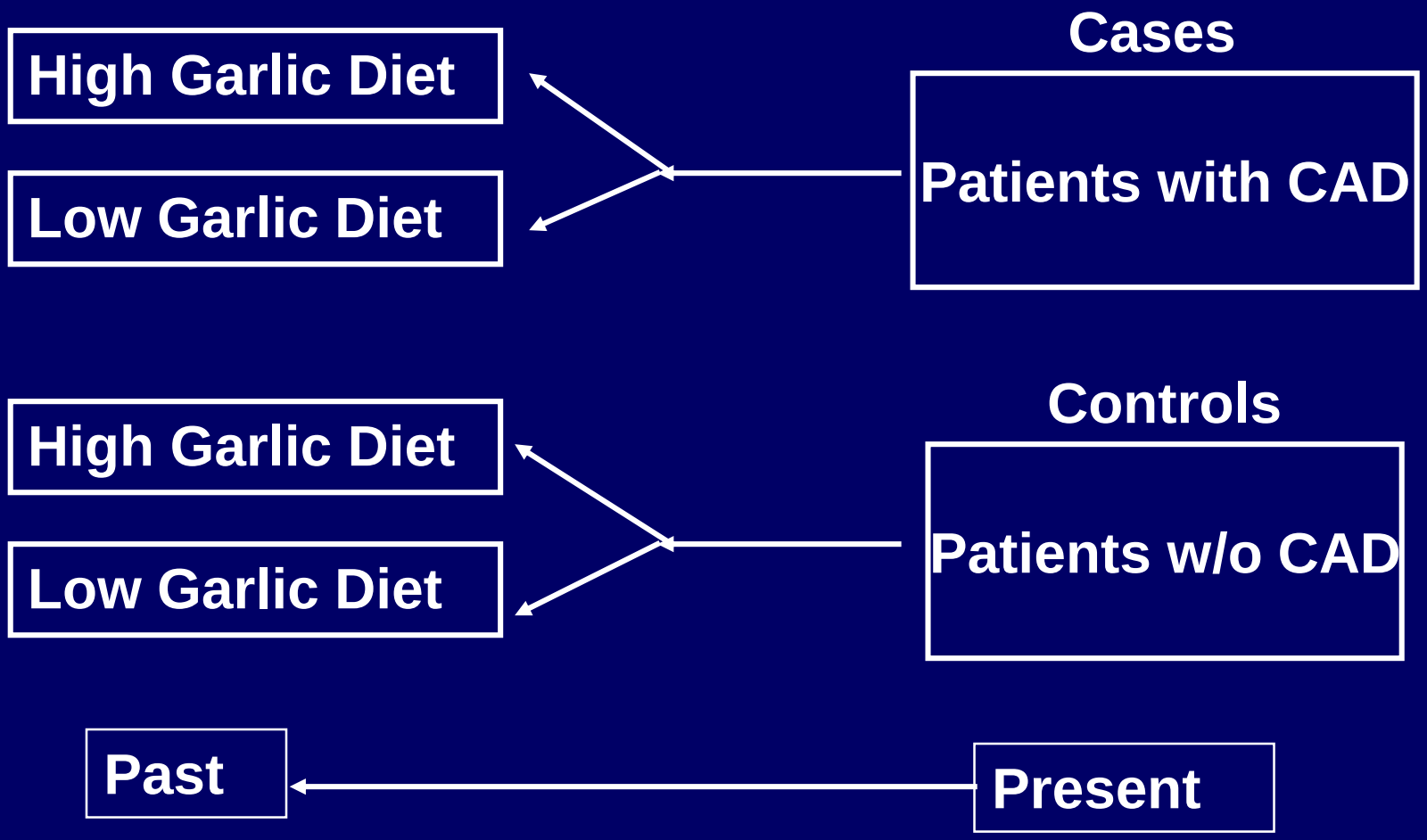
Example of a Case-Control Study

Are those with CAD less likely to have consumed garlic?

