Case-control studies

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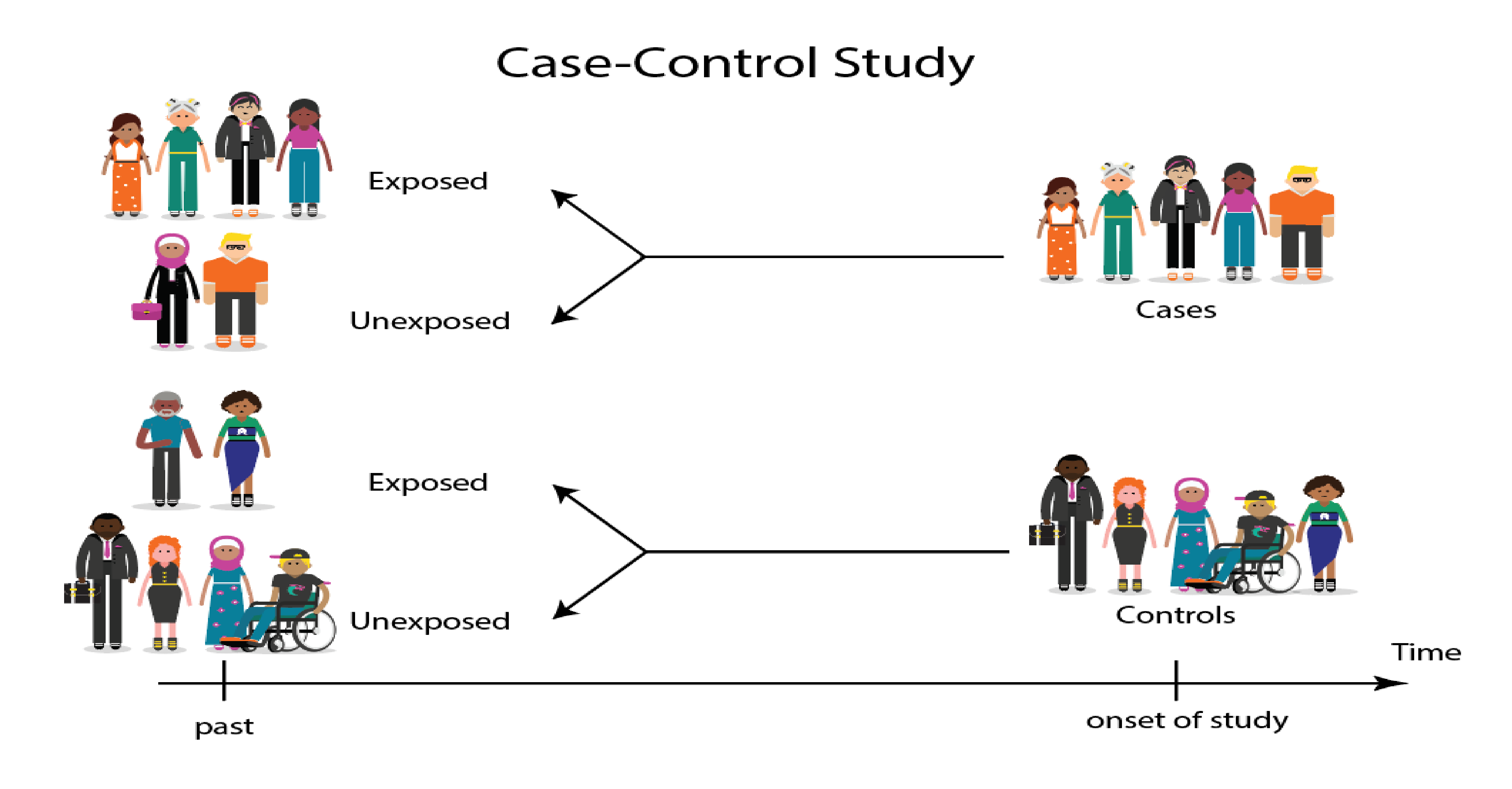
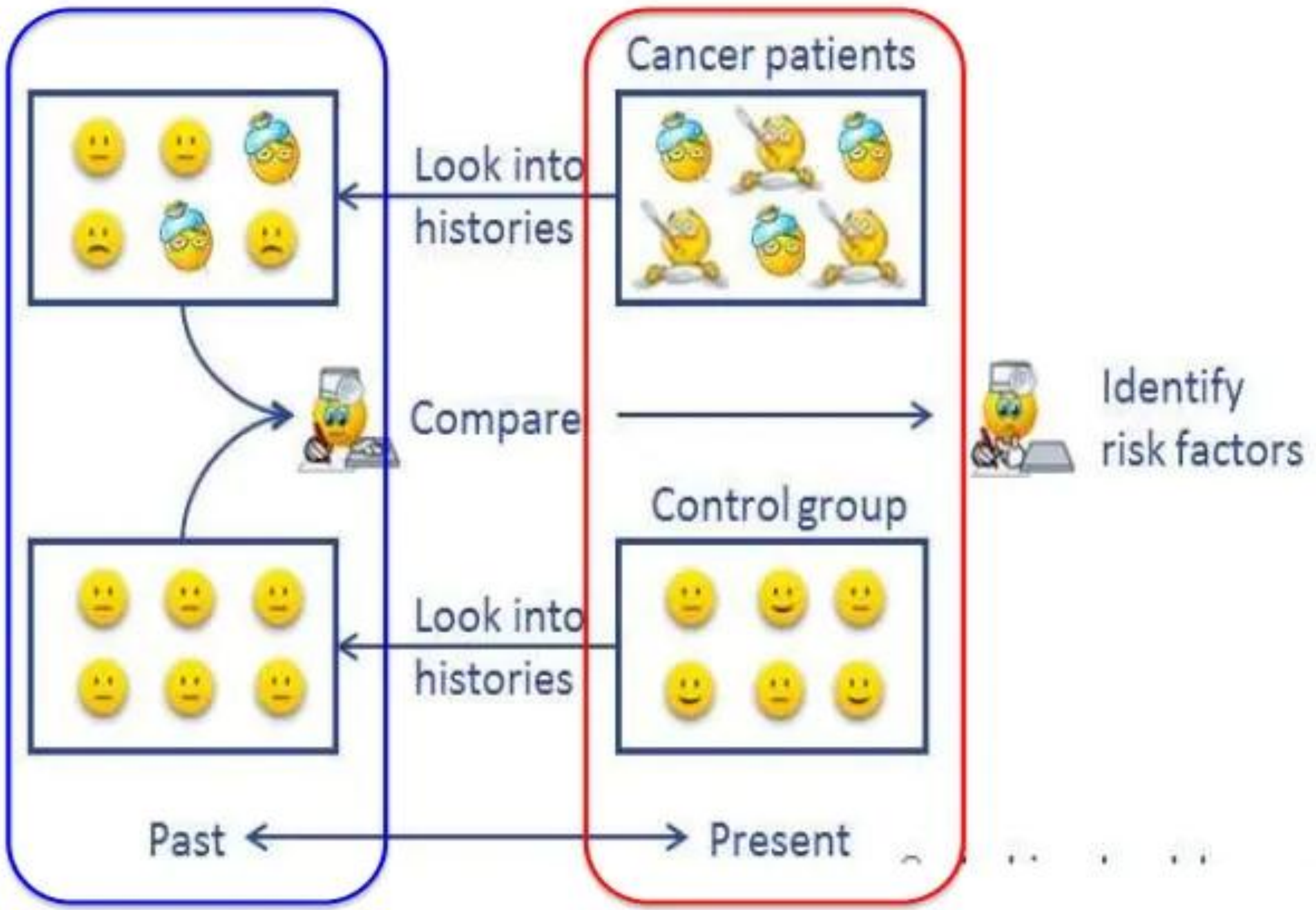


