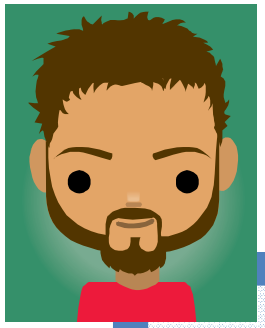
Case Control Study

Study design in epidemiology



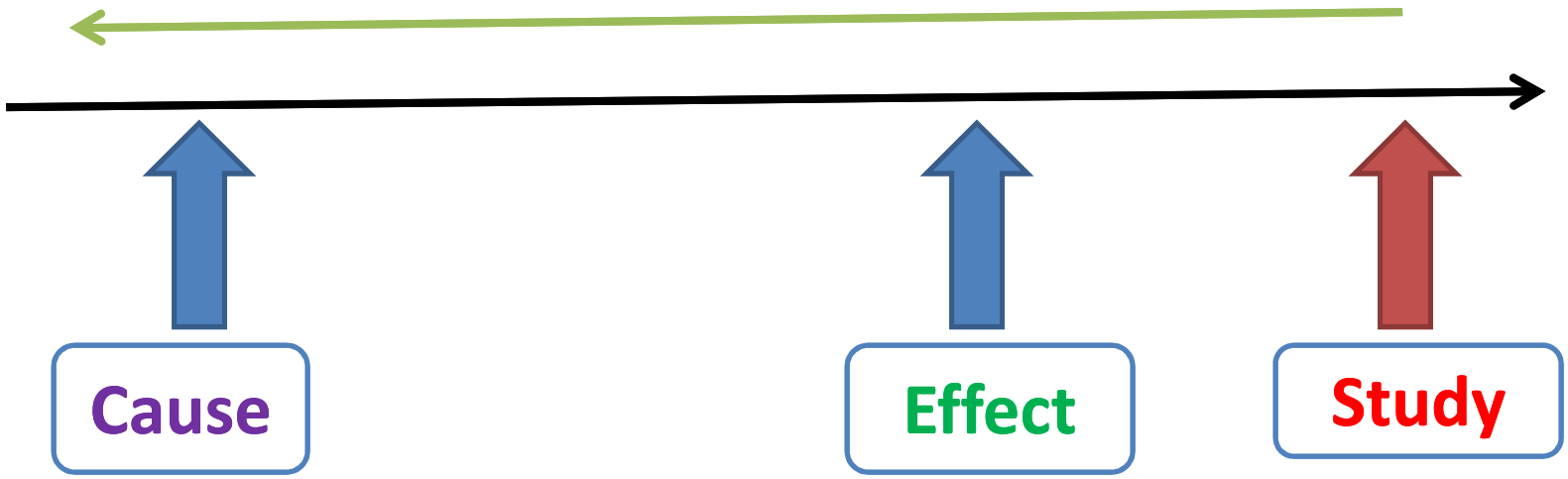
- Observational study
  - individual
    - Case-control study
    - Cohort study
  - population
    - Ecological study
- intervention

Case Control Study

- Start with a disease and work backwards to find associations between exposures and the disease.
- Compare patients with and without diseases to determine how they may differ in what they were exposed to.

