STATISTICS
TEXAS A&M UNIVERSITY

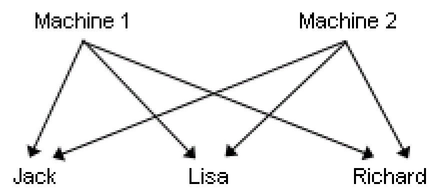
Handout 08

Mixed Models Analyses

Nested and Crossover Designs

Crossed Design

Each subject sees each level of the treatment conditions.



If you study the effects of caffeine on alertness, each subject would be exposed to both a caffeine condition and a no caffeine condition. Using the members of a statistics class as subjects, the experiment might be conducted as follows:

- On the first day of the experiment, the class is divided in half with one half of the class getting coffee with caffeine and the other half getting coffee without caffeine. A measure of alertness is taken for each individual, such as the number of yawns during the class period.
- On the second day the conditions are reversed; that is, the individuals who received coffee with caffeine are now given coffee without and vice-versa. The size of the effect will be the difference of alertness on the days with and without caffeine.

Crossed Design

The distinguishing feature of crossed designs is that each individual will have more than one score. The effect occurs within each subject.

- Crossed designs have two advantages:

(i) require fewer subjects, because each subject is used a number of times in the experiment.

(ii) more likely to result in a significant effect, given the effects are real.

- Crossed designs also have disadvantages : carry-over effects.

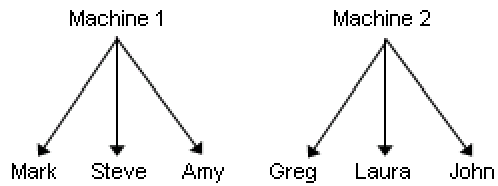
(i) Individuals not used to caffeine may still feel the effects of caffeine on the second day, even though they did not receive the drug.

(ii) the first measurements taken may influence the second. For example, if the measurement of interest was score on a statistics test, taking the test once may influence performance the second time the test is taken.

(iii) the assumptions necessary when more than two treatment levels are employed in a crossed design may be restrictive.

Nested Design

Each subject receives one, and only one, treatment condition.



- The critical difference in the simple experiment described for crossed design would be that the experiment would be performed on a single day, with half the individuals receiving coffee with caffeine and half without receiving caffeine. The size of effect in this case is determined by comparing average alertness between the two groups.
- The major distinguishing feature of nested designs is that each subject has a single score.
- The relative advantages and disadvantages of nested designs are opposite those of crossed designs.

(i) carry over effects are not a problem, as individuals are measured only once.

(ii) the number of subjects needed to discover effects is greater than with crossed designs.

Nested Design

Some treatments by their nature are nested.

The effect of sex in the case of subjects, for example, is necessarily nested. One is either a male or a female, but not both. Current religious preference is another example.

Treatment conditions which rely on a pre-existing condition are sometimes called demographic or blocking factors.

Nested classifications have some levels of one factor occur only within certain levels of a first factor. Individual children are selected within classrooms (but the children from classroom B can never be selected from the population of classroom A); classrooms may occur within schools, which may occur within districts that occur within states, etc. Observations of Y are nested within classrooms, which are nested in schools.........

Crossed, Nested, Repeated

group Groups * Time Pre-Post Crosstabulation

Count

		Time Pre-Post 1	Time Pre-Post 2	Total
group Groups	1 Endurance	9	9	18
	2 Strength	9	9	18
	3 Concurrent	9	9	18
	Total	27	27	54

id * Time Pre-Post Crosstabulation

Count

		Time Pre-Post 1	Time Pre-Post 2	Total
id	1	1	1	2
	2	1	1	2
	3	1	1	2
	4	1	1	2
	5	1	1	2
	6	1	1	2
	7	1	1	2
	8	1	1	2
	9	1	1	2
	10	1	1	2
	11	1	1	2
	12	1	1	2
	13	1	1	2
	14	1	1	2
	15	1	1	2
	16	1	1	2
	17	1	1	2
	18	1	1	2
	19	1	1	2
	20	1	1	2
	21	1	1	2