Case-Control Study



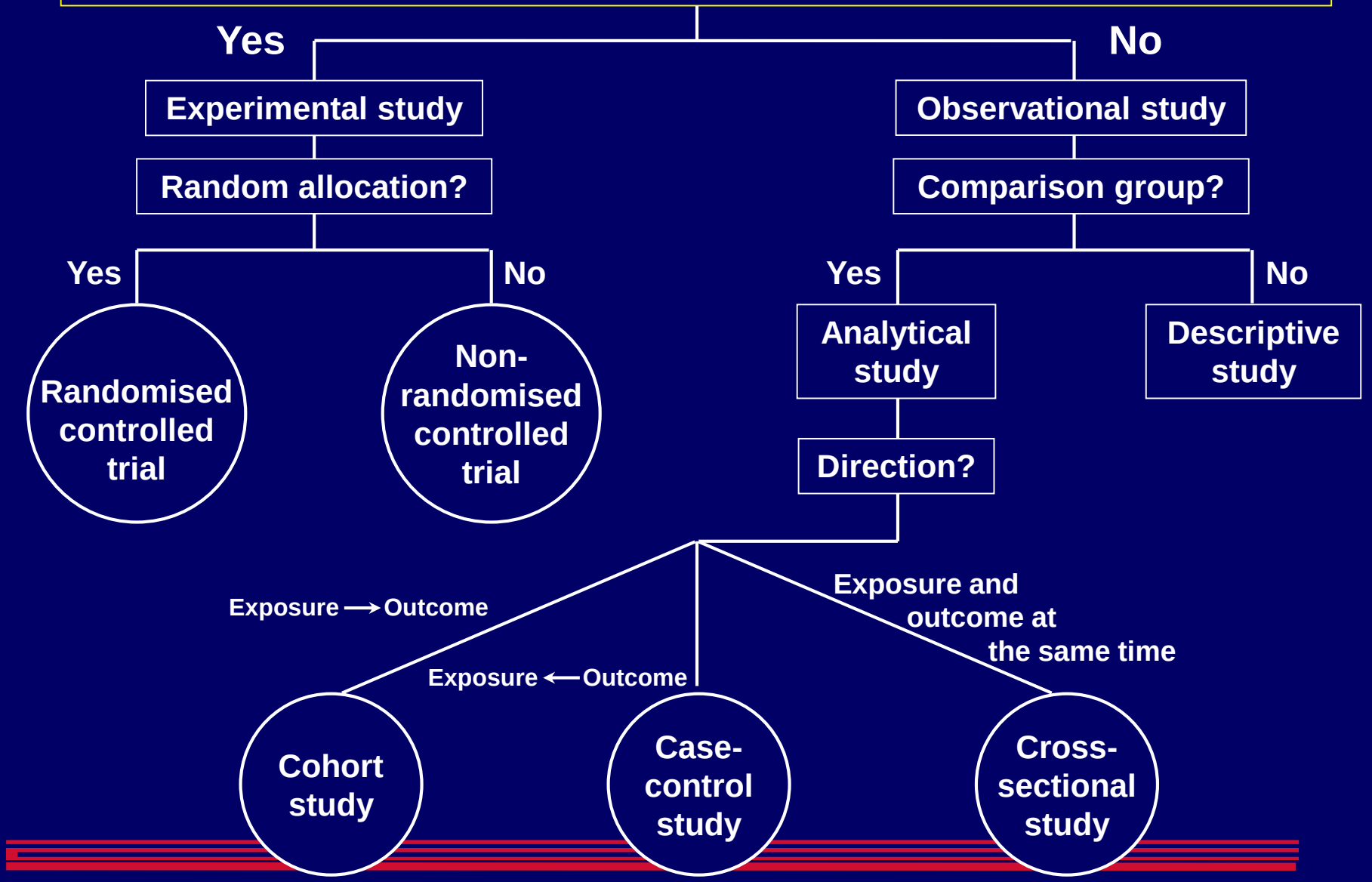
Case-control study: thinking backwards

- prevalence (or amount) of exposure to a risk factor
- Case-control studies are especially useful for outcomes that are rare or that take a long time to develop, such as CVD and cancer.
- The Achilles heel of case-control studies is choosing an appropriate control group.

Case-control study: thinking backwards

- Additionally, recall bias (better recollection of exposures among the cases than among the controls) is a persistent difficulty in studies that rely on memory
- Because the case-control study lacks denominators, investigators cannot calculate incidence rates, relative risks, or attributable risks.

Did Investigator Assign Exposures?