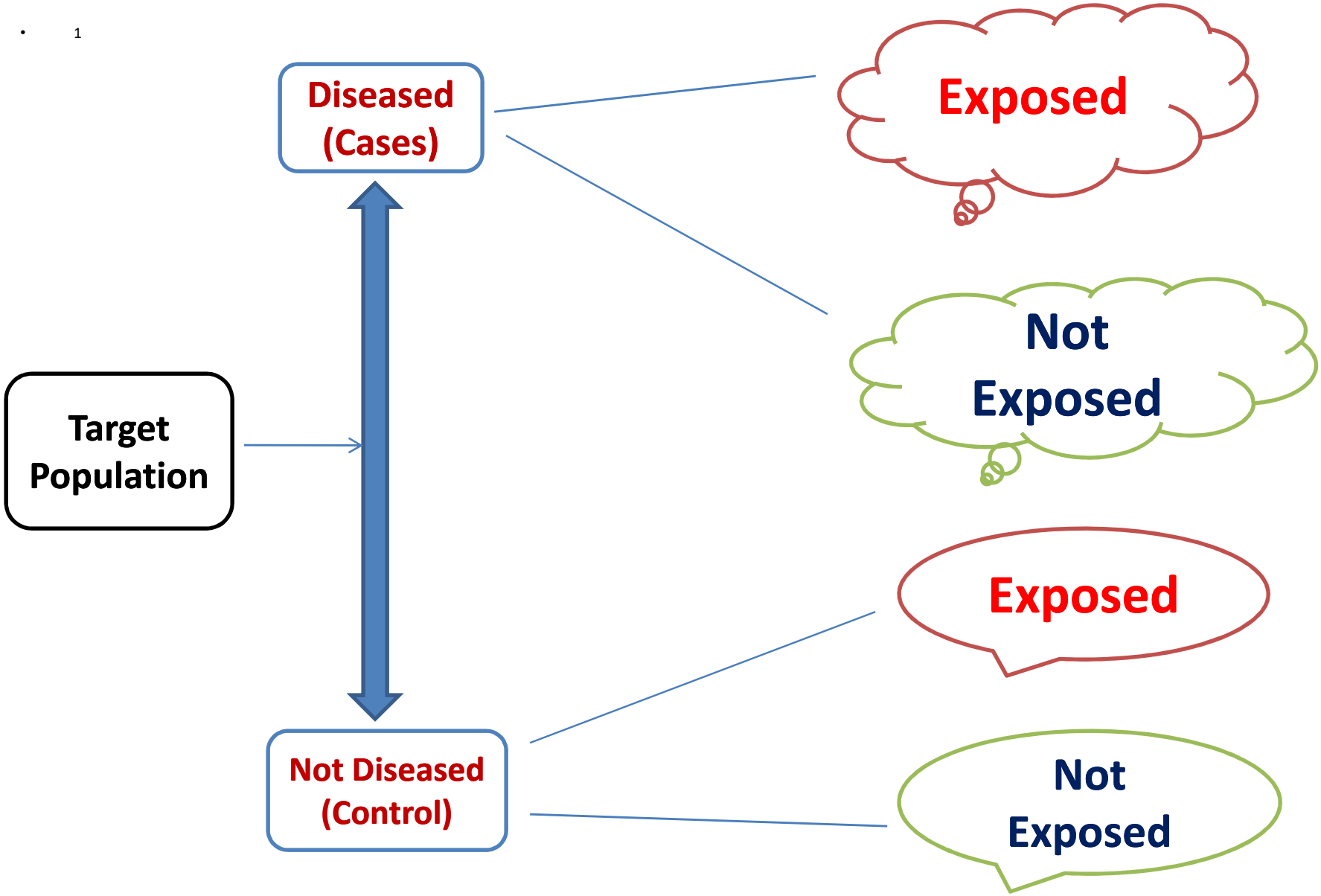
Retrospective Study

- From effect to cause



- Uses comparison group to support or refute an inference.

Study Design (Looking Backward)



Steps In Case Control Study

1. Selection of Cases and Controls.
2. Matching – Making two groups comparable.
3. Measurement of exposure.
4. Analysis and interpretation.

Selection of Cases

- **Diagnostic Criteria**

➢ Establish Diagnostic criteria and definition of diseases and stage of disease.

➢ Once established diagnostic criteria should not be changed.

➢ Study cases should be representatives of all cases.

➢ Sources of cases can be hospital or general hospital.

Eligibility criteria

- Incident cases are preferred to prevalent cases to reduce-

❑ **Recall Bias**

❑ **Over representation of cases of long duration**

- Most desirable way is to include all incident cases in the population in a specific time period.

Selection of Control

- From same population at risk for the diseases as the cases.
- Should be representative of population.
- Help to estimate exposure rate to be exposed.
- Sources can be hospitals, relative, neighbours,or general population.
- **Best possible ratio for number of cases to controls is 1:1.**
- **Maximum permissible option is 1:4 (for rare diseases)**

Measurement

- It is estimate unless past measurements are available.
- It has to be assumed that exposure incurred at the time the disease process began.
- Subjected to recall or interviewer bias.
- Potential confounders need to be assessed.

