Case Control Studies

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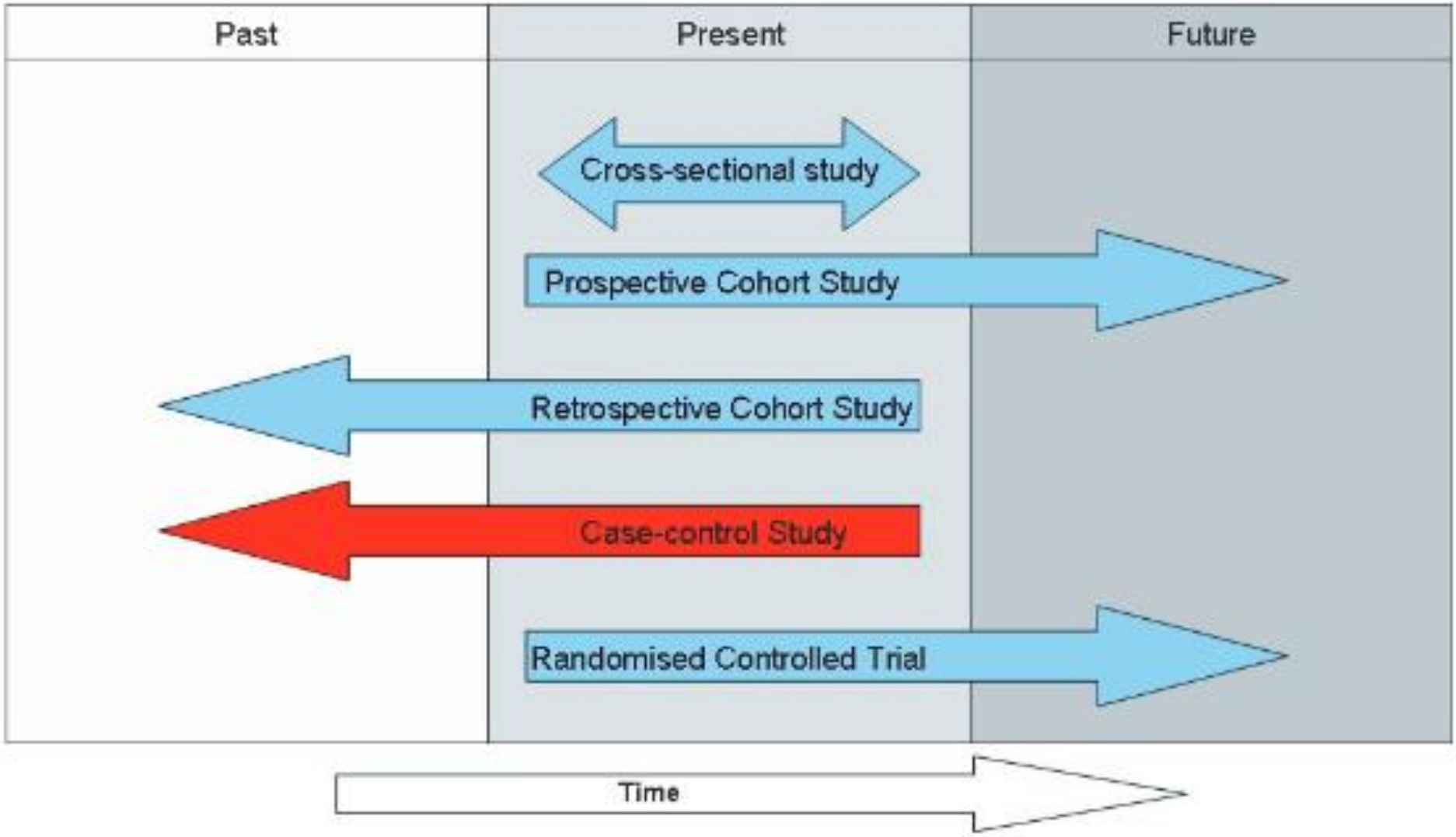
Contents

