Chapter 7: Study Design

Introduction

Two distinct types of study

- **Observational studies** in which we just observe ‘nature’.
- **Designed experiments** in which we intervene and assign treatments to the experimental units.

The main difference between the two types is the ability to deduce causality.

The goal of experimental design is to get the best information with the least effort.
Example  Comparing cattle feeds.

Which cattle feed is best, A or B?

Example  Comparing cattle feeds: candidate strategies.

Ask all farmers in an area
▶ what feed they use
▶ the average weight of their cows

What can we conclude if it turns out that cows on feed A are heavier, on average?

(... and that large farms use feed A while small ones use feed B)?

Explain your answer in terms of estimability in a linear model.

Example  Comparing cattle feeds: candidate strategies.

Assign each of the 40 farms in the region either feed A or feed B.

Later, determine the average weight of the cows on the farms.

How should the feeds be allocated to the farms, and why?

How many farms should be allocated feed A (feed B), and why?
Comparing cattle feeds: candidate strategies.

(c) If there are any characteristics of the farms that you think could affect the outcome, such as location within the region or size of farm, how would/should this affect your design?

Designed Experiments - Principles

Objective: to achieve validity and precision through the use of
▶ Control of the effects of confounding variables; most simply by comparing several treatments under similar conditions.
▶ Randomisation of experimental units to treatments, for validity — to (try to) avoid confounding.
▶ Replication of treatments to avoid confounding, increase precision AND provide a measure of precision.
▶ Balance — use each treatment the same number of times to increase precision and to simplify the analysis, and interpretation.
▶ Blocking of similar experimental units (repeating the experiment in each block) to avoid (partial) confounding and increase precision.

Fuel economy.

(a) (Three) fuels only. Fuel

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>19.5</td>
<td>16.0</td>
<td>23.2</td>
<td></td>
</tr>
<tr>
<td>20.7</td>
<td>17.4</td>
<td>22.5</td>
<td></td>
</tr>
<tr>
<td>26.2</td>
<td>15.5</td>
<td>22.5</td>
<td></td>
</tr>
<tr>
<td>29.4</td>
<td>27.6</td>
<td>35.6</td>
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</tbody>
</table>

Analysis:

<table>
<thead>
<tr>
<th>Source</th>
<th>df</th>
<th>SS</th>
<th>MS</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fuels</td>
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<td>98.48</td>
<td>49.24</td>
<td>1.54</td>
</tr>
<tr>
<td>Residual</td>
<td>9</td>
<td>287.33</td>
<td>31.93</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>385.81</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

How many cars should have been used to justify this analysis of the design (1, 2, 3, 4, 6, 12)?
Example Fuel economy.

(b) (Three) fuels and four vehicle types.

<table>
<thead>
<tr>
<th>Vehicle type</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>19.5</td>
<td>16.0</td>
<td>23.2</td>
</tr>
<tr>
<td>2</td>
<td>20.7</td>
<td>17.4</td>
<td>22.5</td>
</tr>
<tr>
<td>3</td>
<td>26.2</td>
<td>15.5</td>
<td>22.5</td>
</tr>
<tr>
<td>4</td>
<td>29.4</td>
<td>27.6</td>
<td>35.6</td>
</tr>
</tbody>
</table>

Analysis:

<table>
<thead>
<tr>
<th>Source</th>
<th>df</th>
<th>SS</th>
<th>MS</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fuels</td>
<td>2</td>
<td>98.48</td>
<td>49.24</td>
<td>8.42</td>
</tr>
<tr>
<td>Vehicle type</td>
<td>3</td>
<td>252.22</td>
<td>84.07</td>
<td>14.37</td>
</tr>
<tr>
<td>Residual</td>
<td>6</td>
<td>35.11</td>
<td>5.85</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>385.81</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

How many cars should have been used to justify this analysis of the design (1, 2, 3, 4, 6, 12)?

Single-factor designs I

Completely randomised designs

- assign study units to treatments, at random
- analyse as a one-way ANOVA
- preferable to use each treatment the same number of times (balance)

Completely Randomised Design in R.

