



## Cross-over / Repeated measures study

The administration of two or more experimental therapies one after the other in a specified or random order to the same group of patients.

e.g. of “2 treatment, 2 period design” or “AB/BA design”

|                | Period 1 | Wash-out | Period 2 |
|----------------|----------|----------|----------|
| <b>Group 1</b> | A        | -        | B        |
| <b>Group 2</b> | B        | -        | A        |

### Requirements

- Disease under study must be chronic and treatable but not curable
- Disease must be stable over course of study
- Patients: population well defined, at similar point in disease
- Intervention: randomized and double-blinded assignment to treatment sequence
- Outcome: blinded assessment

### Advantages

- Need fewer patients*
  - Each patient acts as his/her own control
  - May be preferred design if disease is rare
- Decreased cost*

### Disadvantages

- Period effect*
  - If disease changes (deteriorates or improves) over the course of the study, the patients may respond differently to treatment in period 1 as compared to period 2
- Carry-over effect*
  - Effects of the first treatment might carry over into the second treatment period and thereby confound the detection of treatment effects
  - May be physiological or psychological
    - e.g., not all of the drug administered during the first study period is eliminated from the subject's system before the second treatment is administered
    - e.g. the people that received the more effective treatment first, may rate the second treatment as much less effective since it will be compared to the effective drug
  - Carry-over can be dealt with by use of a *wash-out* period between treatments, or by making observations sufficiently late after the start of a treatment period that any carry-over effect is minimised.
- Length of trial*
  - May be longer than in a parallel group study since each patient must be studied during at least 2 study periods
- Missing data / Dropouts / Outliers*
  - Have a much greater effect on the analysis than they would in a parallel group study

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