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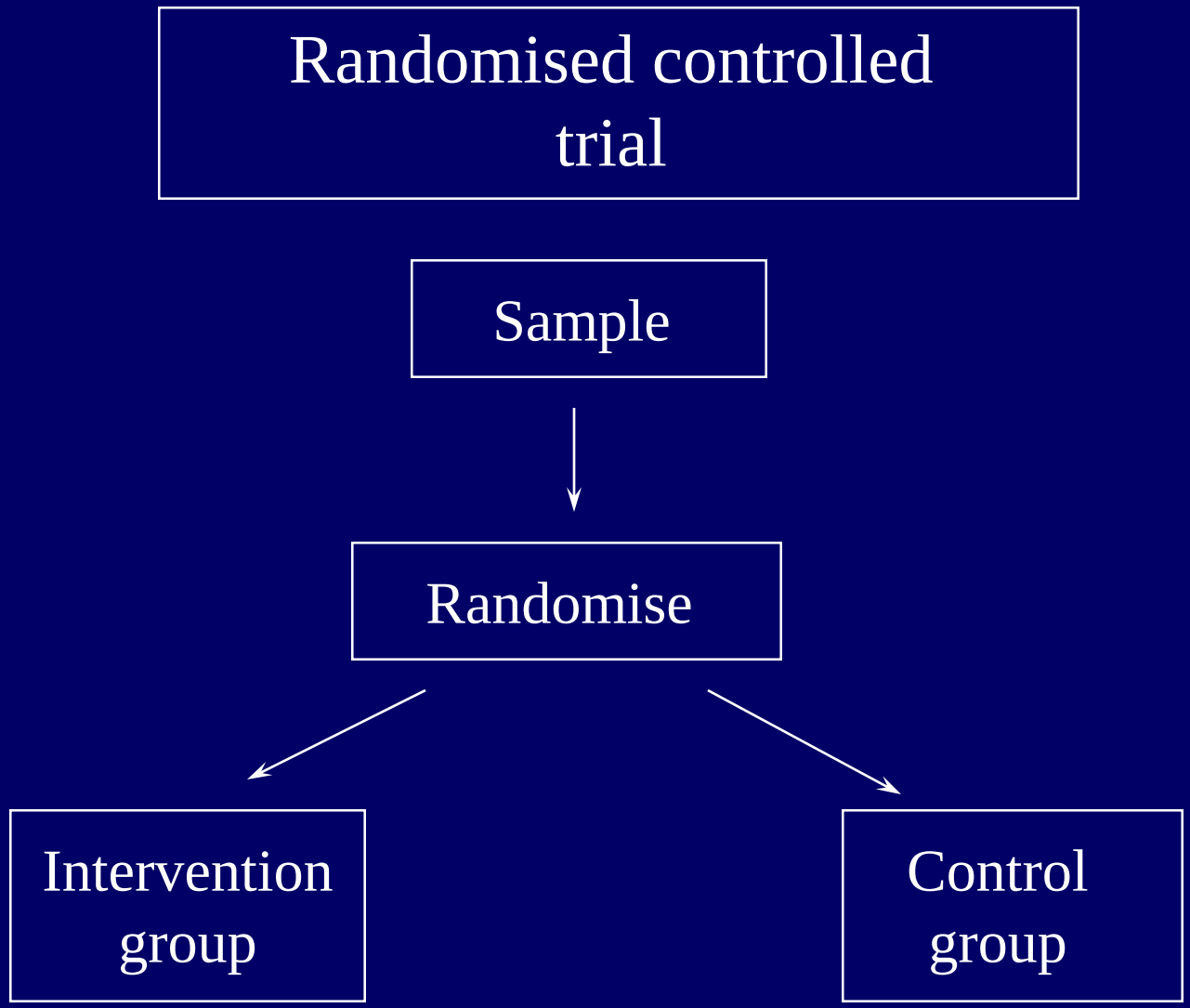
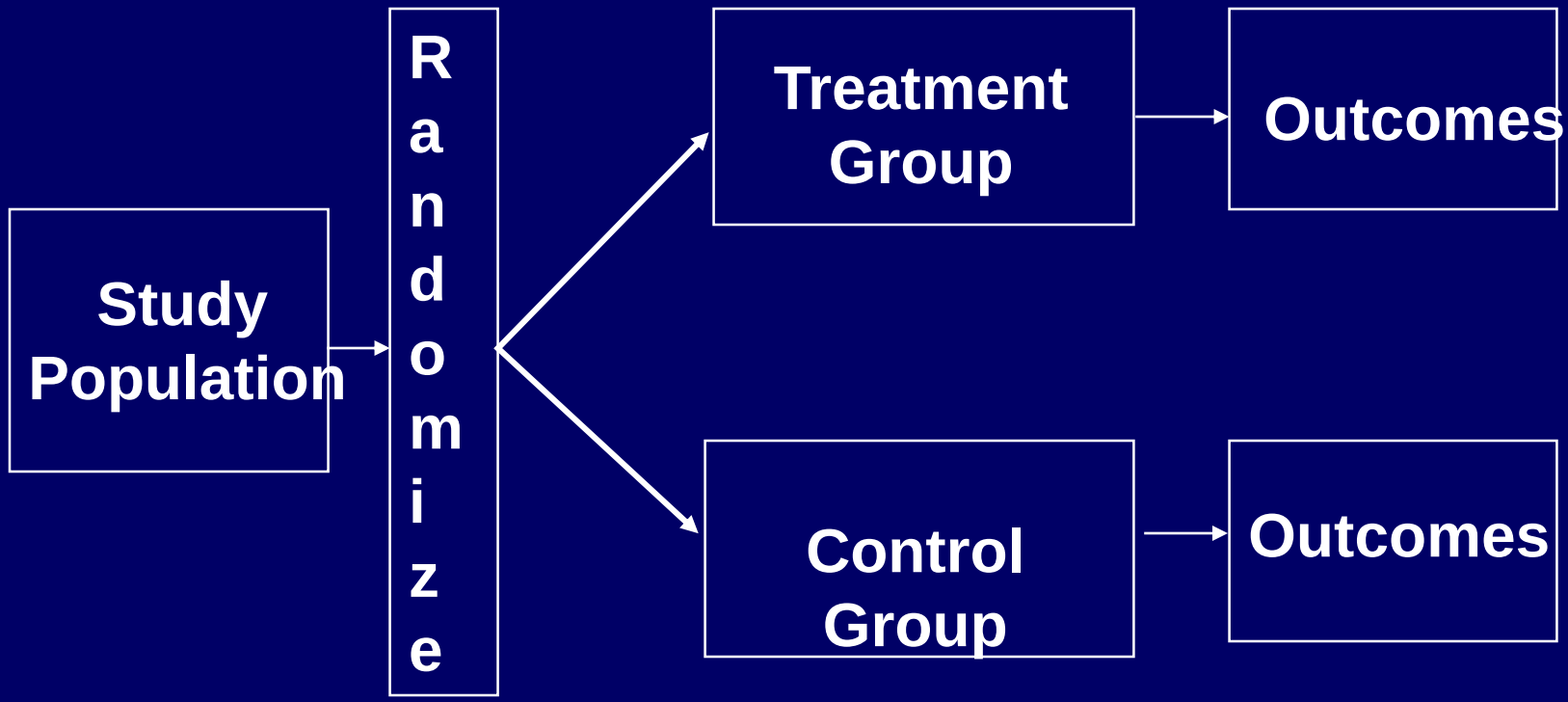