Write the model

\[ y_{ij} = \mu + \alpha_i + \epsilon_{ij}; \quad \epsilon_{ij} \sim \mathcal{N}(0, \sigma^2) \]

```r
> cars <- data.frame(eff = c(19.5, 20.7, 26.2, 29.4, 16.0, 17.4, 15.5, 22.5, 22.5, 27.6, 22.5, 35.6),
+ fuel = factor(rep(1:3, each = 4)))
> cars.crd <- lm(eff ~ fuel, data = cars)
> anova(cars.crd)
```

Analysis of Variance Table

<table>
<thead>
<tr>
<th>Response: eff</th>
<th>Df</th>
<th>Sum Sq</th>
<th>Mean Sq</th>
<th>F value</th>
<th>Pr(&gt;F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>fuel</td>
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<td>98.482</td>
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<td>1.5424</td>
<td>0.2655</td>
</tr>
<tr>
<td>Residuals</td>
<td>9</td>
<td>287.327</td>
<td>31.925</td>
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</tbody>
</table>
**Single-factor designs II**

**Complete randomised block designs**
- assign the same number of study units (usually one) to treatments, at random, within each block
- analyse as a (balanced) 2-way ANOVA using the strictly additive model (ie, no interaction)

**Randomised Block Design in R.**

Write the model

\[ y_{ij} = \mu + \alpha_i + \gamma_j + \epsilon_{ij}; \quad \gamma_j \sim N(0, \sigma_j^2); \quad \epsilon_{ij} \sim N(0, \sigma^2) \]

NB: Vehicle is a blocking effect.

```r
> cars$vehicle <- factor(rep(1:4, 3))
> cars.rbd <- lm(eff ~ vehicle + fuel, data = cars)
> anova(cars.rbd)
```

Analysis of Variance Table

<table>
<thead>
<tr>
<th></th>
<th>Df</th>
<th>Sum Sq</th>
<th>Mean Sq</th>
<th>F value</th>
<th>Pr(&gt;F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>vehicle</td>
<td>3</td>
<td>252.216</td>
<td>84.072</td>
<td>14.3665</td>
<td>0.0038</td>
</tr>
<tr>
<td>fuel</td>
<td>2</td>
<td>98.482</td>
<td>49.241</td>
<td>8.4144</td>
<td>0.0182</td>
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<tr>
<td>Residuals</td>
<td>6</td>
<td>35.112</td>
<td>5.852</td>
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</tr>
</tbody>
</table>

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Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

**Single-factor designs III**

**Incomplete block designs**
- it is generally better to use ‘natural’ blocks than to impose balance
- it is sometimes better to use small blocks rather than to impose balance.
- if possible, use a balanced incomplete block design (BIBD) each treatment used the same number of times, plus each pair of treatments appear together in a block the same number of times
- if a BIBD is not possible, then get as close to one as possible
- analyse as an unbalanced ANOVA (with no interaction)
- always put the block terms first, and pay little or no attention to their tests.
Incomplete Randomised Block Design in R.

Write the model

\[ y_{ij} = \mu + \alpha_i + \gamma_j + \epsilon_{ij} \]

\[ \gamma_j \sim N(0, \sigma^2_j); \quad \epsilon_{ij} \sim N(0, \sigma^2) \]

```r
> cars$vehicle <- factor(rep(1:4, 3))
> cars.ibd <- cars[-1, ]
> cars.rbd <- lm(eff ~ vehicle + fuel, data = cars.ibd)
> anova(cars.rbd)
```

Analysis of Variance Table

Response: eff

<table>
<thead>
<tr>
<th></th>
<th>Df</th>
<th>Sum Sq</th>
<th>Mean Sq</th>
<th>F value</th>
<th>Pr(&gt;F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>vehicle</td>
<td>3</td>
<td>238.795</td>
<td>79.598</td>
<td>12.0319</td>
<td>0.01005*</td>
</tr>
<tr>
<td>fuel</td>
<td>2</td>
<td>100.508</td>
<td>50.254</td>
<td>7.5963</td>
<td>0.03051*</td>
</tr>
<tr>
<td>Residuals</td>
<td>5</td>
<td>33.078</td>
<td>6.616</td>
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</tr>
</tbody>
</table>

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Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Single-factor designs IV

**Latin square design**

- 'two-directional' blocking (rows and columns)
- need as many rows and columns, in a square, as there are treatments
- randomisation: choose a square, then randomise the order of rows, then columns
- analyse as a (balanced) 3-way ANOVA, with no interactions

```r
> tld <- data.frame(response = c(12, 10, 4, 11, 10, 3, 9, 9, 1),
+                    rows = factor(rep(1:3, each=3)),
+                    cols = factor(rep(1:3, 3)),
+                    treatment = factor(c(1, 2, 3, 2, 3, 1, 3, 1, 2)))
> tld.lm <- lm(response ~ rows + cols + treatment, data=tld)
> anova(tld.lm)
```