Case-control studies

Are studies in which a group of people with a particular disease (the cases) are compared with a group of people without the disease (the controls). The purpose of the comparison is to determine whether, in the past, the cases have been exposed more (or less) often to a specific factor than the controls

- This type of study is done to identify factors that could be responsible for the development of a disease or drug use problem.


Cancer patients
Look into histories
Compare
Identify risk factors
Control group
Look into histories
Past
Present

CASE-CONTROL STUDIES

- The direction of time
- Cases identified now
- Data on past events collected

CASE-CONTROL STUDY DESIGN

- Designed to assess association between disease occurrence and exposures (e.g., causative agents, risk factors) suspected of causing or preventing the disease.

Case-control studies

- A group of people with a disease are compared to a group without the disease from the same population.
- Compare exposure to risk factors in both groups
- Able to look at many different possible risk factors
- Able to study diseases with a long latency period
- Most common analytic study design seen in the medical literature today

Case-control studies

- In general, the cases included in a case-control study include people with one specific disease only
- But, a case-control study can provide information on a wide range of possible exposures that could be associated with that particular disease
- Useful for the study of rare diseases
- Not suitable for the study of rare exposure
- Relatively small and inexpensive
- Takes a relatively short time to complete
- Can test current hypotheses
- Cannot measure disease incidence

