DESIGN OF EXPERIMENTS

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1. Idealized sequence

- Research question
- Availability of data
- Design of study
- Measurement issues
- Various stages of analysis
- Conclusions
- Interpretation

Why this is idealized.

2. Comparative research question

What is the effect of such and such a treatment (condition, exposure, . . .) on a response?

In observational study investigator may control who is measured and what is recorded but not the assignment of the treatment. In an experiment all important aspects are under control of investigator.

Example. Long-term use of HRT and its effect on cardio-vascular health and cancer.

Crucial distinction

3. Elements of an experiment

- Experimental units $U_1, \ldots, U_n$
- Background variable $z_1, \ldots, z_n$
- Treatments $T_1, \ldots, T_p$
- One treatment applied to each unit and response $y_{1t_1}, \ldots, y_{nt_n}$ observed. Here t_j is treatment applied to U_j.

1. Experimental unit is smallest subdivision of material such that any two units *might* be allocated a different treatment

2. Any treatment might be applied to any unit but in fact each unit receives just one treatment

3. Response on U_j does not depend on allocation to other units

4. Object is to assess the effect of treatments on y, often on $E(Y)$

4. Examples

- experimental unit: a plot in a field; treatment : level of fertiliser; z yield last year; y yield this year

- experimental unit: a patient; treatment: new drug or placebo; y: two-year survival

- experimental unit: a class of children; treatment: method of instruction. Note a unit is *not* a child

- experimental unit: subject-period combination in an investigation in which in each period each subject is given a signal to which they must respond

Examples ctd

experimental unit: batch of reactants in a chemical reaction: treatments: concentrations of reactants, catalyst, temperature, etc.; Response; yield of product or rate of reaction

in ophthalmological investigation, experimental unit might be a patient or might be a patient-eye combination, when each patient contributes two units, i.e. left and right eye may be treated differently.

in a computer large-scale simulation study, experimental unit: simulation run; treatment: model parameters.

Typically the units have structure by space, by time, by observers, etc and it is essential to recognize this. Partly this may be done by concomitant variable, z.

5. Objectives and their achievement

Of course the key requirement for a good experiment is that it addresses interesting questions. Only rarely do single experiments stand on their own.

To achieve a secure answer we need

- freedom from systematic error
- control of haphazard error
- appropriate size
- in technological experiments, good range of validity

There is a very important further consideration, the factorial concept, which is discussed later

6. Variation control

There are two aspects to this. First we aim typically by balancing to ensure that systematic structure in the units affects all treatments equally. Then remaining sources of variation, and particularly personal selection biases, are neutralised by randomization, Principle underlying first is

Compare like with like.

7. Implementation

For simplicity suppose for some of the discussion just two treatments, T and C

Matched pair design

Group the units into pairs, the two units in a pair being as similar as possible. Randomize the treatments between T, C and C, T

$Pair 1$	T	C
$Pair 2$	T	C
$Pair 3$	C	T
.	.	.
.	.	.
.	.	.

Comparison unaffected by large inter-pair differences

Randomization needed at all stages at which error might enter and often concealment is important

Randomized block design

Similar principles with $p > 2$ treatments.

Randomized block design with $p = 4$

$$
\begin{array}{ccccc}
Block1 & T_3 & T_1 & T_4 & T_1 \\
Block2 & T_1 & T_3 & T_4 & T_2 \\
. & . & . & . & . \\
. & . & . & . & . \\
. & . & . & . & .
\end{array}
$$

Two-way elimination: Latin square design

Simple example with four treatments, $A, \ldots, D$.

$Column(Session)$	1	2	3	4
$Row(Subject)$ 1	B	C	D	A
2	D	B	A	C
3	A	D	C	B
4	C	A	B	D

8. General principle of analysis

Any source of variability balanced out by design should be represented in the statistical model used for analysis.

For Latin square with continuous response analysed by linear model, if t_{ij} is the treatment applied in row i and column j and $Y_{ijt_{ij}}$ is a random variable representing the response, then

$$E(Y_{ijt_{ij}}) = \mu + \alpha_i + \beta_j + \tau_{t_{ij}}.$$

Interest lies in contrasts among the $\tau_1, \ldots, \tau_p$.

9. Adjustment for base-line z

Add regression term to model, for example

$$E(Y_{ijt_{ij}}) = \mu + \alpha_i + \beta_j + \tau_{t_{ij}} + \gamma^T z_{ij}.$$

10. Factorial experiments

Suppose that we have three treatments, A, B, C each at two possible levels called conventionally absent and present. With 24 units we have the following possibilities:

- Fix B, C possibly at absent levels and randomize 4 units to each level of A. Repeat in turn for B, C to give in effect three separate experiments

- Consider the full set of 2^3 possible combinations denoted conventionally

$$1, a, b, ab, c, ac, bc, abc.$$

Run 3 replicates of this.

Two large advantages of the second approach.

11. Some extensions

Implementation of the above ideas in more complex cases can become quite complicated and involves possibly intricate combinatorial considerations. There is also a formal theory of optimal design. These are not the most important aspect of design, however.

REFERENCES

Bailey, R.A. (2008). Design of comparative experiments. Cambridge University Press.

Cox, D.R (1958). Planning of experiments. New York: Wiley.

Cox, D.R. and Reid, N. (2000). The theory of the design of experiments. London: Chapman and Hall/CRC.

EXERCISES

1. To compare the effects of the ingestion of two different substances A and B on an important blood constituent, y, volunteers are injected either with A or with B and two hours later a blood sample is taken, clearly labelled with the subjects name, which of A or B was used, and other details and sent to a lab for measurement of y. Just two subjects could be dealt with in one day, A being used in morning sessions and B in the afternoon. The data were analysed by a two sample Student t test and associated confidence intervals.

How might the design and analysis be improved?

EXERCISES (ctd)

2. A very complex computer model takes a long time (several days or more) for one run to be complete and only one run can be in progress at a time. There are seven adjustable parameters in the model for each of which a low value and a high value are specified. It is decided to undertake 8 computer runs.

What might be a good procedure?