Analysis of Variance Table

Response: response

<table>
<thead>
<tr>
<th></th>
<th>Df</th>
<th>Sum Sq</th>
<th>Mean Sq</th>
<th>F value</th>
<th>Pr(&gt;F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>rows</td>
<td>2</td>
<td>8.667</td>
<td>4.333</td>
<td>13 0.071429</td>
<td></td>
</tr>
<tr>
<td>cols</td>
<td>2</td>
<td>114.000</td>
<td>57.000</td>
<td>171 0.005816**</td>
<td></td>
</tr>
<tr>
<td>treatment</td>
<td>2</td>
<td>0.667</td>
<td>0.333</td>
<td>1 0.5000000</td>
<td></td>
</tr>
<tr>
<td>Residuals</td>
<td>2</td>
<td>0.667</td>
<td>0.333</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Single-factor designs V

**Row and column designs**
- extension of latin squares when we don’t have
  \(#\text{rows} = \#\text{columns} = \#\text{treatments}\)
- a balanced (orthogonal) design is ‘best’, but if not possible
  then try to get as close to orthogonal as possible
- analyse as an unbalanced 3-way ANOVA, with no interactions
- always put the blocking terms first, and pay little attention to
  their tests.

Single-factor designs VI

**Cyclic and Alpha designs**
- extension of unbalanced incomplete block designs.
- computer-aided design for greater optimality but less
  robustness to failure.
- popular in expensive genetics field trials, for example.
- analyse as they come.

Factorial experiments

Is it better to consider one factor at a time (holding the levels of
the other factors constant) or to use a so-called factorial
experiment, and why?
Factor types

It is necessary to distinguish between different types of factors:

- crossed and nested factors
- fixed and random factors

and the effects of these on the analysis.

Example Machines and operators

<table>
<thead>
<tr>
<th>Machine</th>
<th>Operator</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>M₁</td>
<td>O₁₁</td>
<td>205 200</td>
</tr>
<tr>
<td></td>
<td>O₁₂</td>
<td>207 208</td>
</tr>
<tr>
<td></td>
<td>O₁₃</td>
<td>202 204</td>
</tr>
<tr>
<td>M₂</td>
<td>O₂₁</td>
<td>196 194</td>
</tr>
<tr>
<td></td>
<td>O₂₂</td>
<td>203 205</td>
</tr>
<tr>
<td></td>
<td>O₂₃</td>
<td>199 197</td>
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<tr>
<td>M₃</td>
<td>O₃₁</td>
<td>174 170</td>
</tr>
<tr>
<td></td>
<td>O₃₂</td>
<td>181 178</td>
</tr>
<tr>
<td></td>
<td>O₃₃</td>
<td>172 175</td>
</tr>
<tr>
<td>M₄</td>
<td>O₄₁</td>
<td>170 177</td>
</tr>
<tr>
<td></td>
<td>O₄₂</td>
<td>180 175</td>
</tr>
<tr>
<td></td>
<td>O₄₃</td>
<td>172 174</td>
</tr>
</tbody>
</table>

Example Drugs, diagnostic groups and hospitals

At each of four hospitals, five patients are recruited in each of three diagnostic groups (mild, moderate, severe) — a total of 60 patients.
Each hospital uses only one of two drugs.
Cell entries are means of 5 patients.

<table>
<thead>
<tr>
<th>G₁</th>
<th>H₁(D₂)</th>
<th>H₂(D₂)</th>
<th>H₁(D₁)</th>
<th>H₂(D₁)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.0</td>
<td>3.6</td>
<td></td>
<td>2.0</td>
<td>2.8</td>
</tr>
<tr>
<td>4.4</td>
<td>5.0</td>
<td>4.2</td>
<td>4.8</td>
<td></td>
</tr>
<tr>
<td>7.6</td>
<td>8.2</td>
<td>6.0</td>
<td>7.0</td>
<td></td>
</tr>
</tbody>
</table>
Crossed and Nested factors

“Crossed” and “Nested” describe the relationships between pairs of factors.

Crossed factors
Two factors are crossed if the levels of one factor are used in combination with (usually) all levels of the other factor. It is possible to study interaction between crossed factors.

Nested factors
Factor B is nested within factor A if a different set of levels of factor B is used for each level of factor A. It is not possible to study the interaction between nested factors.

Notation: For factor B nested within factor A B %in% A

Exercise
Which factors are crossed and which are nested in:

Machines and Operators?

Hospitals?

Practical Design Policies.

- Use simulation wherever possible.
  - To force your collaborators to think about the design.
  - To prepare for model fitting.
  - To support selection of the most powerful design.
  - Cycles are cheap.
- Grasp the expectations - what tests are the most important?
- Replicate at the highest feasible level.
- Randomize craftily - don’t leave it to chance!
- Use any previous information available - prior studies, simulations, hunches, to help you make the important decisions.