Analysis

Entering Data

	Cases	Controls
Exposed	a	b
Not Exposed	c	d
Total	a+c	b+d
Proportion Exposed	a/a+c	b/b+d

Analysis

- **Odds Ratio**
- Odds of exposure for cases compared to controls.
- **Odds ratio= ad/bc**
- Interpretation of OR

If OR=n , then the cases are “n “times more likely to be exposed than the controls.

Why case-control study?

- In a **cohort study**, you need a large number of the subjects to obtain a sufficient number of case, especially if you are interested in a rare disease.
  - Gastric cancer incidence in Japanese male:
    128.5 / 100,000 person year

- A **case-control study** is more efficient in terms of study operation, time, and cost.

Case-control study - subjects

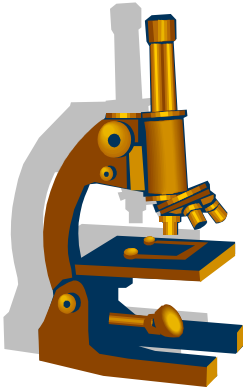
- Start with identifying the **cases of your research interest.**
  - If you can identify the cases systematically, such as a cancer registration, that would be better.
  - Incident cases (newly diagnosed cases) are better than prevalent cases (=survivors).
- Recruitment of appropriate **controls**
  - From residents, patients with other disease(s), cohort members who do not develop the disease yet.

Case ascertainment

- Who is your case?
  - Patient?
  - Deceased person?

- What is the definition of the case?
  - Cancer (clinically? Pathologically?)
  - Virus carriers (Asymptomatic patients)

    → You need to screen the antibody



Who will be controls?

- **Control ≠ non-case**
  - Controls are also at risk of the disease in his(her) future.
  - In a case-control study of gastric cancer, a person who has received the gastrectomy cannot be a control.
  - In a case-control study of car accident, a person who does not drive a car cannot be a control.

Case-control study - information

- Collection of the information

(past information) by **interview, biomarkers,** or **medical records**

  - Exposure (your main interest)
  - Potential confounding factors

Bias

- " **Any systemic error in the determination of the association between the exposure and the disease."**

➢ **Risk estimate may increase or decrease as a result of bias.**

Five types:

1. Bias due to confounding
2. Recall Bias
3. Selection Bias
4. Berkesonian Bias
5. Interviewer Bias

Bias Due to Confounding

- Confounding factor related both with the exposure and outcome.

Removed by matching at the start of study

Recall Bias

- When cases and controls are asked questions about their past events or factors, it may be more likely for the cases to recall the existence of certain events or factors , than the controls who are healthy person.

Example: “Myocardial Infarction”

“Cases may have a different recall of past events than the controls.”

Selection Bias

- Not Representative of cases and controls in the general hospital.
- May be systemic difference in characteristics between cases and controls.
- **Best controlled by its prevention.**

Berkesonian bias

- “ Bias arises because of **the different rates of admission to the hospitals** for people with different diseases.”

Interviewer Bias

- When the interviewer knows the hypothesis and also knows who the cases are leads to more question to the cases than the controls regarding the positive history of the suspected causal factor.

Prevented by:

1. **Taking average duration time for interview.**
2. **Eliminated by Double blinding.**

Why do we have to consider confounding?

- We want to know the “real” causal association but a distorted relationship remains if you do not adjust for the effects of confounding factors.

How can we solve the problem of confounding?

"Prevention" at study design

- ✓**Limitation**
- ✓**Randomization** in an intervention study
- ✓**Matching**

How can we solve the problem of confounding?

"Treatment " at statistical analysis

- ✓**Stratification** by a confounder
- ✓**Multivariate** analysis

Advantages

1. Relatively easy to carry out
2. Rapid and Inexpensive
3. Require comparatively few subjects
4. Particularly suitable to investigate rare disease.
5. No risk to subjects.
6. Allows the study several etiological factors.
7. Risk factors can be identified.

Disadvantages

- Problem of bias relies on memory or past records.

“ Validation of information obtained is difficult or sometimes impossible.”

- Selection of appropriate control group may be difficult.
- Can not measure incidence , **only estimate odds ratio.**
- Not suited to the evaluation of the therapy.