



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
Group 1	A	-	B
Group 2	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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