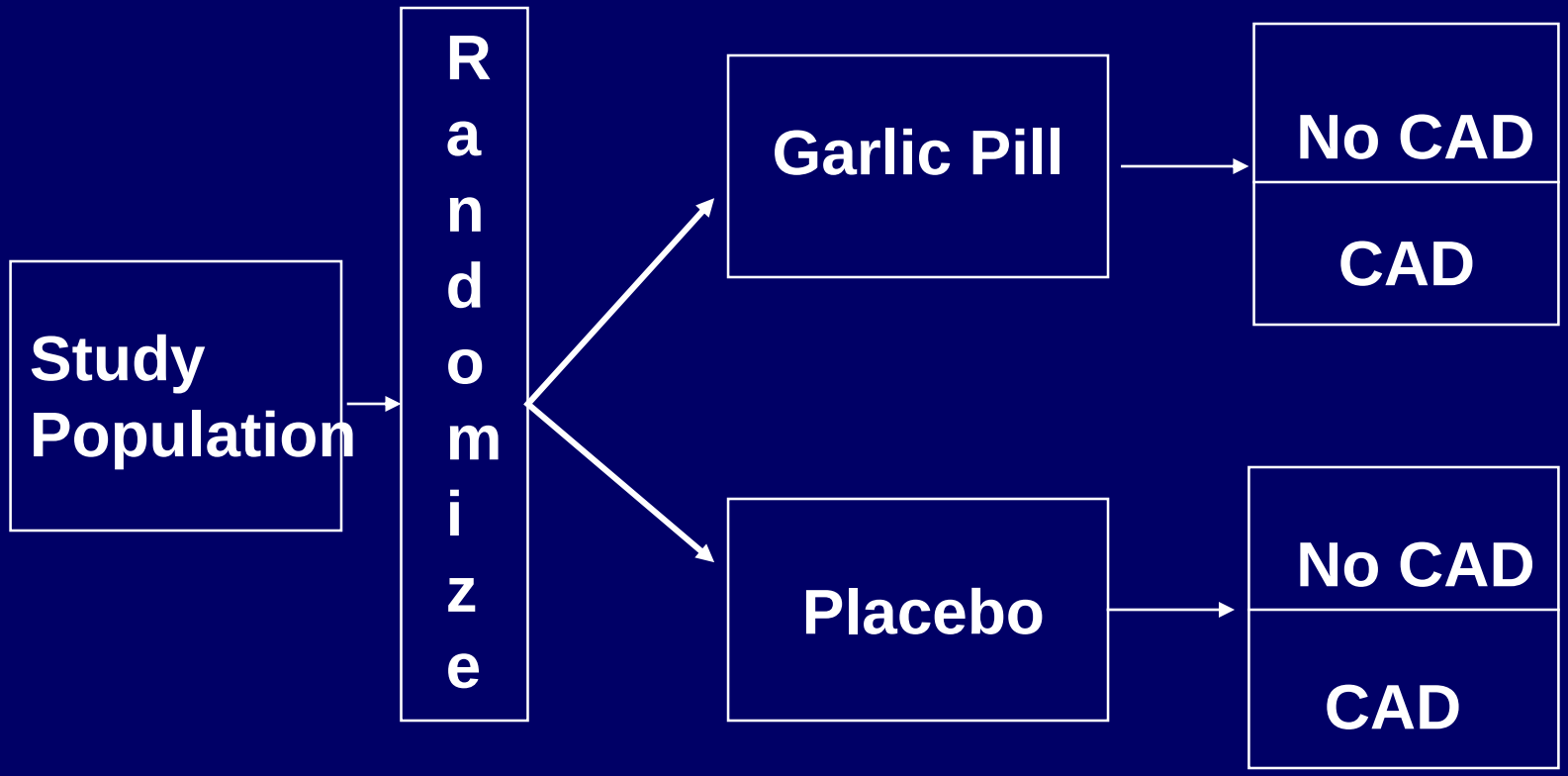