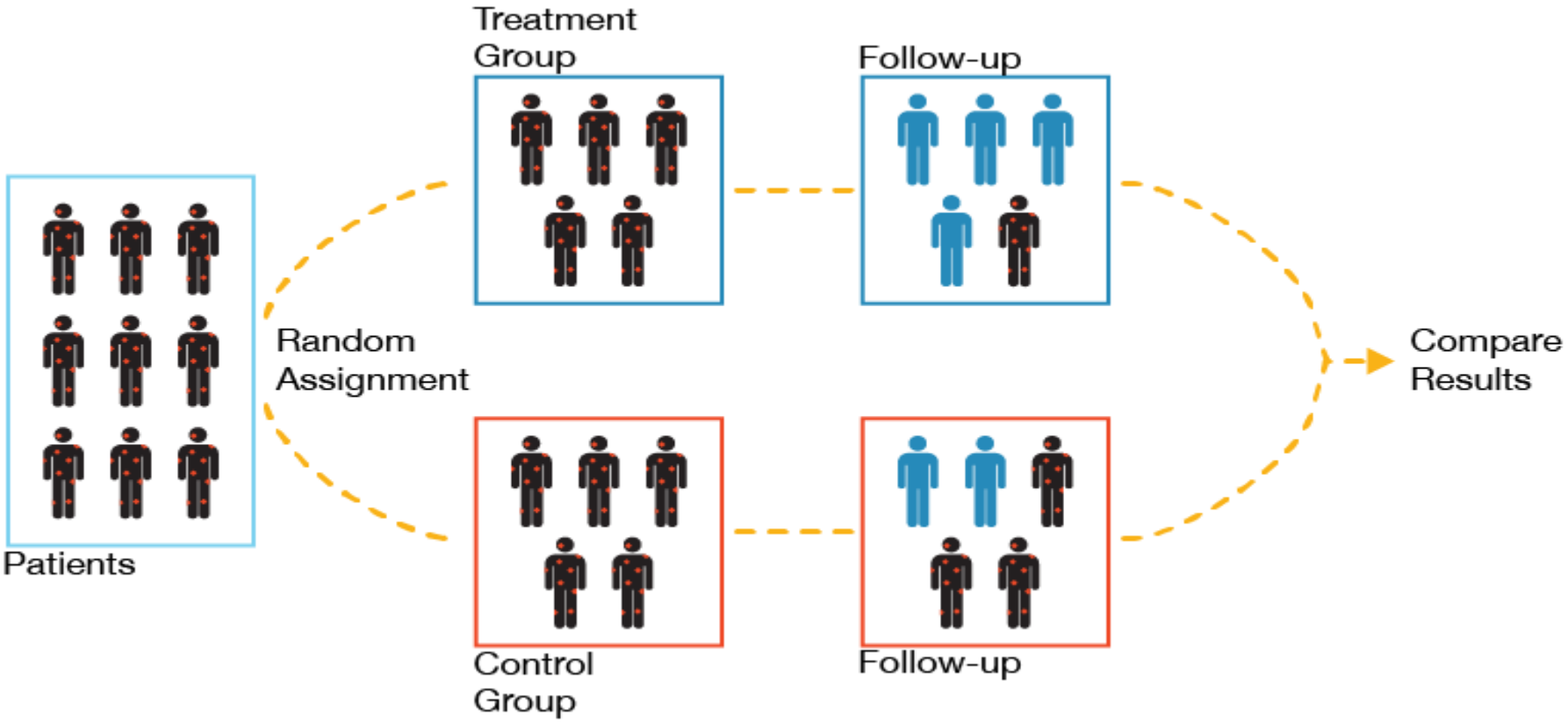
- Basic concepts
- Bias and confounding
- Check list and reporting of case control study

Basic concepts


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

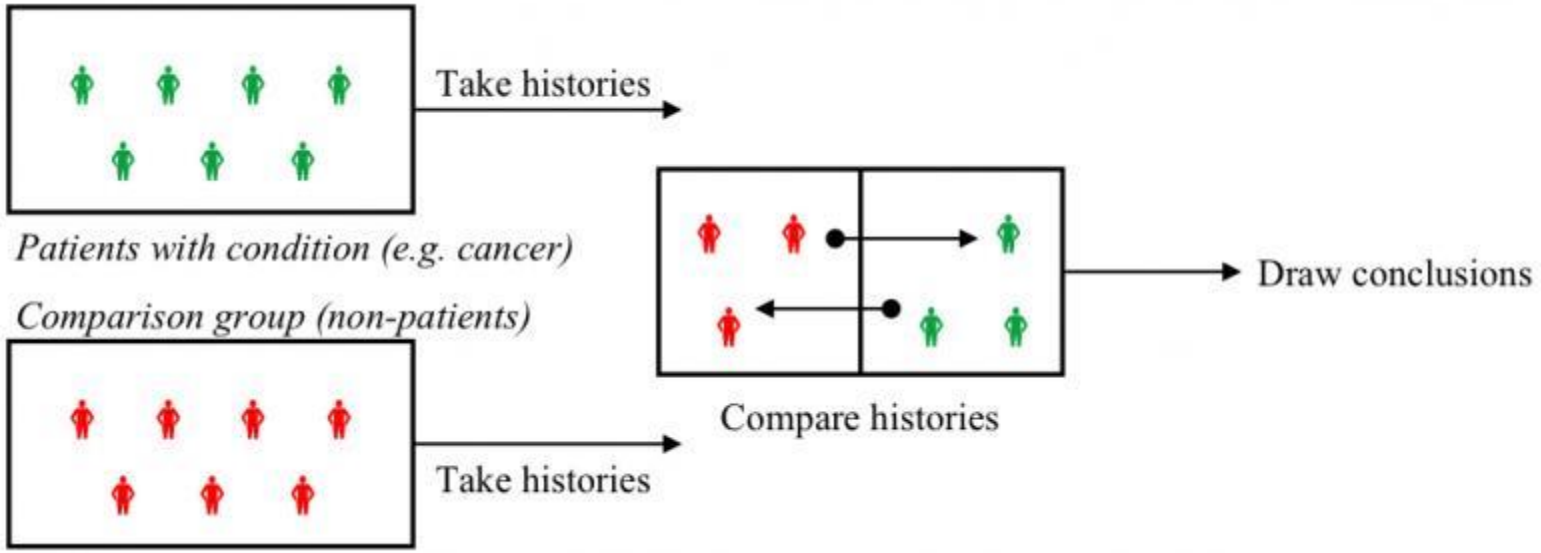
What is case control study?

