Other Special Designs:
Cross-Over Design
Screening Designs

Cross- Over Design

- Experiments in which subjects are administered first one treatment, then ‘crossed over’ to receive a second, and perhaps, subsequently crossed over to receive a third, or even a fourth treatment.

- Advantages
  - each subject is his/her own control
  - appropriate for chronic conditions
- Disadvantages
  - not appropriate for acute conditions (e.g. post-op pain), surgical procedures, treatments with long administration period
  - retention of the patients

- Issues specific to cross over studies
  - washout period– should not vary from subject to subject
  - baseline measurements for each period

Two-period Cross Over Design

- Consider the two-period two-treatment (A and B) cross over design
  - subjects are randomly assigned to one of the two sequences : AB and BA
  - in a large study, the two sequences will be balanced for the number of subjects

- The Analysis compares the two sequences
  - The mean difference compares the baseline measurement (prior to Period 1) with the final measurement (after Period 2)
  - Problem
    - carry-over effect influences the baseline measurement for Period 2 in both sequences, but differently.
    - Example
      - Sequence 1: Pbo followed by Active treatment
      - Sequence 2 : Active treatment followed by Pbo

- If carry-over effect is present, the analysis reduces to comparison after Period 1, therefore design advantages are lost.
- baseline measurements are different by period, crossover is not appropriate: use parallel design

Example

- A crossover design : a set of 10 Latin squares with 2 rows (time periods) and 2 treatments (fluid types)
  - N=10 subjects receiving fluids A and B

A crossover design

Latin Squares

	I		II		III		IV		V		VI		VII		VIII		IX		X	
Subject	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Period 1	*A*	*B*	*B*	*A*	*B*	*A*	*A*	*B*	*A*	*B*	*B*	*A*	*A*	*B*	*A*	*B*	*A*	*B*	*A*	*B*
Period 2	*B*	*A*	*A*	*B*	*A*	*B*	*B*	*A*	*B*	*A*	*A*	*B*	*B*	*A*	*B*	*A*	*B*	*A*	*B*	*A*

Figure 4-7 A crossover design.

The 10 subjects receiving fluid A first (1, 4,6,7,9,12,13,15,17,19) are randomly chosen

ANOVA –Table

Table 4-17 Analysis of Variance for the Crossover Design in Figure 4-7

Source of Validation	Degrees of Freedom
Subjects (columns)	19
Periods (rows)	1
Fluids (letters)	1
Error	18
Total	39

Conclusion

- Importance of correct choice of design:
  - Cross over
  - Randomized block design
  - Factorial design (with one or more factors)
  - Fractional factorial design

Screening designs

Screening designs

- The term `Screening Design' refers to an experimental plan that is intended to find the few significant factors from a list of many potential ones.
- Alternatively, we refer to a design as a screening design if its primary purpose is to identify significant *main effects*, rather than interaction effects, the latter being assumed an order of magnitude less important.

Screening designs

- As the number of factors in a factorial design increases , the number of runs needed for a complete replicate can rapidly outgrow the resources of an experimenter.
- If the experimenter can make assumptions regarding the higher order interactions, then a ***fractional factorial design*** can be run instead of a full fractional design
  - Importance as a screening design
- Another common family of screening designs is the ***Plackett-Burman*** set of designs, so named after its inventors
- In general, screening designs are *economical* experimental plans that focus on determining the relative significance of many main effects.