Taxonomy of Clinical Research Design

Experimental	Observational
Clinical trials • Parallel randomised • Parallel non-randomised • Cross-over Community trials Historical controlled trials	Cohort study • Prospective • Retrospective Case-control Cross-sectional

Observational Studies

Investigator does not assign exposures. A descriptive study provides a description of exposures and outcomes, whereas an analytic study provides a measure of the association between exposure and outcome. Observational studies are hypothesis generating and cannot establish causal association.

Case-control study: compares subjects with disease (cases) to those without disease (controls) for risk factors. It is useful for establishing hypotheses about aetiology, especially when a disease is rare. It cannot estimate the prevalence of disease. Controls and cases should be sufficiently similar in prognostic factors other than the risks of interest.

- Nested case-control study: defines a cohort with suspected risk factors and a control is assigned for each case from within the cohort. Cases and controls are matched on calendar time and length of follow-up.
- Case-cohort study: cases are not matched on calendar time or length of follow-up to controls.

Cohort study:

- Prospective follows and assesses outcomes in exposed and unexposed groups over time.
- Retrospective identifies populations with and without the exposure based on past records and assesses outcomes at the time of study.

Before and after (pre-post) observational study: outcomes are measured before and after an exposure, that is not assigned by the investigator. Study participants in the pre- and post-periods may be the same or different.

- Controlled before and after: the before-after effect of implementation in the intervention group is compared with a control group that has no intervention.

Cross-sectional (prevalence) study: evaluates the prevalence of exposures and outcomes at the same time. Temporal association is difficult to establish.

Experimental

Investigator assigns exposures (treatments).

Clinical trial: subjects with disease are placed in different treatment groups. The study population must be sufficiently similar and representative of the general population of patients. The intervention is compared to a placebo, no treatment or an alternative treatment.

- Parallel randomised trial: subjects are unpredictably (randomly) allocated to intervention and control groups. This minimises the selection bias and confounding.
- Parallel non-randomised trial: controls are selected using some predictable pattern, e.g., certain days of the week.
- Historically controlled trial: controls are adopted from the past, e.g., medical records, or previous studies.
- Cross-over trial: two groups undergo the same treatments at different time periods, i.e., each group serves as a control while the other group is undergoing intervention. The effect of the treatments needs to be reversible.
- Factorial trial: different treatments are tested at the same time in the same population. The treatment effects should be independent.

Community trial: groups of subjects are assigned to different treatments.

Field trial: subjects without disease are placed in different preventative intervention groups.

Bias

References

- Essentials of Clinical Research Design (Pediatr Invest 2019)
- Classification of Observational Studies (Lancet 2002)
- NICE Glossary of Study Designs