CASE-CONTROL STUDIES

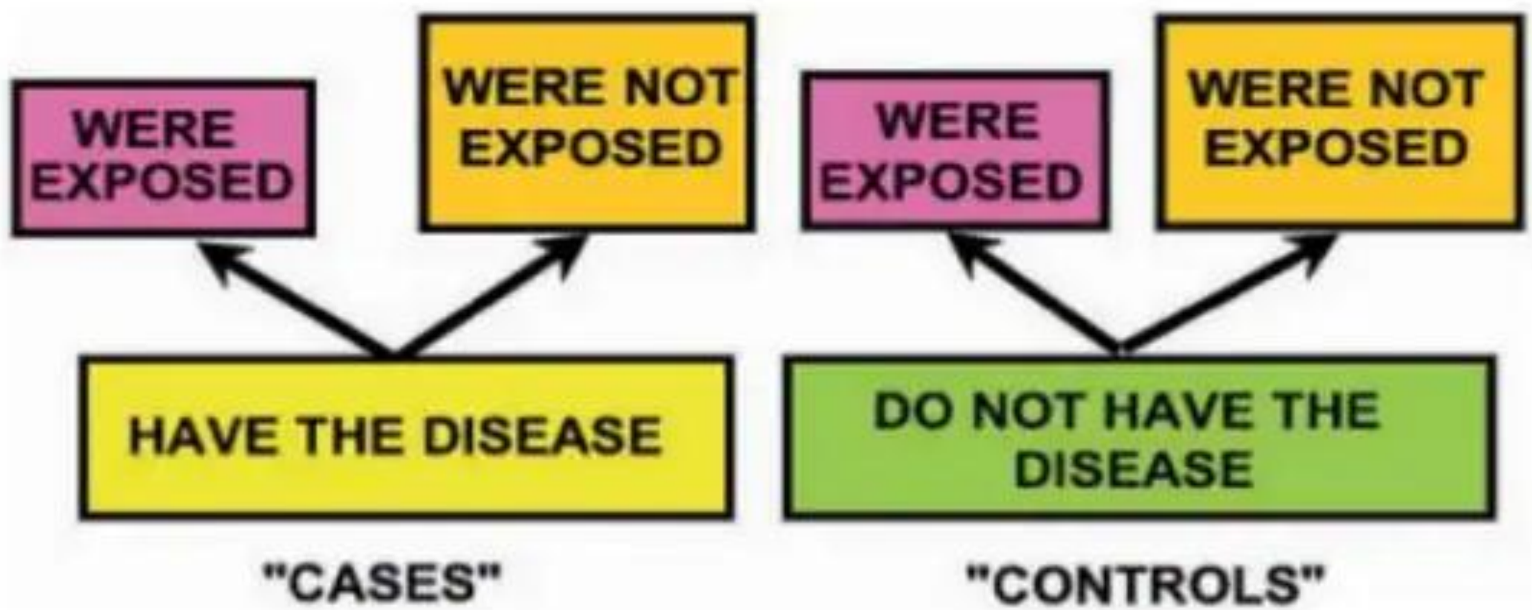
- Cases have the disease of interest

Eg. Cerebral palsy

- Controls do not have the disease

Eg. Healthy babies born at the same time

Design of a case-control study



Hallmark of Case Control Study:
from cases and controls and searches for exposure.

Example

Alcohol Consumption and Risk of Tuberculosis: Seattle/King County, Washington, 1988 through 1990

