R16 - Crossover designs

HCI/PSYCH 522
Iowa State University

May 5, 2022

Crossover designs

`https://en.wikipedia.org/wiki/Crossover_study`

Definition

A crossover study is one in which each subject receives a sequence of different treatments.

Crossover designs

`https://en.wikipedia.org/wiki/Crossover_study`

Definition

A crossover study is one in which each subject receives a sequence of different treatments.

- Crossover designs can increase precision and reduce costs
  - subjects being used as blocks

Crossover designs

https://en.wikipedia.org/wiki/Crossover_study

Definition

A crossover study is one in which each subject receives a sequence of different treatments.

- Crossover designs can increase precision and reduce costs
  - subjects being used as blocks
- Design to avoid confounding time period effects with treatments
  - each treatment in every period

Crossover designs

https://en.wikipedia.org/wiki/Crossover_study

Definition

A crossover study is one in which each subject receives a sequence of different treatments.

- Crossover designs can increase precision and reduce costs
  - subjects being used as blocks
- Design to avoid confounding time period effects with treatments
  - each treatment in every period
- Carryover effect can persist after the treatment period
  - increase washout period between treatment periods

Crossover designs

https://en.wikipedia.org/wiki/Crossover_study

Definition

A crossover study is one in which each subject receives a sequence of different treatments.

- Crossover designs can increase precision and reduce costs
  - subjects being used as blocks
- Design to avoid confounding time period effects with treatments
  - each treatment in every period
- Carryover effect can persist after the treatment period
  - increase washout period between treatment periods

Confounding

Definition
A confounding variable is a variable the influences both the dependent and the independent variable.

Confounding

Definition
A confounding variable is a variable the influences both the dependent and the independent variable.

```
##    period sequence
## 1      I          A
## 2     II          B
```

Confounding

Definition
A confounding variable is a variable the influences both the dependent and the independent variable.

```
##    period sequence
## 1       I        A
## 2      II        B
```

In this example, period is a confounding variable since it determines the treatment order (A $\rightarrow$ B) and (may) have an effect on the dependent variable.

Confounding

Definition
A confounding variable is a variable the influences both the dependent and the independent variable.

```
##    period sequence
## 1      I         A
## 2     II         B
```

In this example, period is a confounding variable since it determines the treatment order (A → B) and (may) have an effect on the dependent variable. Treatment and period are said to be confounded with each other.

Example balanced 3 treatment in 3 period design

```
##     period seq1 seq2 seq3 seq4 seq5 seq6
## 1        I    A    B    C    A    B    C
## 2       II    B    C    A    C    A    B
## 3      III    C    A    B    B    C    A
```

Example balanced 3 treatment in 3 period design

```
##    period seq1 seq2 seq3 seq4 seq5 seq6
## 1      I    A    B    C    A    B    C
## 2     II    B    C    A    C    A    B
## 3    III    C    A    B    B    C    A
```

Definition

A crossover design is balanced for carryover effects when each treatment follows each of the other treatments an equal number of times.

Analysis

In general, an analysis of a crossover design wants to account for the following

- Fixed effects
    - treatment
    - period
    - carryover
    - sequence (= treatment:period interaction)

Analysis

In general, an analysis of a crossover design wants to account for the following

- Fixed effects
    - treatment
    - period
    - carryover
    - sequence (= treatment:period interaction)
- Random effects
    - subject

Analysis

In general, an analysis of a crossover design wants to account for the following

- Fixed effects
  - treatment
  - period
  - carryover
  - sequence (= treatment:period interaction)
- Random effects
  - subject

Simpler analyses are possible if you can assume negligible effects of

- sequence
- carryover

Analysis

In general, an analysis of a crossover design wants to account for the following

- Fixed effects
  - treatment
  - period
  - carryover
  - sequence (= treatment:period interaction)
- Random effects
  - subject

Simpler analyses are possible if you can assume negligible effects of

- sequence

- carryover

But these assumptions may be dubious.

2x2 Crossover

```
##    period seqAB seqBA
## 1      I     A     B
## 2     II     B     A
```

Consider a regression model with period, treatment, sequence, and carryover.

2x2 Crossover

```
##    period seqAB seqBA
## 1      I     A     B
## 2     II     B     A
```

Consider a regression model with period, treatment, sequence, and carryover. You will have the following terms

- Intercept (reference level: I, A, AB, carryover from A)
- Indicator for period II
- Indicator for treatment B
- Indicator for sequence BA
- Indicator for carryover from B

2x2 Crossover

```
##    period seqAB seqBA
## 1      I     A     B
## 2     II     B     A
```

Consider a regression model with period, treatment, sequence, and carryover. You will have the following terms

- Intercept (reference level: I, A, AB, carryover from A)
- Indicator for period II
- Indicator for treatment B
- Indicator for sequence BA
- Indicator for carryover from B

Since there are only 4 combinations of period and treatment, we only have 4 means.

2x2 Crossover

```
##    period seqAB seqBA
## 1      I     A     B
## 2     II     B     A
```

Consider a regression model with period, treatment, sequence, and carryover. You will have the following terms

- Intercept (reference level: I, A, AB, carryover from A)
- Indicator for period II
- Indicator for treatment B
- Indicator for sequence BA
- Indicator for carryover from B

Since there are only 4 combinations of period and treatment, we only have 4 means. Thus, we cannot estimate all of the terms in this model.

Extra Period Design

```
##     period seqABB seqBAA
## 1      I      A      B
## 2     II      B      A
## 3    III      B      A
```

Consider a regression model with period, treatment, sequence, and carryover.

Extra Period Design

```
##    period seqABB seqBAA
## 1      I      A      B
## 2     II      B      A
## 3    III      B      A
```

Consider a regression model with period, treatment, sequence, and carryover. You will have the following terms

- Intercept (reference level: I, A, AB, carryover from A)
- Indicators for period II and III
- Indicator for treatment B
- Indicator for sequence BA
- Indicator for carryover from B

Extra Period Design

```
##    period seqABB seqBAA
## 1      I      A      B
## 2     II      B      A
## 3    III      B      A
```

Consider a regression model with period, treatment, sequence, and carryover. You will have the following terms

- Intercept (reference level: I, A, AB, carryover from A)
- Indicators for period II and III
- Indicator for treatment B
- Indicator for sequence BA
- Indicator for carryover from B

Since we now have 6 means we can estimate all of the terms in this model.

R Code for Extra Period Design

```r
library(lme4) # library(lmerTest)?
m <- lmer(y ~
            # fixed effects
            treatment + period + sequence +
            carryover + # carryover missing in first period

            # random effect
            (1|subject),

          data = d)


anova(m) # Type III ?
em <- emmeans(m, pairwise ~ treatment) # ??
confint(em) # ??
```