Randomised controlled trial
Sample
Randomise
Intervention group
Control group

Clinical Trial



Clinical Trial



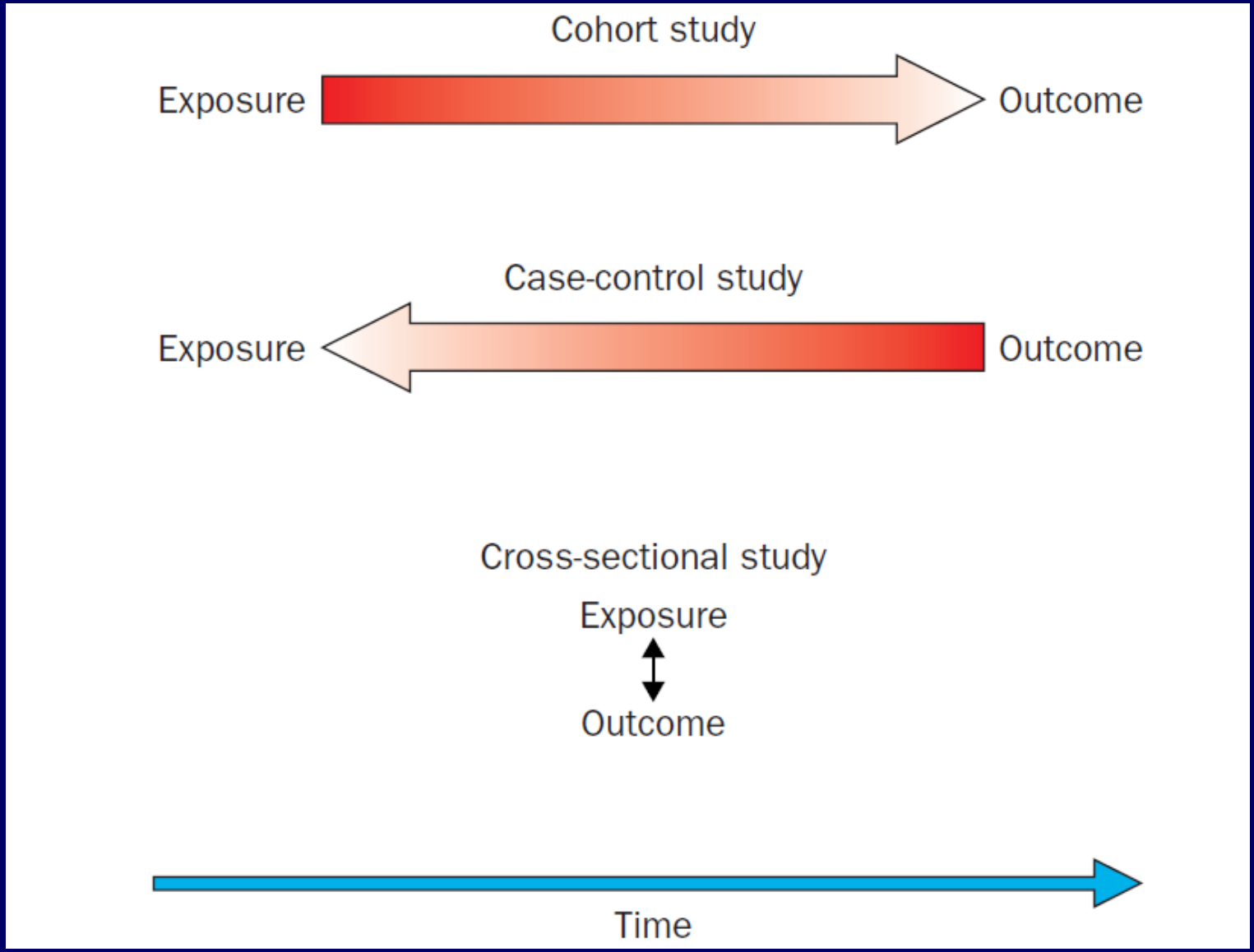
Randomised controlled trial: gold standard

- The RCT is the only known way to avoid selection and confounding biases in clinical research.
- When properly implemented, random allocation precludes selection bias.

Randomised controlled trial: gold standard

- If properly designed and done, a randomised controlled trial is likely to be free of bias and is thus especially useful for examination of small or moderate effects.

- Drawbacks :external validity(volunteers)- cannot be used for harmful substances


Cohort study
Exposure
Outcome
Case-control study
Exposure
Outcome
Cross-sectional study
Exposure
Outcome
Time

Study Designs

Type of Study	Descriptive	Analytical
Case study	Yes	No
Case series	Yes	No
Cross-sectional	Yes	Yes
Case-control	Yes	Yes
Cohort	Yes	Yes
Randomised control trial	Yes	Yes

Measures of associations

Relative Risk

$$RR = \frac{Incidence_{exposed}}{Incidence_{unexposed}} = \frac{\frac{a}{a+b}}{\frac{c}{c+d}}$$

Relative Risk

$$\text{Relative risk} = \frac{\text{disease "rate" in exposed}}{\text{disease "rate" in unexposed}}$$