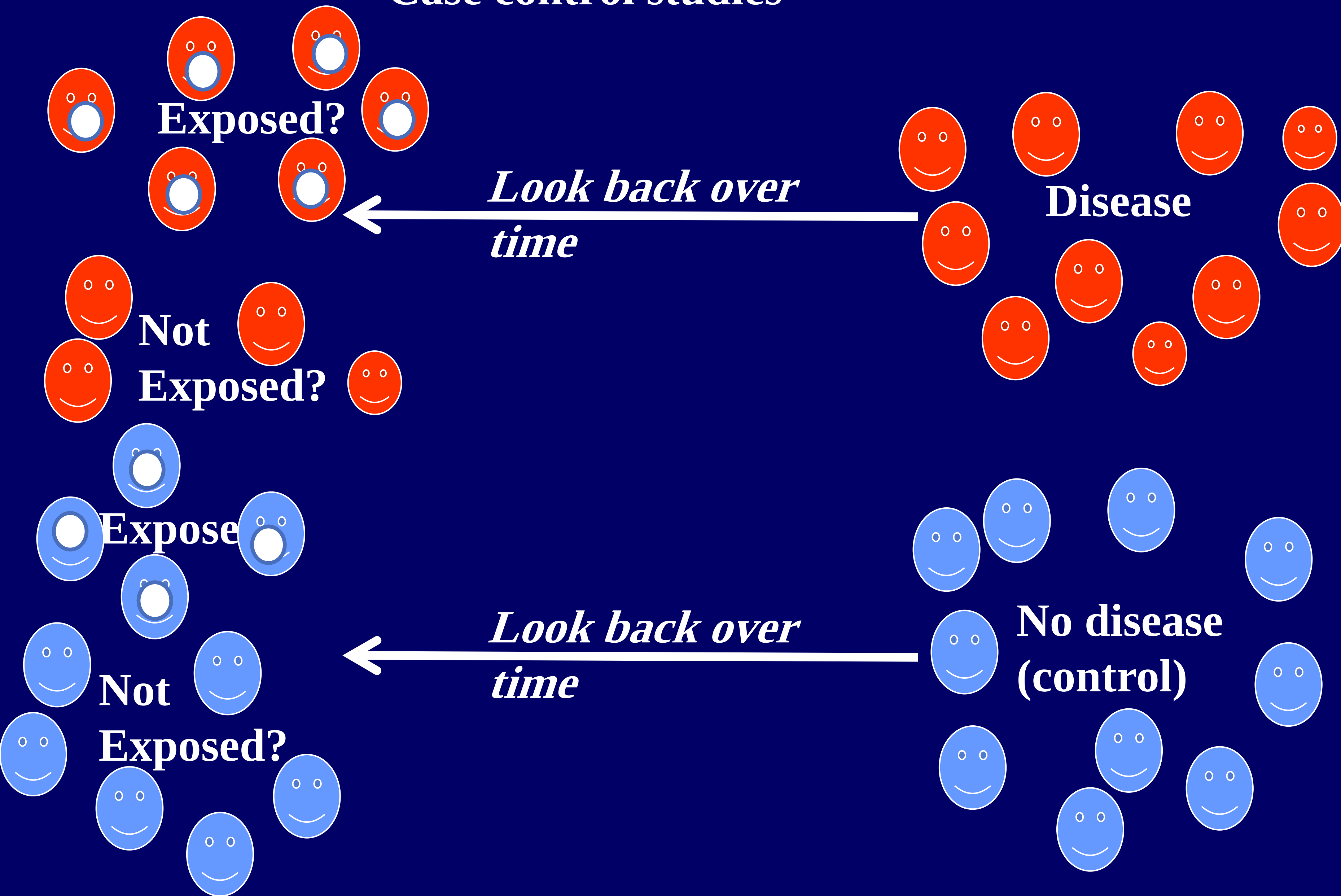
Alcohol Consumption[a]	Case Patients (n = 151)	Control Patients (n = 545)	Adjusted for Age		Adjusted for Age and Smoking[b]	
			OR	95% CI	OR	95% CI
None	60	263	1.0	Reference	1.0	Reference
Light to moderate	52	214	1.1	0.7, 1.7	0.9	0.6, 1.5
Heavy	39	68	2.8	1.7, 4.8	2.0	1.1, 3.7

Buskin et al (1994). *American Journal of Public Health*,84, No. 1 1

CASE-CONTROL STUDY DESIGN

- More efficient than a cohort study because a smaller sample size is required.
- One key feature of a case-control study, which distinguishes it from a cohort study, is the selection of subjects based on disease status.
- Controls are chosen from the same population yielding the cases

Case control studies



CASE-CONTROL STUDIES

Strengths

- Suited to study disease with long latency periods, but can be used in outbreaks investigations
- Optimal for rare diseases
- Efficient in terms of time and costs: relatively quick and inexpensive
- Allows for evaluation of a wide range of possible causative factors that might relate to the disease being studied
- Odds ratio estimated

CASE-CONTROL STUDIES

Limitations

- Very susceptible to bias (especially selection and recall bias) as both the disease and the exposure have already occurred when participants enter the study. Cases and controls might not be representative of the whole population
- We cannot calculate incidence or prevalence rate of disease
- We cannot be certain that exposure came before disease
- Choice of controls difficult
- Controls do not usually represent non-exposed population
- Past records incomplete
- No absolute risk estimates

Design of case control studies

- **Comparability:Two groups must be as similar to each other as possible so selection of controls is very important. Controls must be as similar as possible to cases – except that they do not have the outcome (disease). (matching)**
- **Outcome (disease) must be very clearly defined. (Diagnostic criteria must be clear)**
- **Use objective data about exposure status wherever possible, to reduce the risk of bias (biological or environmental indicators)**

2.Matching

How many controls?

- **control-to-case ratio is 1 : 1**

    is the optimal when the number of available cases and controls is large and the cost of obtaining information from both groups is comparable
- **control-to-case ratio is 1 : n**

    When the number of cases is limited or when the cost of obtaining information is greater for cases or controls

- **As the number of controls per case increases, the power of the study also increase**

- **It is not recommended that this ratio increase beyond 4 : 1**

CASE-CONTROL STUDY DESIGN

- The first step in a case-control study, beyond the research question, is to identify and select cases
- The most important step in designing a case-control study is to specify the case definition.
- In some situations, complete identification of cases in a well-defined source population may be too time consuming or otherwise impossible.