id * group Groups Crosstabulation

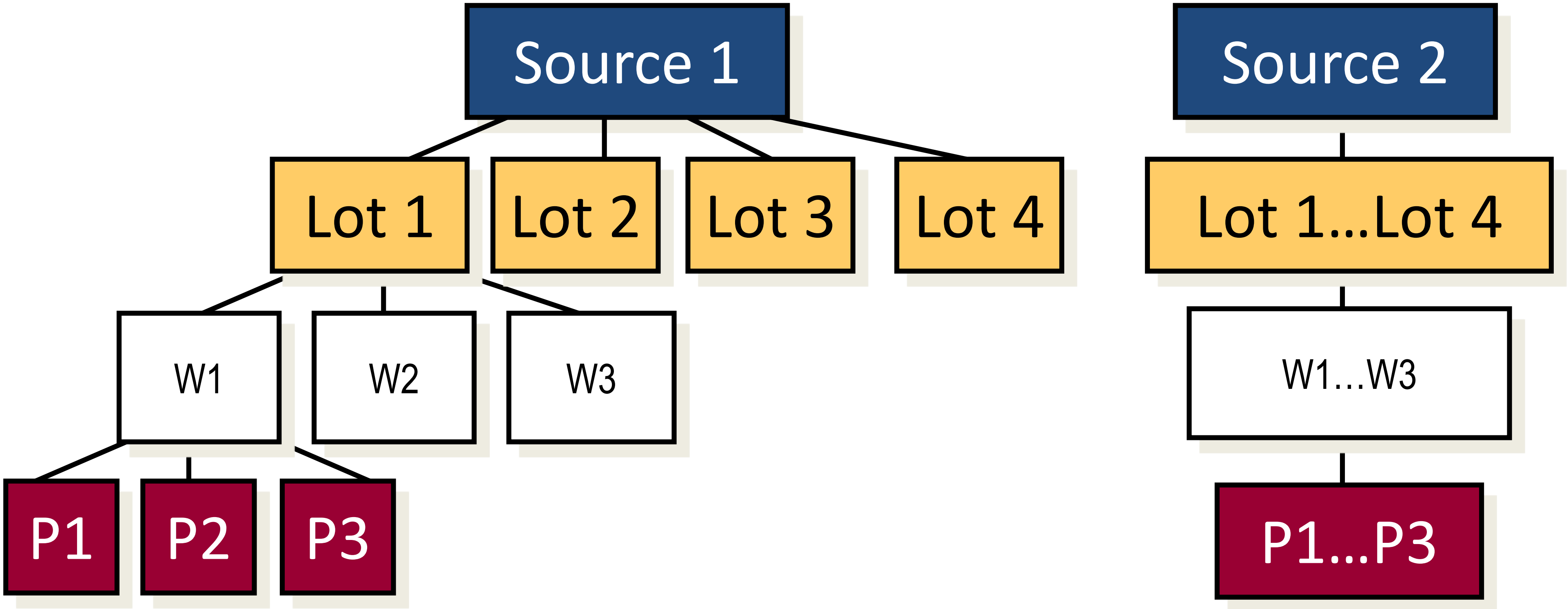
Count

		group Groups 1 Endurance	2 Strength	3 Concurrent	Total
id	1	2	0	0	2
	2	2	0	0	2
	3	2	0	0	2
	4	2	0	0	2
	5	2	0	0	2
	6	2	0	0	2
	7	2	0	0	2
	8	2	0	0	2
	9	2	0	0	2
	10	0	2	0	2
	11	0	2	0	2
	12	0	2	0	2
	13	0	2	0	2
	14	0	2	0	2
	15	0	2	0	2
	16	0	2	0	2
	17	0	2	0	2
	18	0	2	0	2
	19	0	0	2	2
	20	0	0	2	2
	21	0	0	2	2
	22	0	0	2	2
	23	0	0	2	2
	24	0	0	2	2
	25	0	0	2	2
	26	0	0	2	2
	27	0	0	2	2
	Total	18	18	18	54

Semiconductor Example (thickness data)

- A study was conducted in the semiconductor industry to measure the thickness of the oxide layer on silicon wafers determined at three randomly selected positions on each wafer.
- The objective is to determine assignable causes for the observed variability.
- 8 lots of 25 wafers were randomly selected from the population of lots of 25 wafers, with 4 lots from one source and the other 4 lots from the other source.
- Then 3 wafers were randomly selected from each lot of 25 for the use of oxide deposition process.
- After the layer of oxide was deposited, the thickness of the layer was determined at three randomly selected positions on each wafer.

Semiconductor Example



Thickness Data

source	lot	wafer	position	thickness
1	1	1	1	2006
1	1	1	2	1999
1	1	1	3	2007
1	1	2	1	1980
1	1	2	2	1988
1	1	2	3	1982
1	1	3	1	2000
1	1	3	2	1998
1	1	3	3	2007
1	2	1	1	1991
1	2	1	2	1990
1	2	1	3	1988
1	2	2	1	1987
1	2	2	2	1989
1	2	2	3	1988
1	2	3	1	1985
1	2	3	2	1983
1	2	3	3	1989
...	...	...	...	...

Hierarchical Data Structure

Nested designs have a hierarchical data structure.

- There is more than one size of experimental unit.
- A small experimental unit is nested within a larger one.
- The larger unit is typically considered a random effect.