- A study that establishes association between exposure to risk factors and disease.



Study of rare diseases

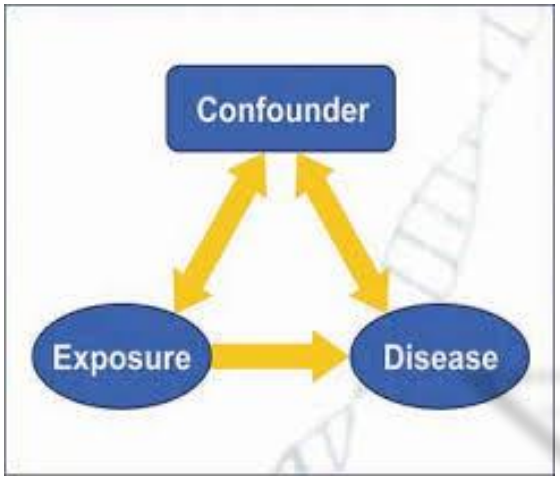
- The case-control study design is often used in the study of rare diseases or as a preliminary study where little is known about the association between the risk factor and

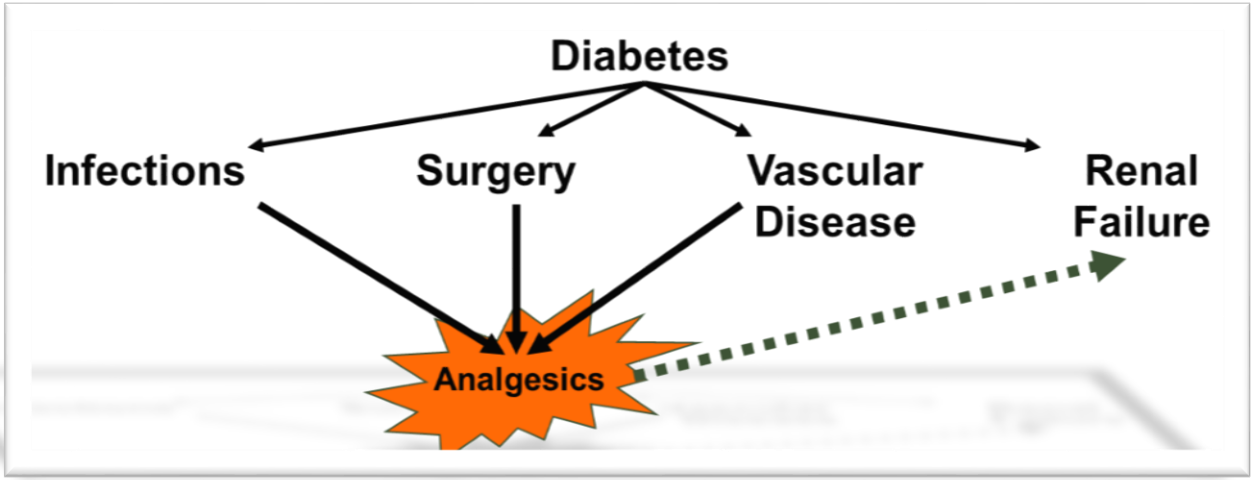


Bias & confounding

Confounding

A situation in which the effect or association between an exposure and outcome is distorted by the presence of another variable.