CASE-CONTROL STUDY DESIGN

- **Selecting Cases and Controls**
- Identification and collection of cases involves specifying the criteria for defining a person as a case—in other words, as having the disease (also called *case definition*).
- This definition consists of a set of criteria, also called *eligibility criteria,* for inclusion in the study. There also are criteria for exclusion from the study.

CASE-CONTROL STUDY DESIGN

Selecting Cases and Controls

- Cases are found through registries, health care systems, and other sources that identify new or incidence cases.

  For example, cases may be sampled from those admitted to particular hospitals or clinics.

- Other sources of cases can be all cases diagnosed in the community ; cases diagnosed in a sample of the general population as from **cross sectional survey**

CASE-CONTROL STUDY DESIGN

The next step is selection of the controls.

- Controls are chosen from the same source population of cases .
- The source population is usually defined by geographic area.
- It is important to select controls so that participation does not depend on exposure.

CASE-CONTROL STUDY DESIGN

Source of controls

- The ideal situation is a random sample from the same source population as the cases.
- Investigators may use more than one control group.
- Controls can be selected by sampling from:

  The general population in the same community; the hospital community (patients in the same hospital); individuals who reside in the same block or neighborhood; and spouses, siblings, or associates (schoolmates, co-workers) of the cases.

Obtaining cases and controls for case control studies

Study	Source of cases	Source of controls
PROM (premature rupture of membrane)	Hospital patients	Hospital patients
Rheumatoid arthritis	Outpatient clinic	Other outpatient clinic
Cervical screening	GP register	GP register

CASE-CONTROL STUDY DESIGN

Matching Cases and Controls

- **Matching is a popular approach to control for confounding and selection bias in case-control studies.**
- **Matching cases and controls helps to ensure that these groups are similar with respect to important risk factors, thereby making case-control comparisons less subject to confounding or selection bias.**

CASE-CONTROL STUDY DESIGN

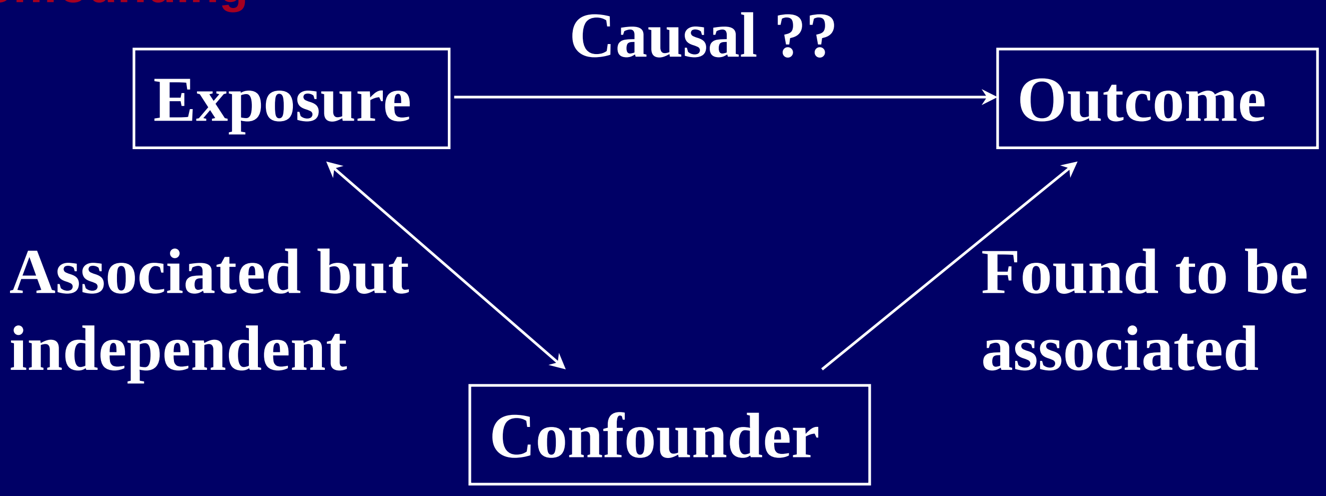
Prior exposure to the risk factor(s) of interest

- Once cases and controls are selected, information must be collected on prior exposure to the risk factor(s) of interest.
- Interviews and questionnaires are the most common means of determining a subject's exposure history and medical records review is another source
- The most objective means for characterizing exposure is the use of a biological marker.