Data is collected for test scores from 3000 students who are grouped into 160 classes. These 160 classes are from 40 different schools. Select all that apply.

a. Students are nested within classes
b. Students are crossed with classes
c. Classes are nested within schools
d. Classes are crossed with schools

A Nested Mixed Model

$$y_{ijkm} = \mu + \alpha_i + l_{j(i)} + w_{k(ij)} + e_{m(ijk)}$$

source, fixed

lot, random

wafer, random

error, or **position**, random

$l_{j(i)} \sim$ *i.i.d.* N(0, σ_l^2)

$w_{k(ij)} \sim$ *i.i.d.* N(0, σ_w^2)

$e_{m(ijk)} \sim$ *i.i.d.* N(0, σ^2)

i = 1, 2 (**source**)

j = 1, 2, 3, 4 (**lot**)

k = 1, 2, 3 (**wafer**)

m = 1, 2 ,3 (**position**)

ThicknessExample.sas
PROC MIXED

Fitted Nested Design

Comfort experiment was conducted to study the effects of temperature and gender on a person's comfort. There is one comfort measurement made on each person.

The three temperatures are randomly assigned to 3 of the 9 available environmental chambers. A chamber is the EU for the levels of temperature and chamber.

18 male and 18 female were randomly assigned to chambers so that 2 male and 2 female were assigned to each of the 9 chambers. The EU for gender is a person.

The model is
$$y_{ijkm} = \mu_{ik} + c_{j(i)} + p_{m(ijk)}$$
$$= \mu + \alpha_i + \beta_k + (\alpha\beta)_{ik} + c_{j(i)} + p_{m(ijk)}$$

i=temperature=1,2,3

j=chambers=1,2,3

k=gender=1,2

m=person=1,2

comfortexample.sas

Nested versus Split

Criteria	Nested	Split
Identical levels	No	Yes
Source of Variation	Many	Minimum
Number of EUs	One	More than one
Randomization	Partially restricted	Restricted
Interaction	Not between nested factors	Yes
Efficiency of the design effecting the budget of the experiment		Economic

Crossover Design

Crossover designs use the same experimental unit for multiple treatments. The common use of this design is where you have subjects (human or animal) on which you want to test a set of drugs -- this is a common situation in clinical trials for examining drugs. In these designs, every treatment is followed by every other treatment exactly the same number of times.

3 treatment 3 period design will have 3!=6 sequences
t treatment t period design will have t! sequences

Carryover parameter will have “o” for the first period data.

Objectives of Crossover Designs

– Recognize a crossover design.
  - A crossover study, also referred to as a crossover trial', is a longitudinal study in which subjects receive a sequence of different treatments (or exposures).
  - While crossover studies can be observational studies, many important crossover studies are controlled experiments.
  - Crossover designs are common for experiments in many scientific disciplines, for example psychology, education, pharmaceutical science, and health-care, especially medicine.
  - At any time, If we have t treatments, we are going to have t factorial possible sequences.

Which of the following is **true**?

a. In crossover design analysis, you treat subjects as a random effect to account for subject-to-subject variance.
b. In the design and analysis of crossover studies, you do not need to be concerned with the sequence of the presentation of the treatments.
c. All of the above
d. None of the above

– Analyze a crossover design using the MIXED procedure.

Heart Rate Example

- A pharmaceutical company conducted clinical trial to assess the effects of the three treatments (p, c, a) on the heart rate patients.

- Each patients received the three treatments in a random order during a time period that was separated from the others so that one treatment did not influence the heart rate measurement obtained after administering the other treatment (ruling out the carry-over effect).

- Each period was a visit to the clinic. The sequences of administering the treatments were A(a p c), B(p c a), C(c a p), D(a c p), E(c p a), F(p a c).

- The drugs were assigned to 24 patients in a three-period crossover design, with four patients for each sequence.

- The change in heart rate at one hour following the treatment was measured.

Heart Rate Example

Subject	1	2	3	4	5	6	. . . 24
Visit 1	a	p	c	a	c	p	. . .
Visit 2	p	c	a	c	p	a	. . .
Visit 3	c	a	p	p	a	c	. . .
Sequence	**A**	**B**	**C**	**D**	**E**	**F**	

p=placebo **c=control** **a=test drug**

`changehr` – change in heart rate

The Data

patient	sequence	visit	drug	changehr
201	B	2	p	-8
201	B	3	c	12
201	B	4	a	4
202	E	2	c	10
202	E	3	p	-10
202	E	4	a	-8
203	F	2	p	-2
203	F	3	a	-10
203	F	4	c	-4
204	D	2	a	0
204	D	3	c	20
204	D	4	p	-16
205	C	2	c	-8
205	C	3	a	-32
205	C	4	p	-12
206	B	2	p	-6
206	B	3	c	8
206	B	4	a	14
207	A	2	a	-32
207	A	3	p	2
...	...	...	...	...

Model for the Heart Rate Example

patients, random

$$y_{ijkm} = \mu + \alpha_i + \beta_j + \gamma_k + p_m + \varepsilon_{ijkm}$$

drug, fixed

visit, fixed

sequence, fixed

i = 1, 2, 3 (drugs)

j = 1, 2, 3 (visits)

k = 1 to 6 (sequences)

m = 1 to 24 (patients)

HeartExample.sas