If relative risk $>$ 1 --- $>$ risk factor

If relative risk $=$ 1 --- $>$ no risk

If relative risk $<$ 1 --- $>$ protective factor

Cohort Studies

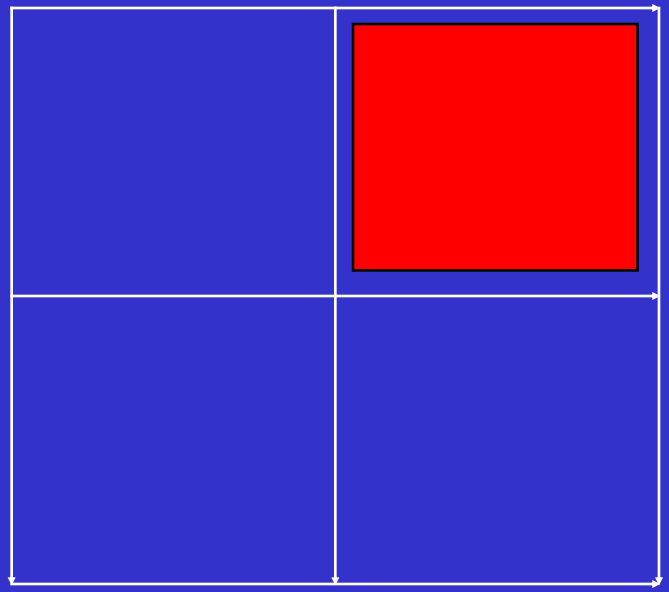
	MI		
	Yes	No	Total
Serum Cholesterol (mg%)			
>250	10	125	135
≤250	21	449	470
Total	31	574	605

Risk Ratio (cum. incidence)=
cum. inc. exp/cum. inc. unexp. (5-yr) =
10/135/21/470 = 0.074/0.045 = 1.66

$$\text{Odds} = \frac{\text{probability}}{1 - \text{probability}}$$

$$\text{Odds Ratio} = \frac{\text{Odds of disease in the exposed group}}{\text{Odds of disease in the unexposed group}}$$

$$\text{Odds} = \frac{\text{The Probability of something happening}}{\text{The Probability of something not happening}}$$



$$\frac{\%۲۵}{۷۵\%}$$

$$P = \frac{Odd}{Odd+1}$$

$$Odd = \frac{P}{1-P}$$

calculation of an odds ratio : example ; artificial sweeteners & bladder cancer

	Cases (Disease)	controls
Exp		
not		

Odds ratio :

$$\frac{0.757}{0.739} = 1.02$$

Odds of exposure in cases $= \frac{1293}{1707} = 0.757$

Odds of exposure in controls $= \frac{2455}{3321} = 0.739$

Case-Control

	Lung Cancer		
	Yes	No	Total
Exposure Usual Industry			
Metal	25	10	35
Sales	55	85	140
Total	80	95	175

Odds ratio = (axd)/(bxc) = (25x85)/(10x55) = 3.86

Breast cancer-specific survival at 7-year follow up

Group	Dead	Alive	Total
Mamography	71	58077	58148
Controls	76	41028	41104
Total	147	99105	99252

Group	Dead	Alive	Total
Mamography	71	58077	58148
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Total	147	99105	99252