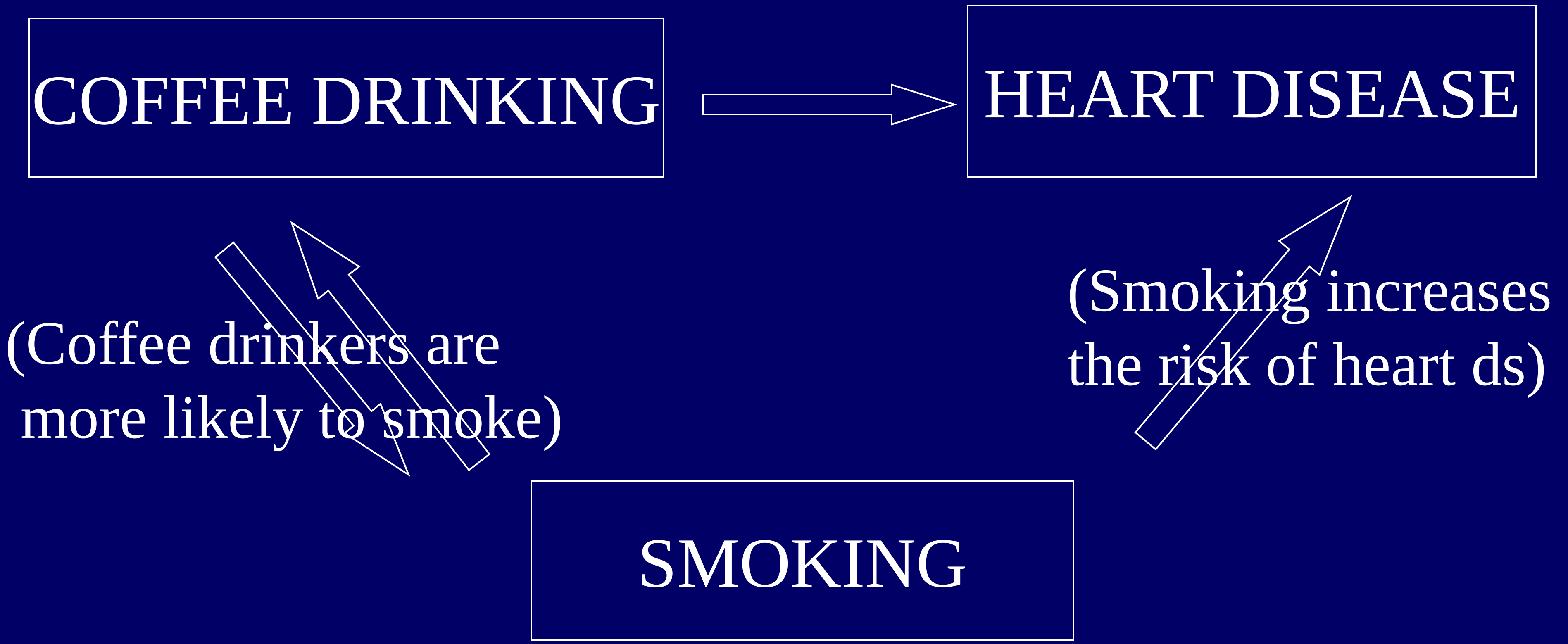
Confounding

A confounding factor is one that is associated with the exposure and that independently affects the risk of developing the outcome, but that is not an intermediate link in the causal chain between the exposure and the outcome under study

Matching - often used in case-control studies to decrease confounding



Examples … confounding



CASE-CONTROL STUDY DESIGN

The disadvantages of matching include

(1) **It is time consuming and expensive**

(2) **Some potential cases and controls may be excluded because matches cannot be made**

(3) **Unmatched cases and controls must be discarded**

(4) **Matched variables cannot be evaluated as risk factors in the study population**

(5) **Continuous matching categories may be too broad, and residual case control differences may persist.**

CASE-CONTROL STUDY DESIGN

- **Data Analysis**
- Data collection and analysis are based on whether the case-control study involves a matched or unmatched design. The measure used typically in case-control studies is the odds ratio.
- **Odds ratio (OR):** odds of a particular exposure among people with a specific condition divided by the corresponding odds of exposure among people without the condition under study

Odds Ratio (OR)

$$OR = \frac{\text{Odds of exposure}_{\text{cases}}}{\text{Odds of exposure}_{\text{controls}}}$$

Analysis

- Find out
  - Exposure rates among cases and controls to suspected factor
  - Estimation of disease risk associated with exposure (Odds Ratio)

Exposure rates

A case control study between smoking and lung cancer

	Cases (with Ca Lung)	Controls (without Ca lung)	Total
Smokers (<5/day)	**33** (a)	**55** **(b)**	**88** (a+b)
Non-smokers	**2** (c)	**27** **(d)**	**29** (c+d)
Total	**35** (a+c)	**82** (b+d)	**117** (a+b+c+d)