Bias and confounding

- Case control studies are prone to bias and confounding.
- **How to minimize bias**:
- Care must be taken in the selection of both cases and controls
- Establishing definitions of disease, risk factors and in ensuring there are no confounding associations between detection of disease and risk factor exposure
- Distinguish between stages or subtypes of disease and to define a measure of health status.
- Incident case design is preferable to reduce recall bias and over-representation of cases with long standing disease

Choosing controls

- Should come from the same population at risk of disease
- Should not have the disease
- Should be representative of the target population.

Choosing cases

- Incident or prevalent cases.

- **Incident cases**
  comprise cases newly diagnosed during a defined time period.
- **Prevalent cases**
  comprise individuals who have had the outcome under investigation for some time

Bias minimization in control selection

- A sampling frame of hospital patients is often used to select controls diseases.
- Selecting controls in this way might **therefore over-estimate population exposure** to a risk factors,
- Using more than one control group helps to overcome this type of issue.
- **Multiple controls can be used for each case**, giving the study greater power, particularly where the number of cases is small, due for example, to the disease being rare.

Recall and interview bias

- Exposure measurements are reliant either on memory where cases and controls are interviewed retrospectively, and/or medical records.
- Exposure estimates are therefore vulnerable to **recall bias**; commonly those with the disease are more likely to remember exposure than those without.
- **Interview or measurement bias**; where the interviewer interviews or reports findings systematically differently between cases and controls and confounding factors

Overcoming interview bias

- Interview and measurement bias can be overcome by including **blinding in the design** so that they do not know who is a case and who is a control at the time of interview.

Reporting a case control study

STROBE Statement

Strengthening the reporting of observational studies in epidemiology

Table. **The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Checklist of Items That Should Be Addressed in Reports of Observational Studies**

Item	Item Number	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract. (b) Provide in the abstract an informative and balanced summary of what was done and what was found.
Introduction		
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported.
Objectives	3	State specific objectives, including any prespecified hypotheses.
Methods		
Study design	4	Present key elements of study design early in the paper.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection.
Participants	6	(a) Cohort study: Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. Case–control study: Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls. Cross-sectional study: Give the eligibility criteria, and the sources and methods of selection of participants. (b) Cohort study: For matched studies, give matching criteria and number of exposed and unexposed. Case–control study: For matched studies, give matching criteria and the number of controls per case.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group.
Bias	9	Describe any efforts to address potential sources of bias.
Study size	10	Explain how the study size was arrived at.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why.
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding. (b) Describe any methods used to examine subgroups and interactions. (c) Explain how missing data were addressed. (d) Cohort study: If applicable, explain how loss to follow-up was addressed. Case–control study: If applicable, explain how matching of cases and controls was addressed. Cross-sectional study: If applicable, describe analytical methods taking account of sampling strategy. (e) Describe any sensitivity analyses.
Results		
Participants	13*	(a) Report the numbers of individuals at each stage of the study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed. (b) Give reasons for nonparticipation at each stage. (c) Consider use of a flow diagram.
Descriptive data	14*	(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders. (b) Indicate the number of participants with missing data for each variable of interest. (c) Cohort study: Summarize follow-up time—e.g., average and total amount.
Outcome data	15*	Cohort study: Report numbers of outcome events or summary measures over time. Case–control study: Report numbers in each exposure category or summary measures of exposure. Cross-sectional study: Report numbers of outcome events or summary measures.
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence intervals). Make clear which confounders were adjusted for and why they were included. (b) Report category boundaries when continuous variables were categorized. (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period.
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions and sensitivity analyses.
Discussion		
Key results	18	Summarize key results with reference to study objectives.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.
Generalizability	21	Discuss the generalizability (external validity) of the study results.
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based.

Give such information separately for cases and controls in case–control studies, and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

An Explanation and Elaboration article (18–20) discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available at www.annals.org and on the Web sites of *PLoS Medicine* [www.plosmedicine.org] and *Epidemiology* [www.epidem.com]). Separate versions of the checklist for cohort, case–control, and cross-sectional studies are available on the STROBE Web site (www.strobe-statement.org).

Overall assessment of paper Checklist

- How well was the study done to **minimise the risk of bias or confounding?**
- Taking into account clinical considerations, **do you think there is clear evidence of an association between exposure and outcome**?
- Are the results of this study **directly applicable** to the patient group targeted by this guideline?

Case control studies in 3 steps

- **Step 1:** Identify the **cases** (a group known to have the outcome) and the **controls** (a group known to be free of the outcome).
- **Step 2:** Look back in time to learn which subjects in each group had the exposure(s), comparing the frequency of the exposure in the case group to the control group
- **Step 3:** Data collections, analysis and reporting

Thank you