Risk(mamography)=71/58148=0.00122

Risk(controls)=76/41104=0.00185

Relative risk= 0.00122/0.00185=0.659

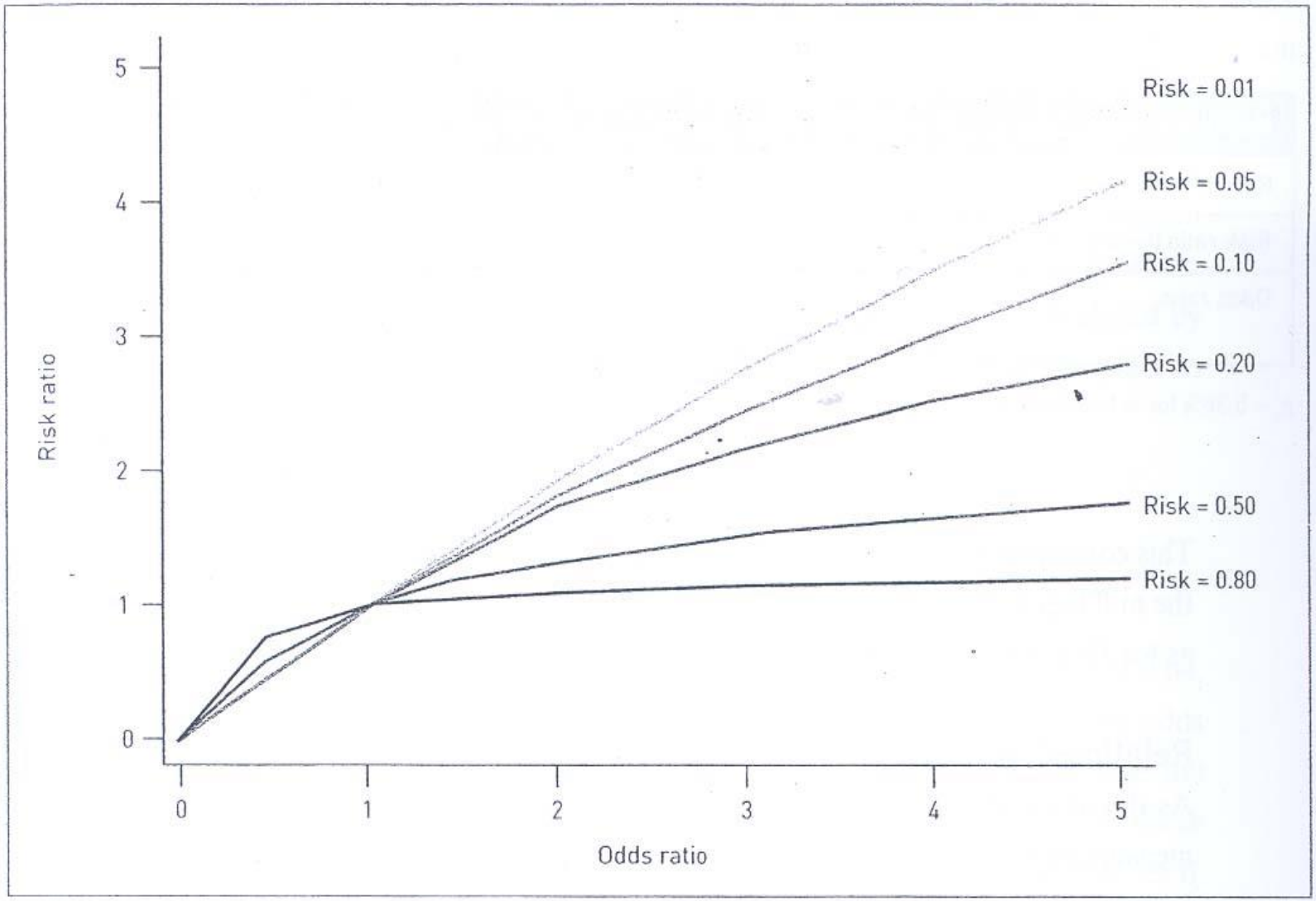
Group	Dead	Alive	Total
Mamography	71	58077	58148
Controls	76	41028	41104
Total	147	99105	99252

Odds(mamography)=71/58077=0.001222

Odds(controls)=76/41028=0.00185

Odds Ratio=0.00122/0.00185=0.659

Figure 1. Relationship between odds ratio and risk ratio.



Measures of association

•An odds ratio can also be calculated for cross-sectional, cohort, and randomised controlled studies. here, the disease-odds ratio is the ratio of the odds in favor of disease in the exposed versus that in the unexposed.

•Odds ratio does not indicate the relative risk when the proportion with the outcome is greater than 5–10%— ie, the term has little clinical relevance or meaning with higher incidence rates.

Conclusion

- Clinical research falls into two general categories:

  experimental and observational, based on whether the investigator assigns the exposures or not.
- Experimental trials can also be subdivided into two: randomised and non-randomised.
- Observational studies can be either analytical or descriptive.
- Analytical studies feature a comparison (control) group, whereas descriptive studies do not.
- Within analytical studies, cohort studies track people forward in time from exposure to outcome. by contrast, case-control studies work in reverse, tracing back from outcome to exposure.

Conclusion

- Cross-sectional studies are like a snapshot, which measures both exposure and outcome at one time point.
- Descriptive studies, such as case-series reports, do not have a comparison group. thus, in this type of study, investigators cannot examine associations, a fact often forgotten or ignored.

Analytical Studies: Summary

	Cross-Sectional	Case-Control	Cohort	RCT
Cost	+	++	+++	++++
Duration	+	++	+++	+++
Sample Size	Varies	Small	Large	Varies
Incidence, Prevalence	Prevalence	None	Incidence	Incidence
Multiple Outcomes	Yes	No	Yes	Yes
Bias Prone	Yes	Yes	No	No
Causality	No	No	No	Yes