Exposure rates

- Cases= a/(a=+c)= 33/35= 94.2 %
- Controls= b/(b+d)= 55/82= 67 %

- So frequency of smoking was definitely higher among lung cancer patients than those without cancer

Outcomes of Case Control Study

- Odds ratio:

	Diseased/ Cases	**Not diseased/ Controls**
Exposed	a	b
Not exposed	c	d

$$\text{Odds ratio} = \frac{\text{Odds that case was exposed}}{\text{Odds that control was exposed}}$$

$= (a/c)/ (b/d) \quad =$ **ad / bc**

Estimation of risk

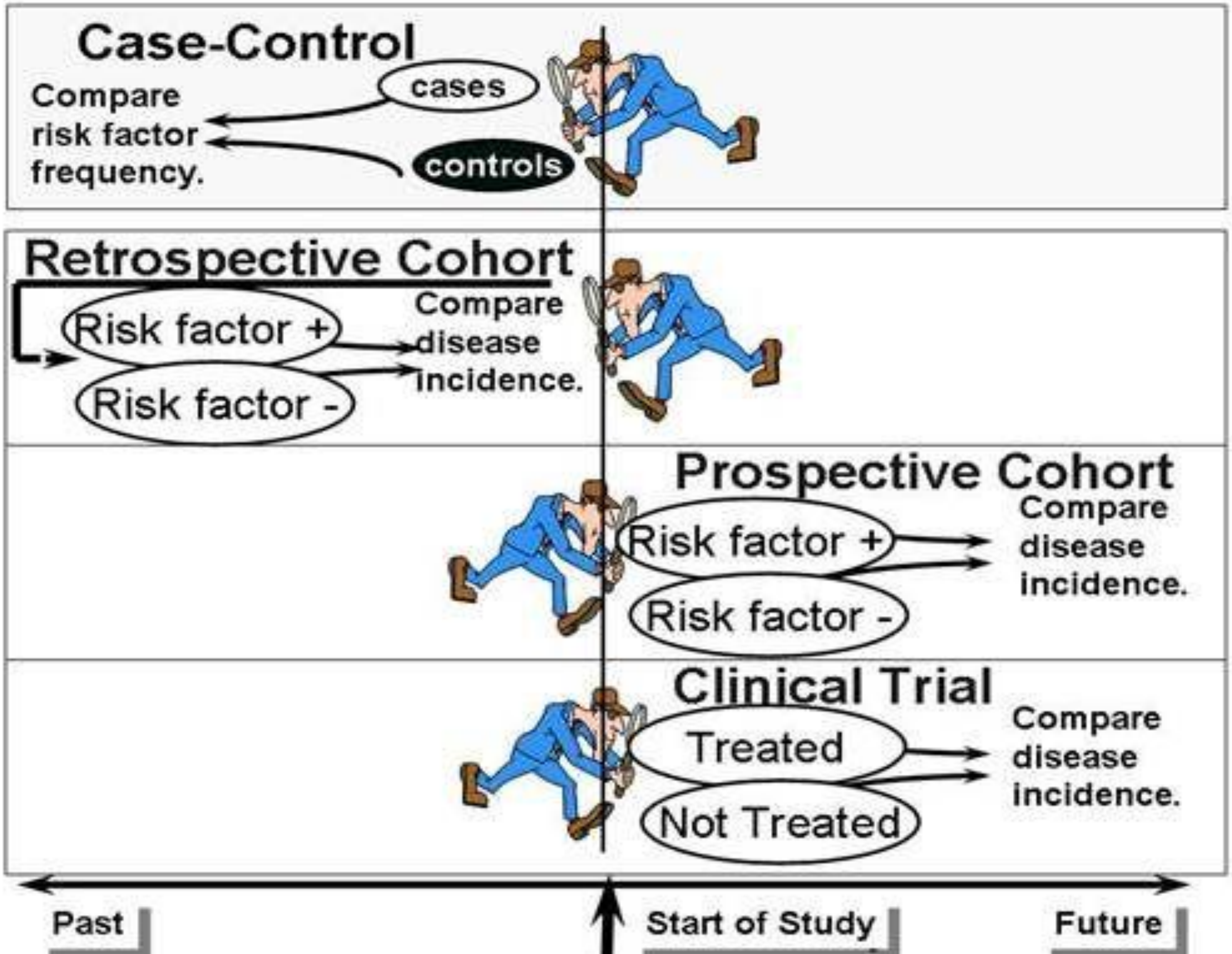
- Odds Ratio (Cross-product ratio)
- Odds that cases were exposed= a/c
- Odds that controls were exposed= b/d
- Odds ratio= (a/c)/(b/d)= ad/bc= 8.1

Interpretation

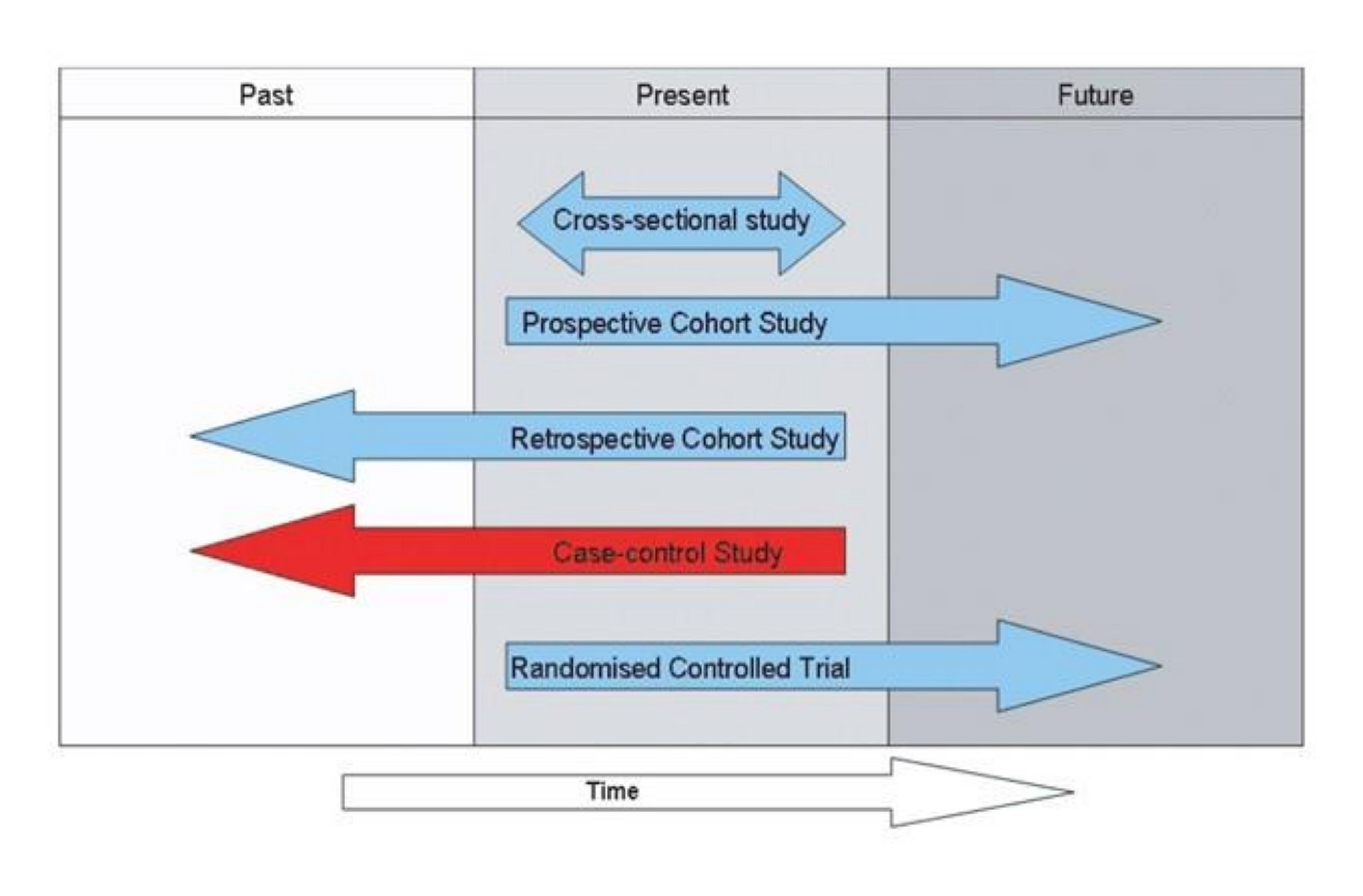
- The odds of smoking more than 5 cigarettes per day was 8.1 times more in the lung cancer patient than those without lung cancer.

OR

- Smoking (>5/day) was found be associated 8.1 times more in patients with lung cancer than those without lung cancer.



Case-Control
Compare risk factor frequency.
cases
controls
Retrospective Cohort
Risk factor +
Risk factor -
Compare disease incidence.
Prospective Cohort
Risk factor +
Risk factor -
Compare disease incidence.
Clinical Trial
Treated
Not Treated
Compare disease incidence.
Past
Start of Study
Future


Past
Present
Future
Cross-sectional study
Prospective Cohort Study
Retrospective Cohort Study
Case-control Study
Randomised Controlled Trial
Time


thank you