Experimental Methods in Health Research

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Introduction

• What is an experiment?
• Components of an experiment
• Classification of experimental designs
• Types of non-randomised design
• Reasons for adopting non-randomised experimental designs
• Disadvantages of non-randomised designs
• Case studies
What is an experiment?

“In an experiment, one investigates the relationship between two (or more) things by deliberately producing a change in one of them and looking at, observing, the change in the other.”

Robson C (1973), *Design and statistics in psychology*, Penguin, Harmondsworth
Components of the experiment

Experiments attempt to test causation rather than association

Hypothesis: change in A leads to corresponding change in B

Cause or independent variable

Effect or dependent variable
Classification of experimental designs

Experimental

Non-randomized

Confounding with baseline imbalance is a major problem

Pre-experimental (Uncontrolled)

Cannot allow for background changes affecting outcomes over time

Interrupted time series

Cannot exclude confounding factors

Randomized

Randomization avoids confounding by known and unknown factors

Changes over time assessed using a control group

Matching or stratification may reduce baseline imbalances

Control group (before and after)

Can account for secular changes in outcome

Cannot exclude bias because of non-random allocation

Stratifying clusters at the design stage may reduce effects of confounding and prognostic factors can be controlled for in baseline analyses

Non-randomised experimental designs

• Pre-experimental designs:
  non-randomized experiments where a particular outcome of interest is measured only in the intervention group:-
  – single group post-intervention design
  – single group pre- and post-intervention design

• Quasi-experimental designs:
  non-randomized experiments where a particular outcome of interest is measured in intervention and control group (or period):-
  – non-randomized control group before and after study
  – interrupted time series design
Reasons for non-randomised experimental designs (1)

- Such strong evidence for an intervention that a placebo group may be unethical
- Strong preference for intervention prevents control
- Educational or other interventions when active participation required
- Less costly than RCTs
- Feasibility studies including Phase II of MRC framework for evaluation of complex interventions
Reasons for non-randomised experimental designs (2)

New service or health technology already introduced

• Intrinsic
  – area-wide change
  – organization-based intervention

• External constraint
  – policy decision to introduce a new service
  – imposed or natural change across a geographical region.
Disadvantages of non-randomised designs

• Confounding (pre-experimental, interrupted time series without control): alternative explanation for change in outcome of interest
  – Secular change (pre-experimental): background change in outcome of interest due to increased awareness of new technologies or processes, local and national influences or demographic factors
  – Hawthorne effect
  – Regression to the mean

• Bias
  – E.g. Volunteer bias
Threats to internal validity

- History
- Maturation (secular trends)
- Testing/Hawthorne effects
- Instrumentation
- Regression to the mean
- Selection bias
- Differential attrition
- Selection maturation interaction
## Threats to internal validity

<table>
<thead>
<tr>
<th>Number of groups</th>
<th>Observation period</th>
<th>Potential major sources of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention group only</td>
<td>After</td>
<td>Selection, attrition, maturation, external influences</td>
</tr>
<tr>
<td>Before and after</td>
<td>maturation, external influences, testing</td>
<td></td>
</tr>
<tr>
<td>Time series</td>
<td>External influences, testing effect on outcomes</td>
<td></td>
</tr>
<tr>
<td>Intervention and non-equivalent control group</td>
<td>After</td>
<td>Maturation, selection, attrition</td>
</tr>
<tr>
<td>Before and after</td>
<td>Residual selection, selection-maturation, regression to mean</td>
<td></td>
</tr>
<tr>
<td>Time series</td>
<td>Residual selection, selection-maturation, regression to mean</td>
<td></td>
</tr>
</tbody>
</table>
Example 1: Pre-experimental

Example 2: Non-randomised control group design


Significant reduction in cannulation rates intervention vs control area (p<0.001)

Reduction in cannulation - intervention area from 9.1% to 6.5% (OR 0.7, 95% CI 1.15 to 1.90, p<0.01)

Increase in cannulation - control area from 13.8 to 19.1% (OR 1.47, 95% CI 1.15 to 1.90, p<0.01)
Example 3: Time series

Example of a simple model

QOF: Interrupted time series


www.lincoln.ac.uk
TARGET: Time series

• To investigate the effect of a large scale educational intervention to primary health care teams to increase prescribing of angiotensin converting enzyme inhibitors for prevention of cardiovascular outcomes in patients with diabetes.

### Table 2  Model for number of prescriptions of 10 mg of ramipril including predictors

<table>
<thead>
<tr>
<th>Effect</th>
<th>Estimate</th>
<th>95% Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Intercept)</td>
<td>17.53</td>
<td>7.91</td>
</tr>
<tr>
<td>GP attended</td>
<td>-1.63</td>
<td>-6.93</td>
</tr>
<tr>
<td>Time</td>
<td>1.27</td>
<td>0.93</td>
</tr>
<tr>
<td>Timepost</td>
<td>1.50</td>
<td>1.07</td>
</tr>
<tr>
<td>Total patient list</td>
<td>0.0000629</td>
<td>-0.000658</td>
</tr>
<tr>
<td>Training</td>
<td>-0.24</td>
<td>-7.12</td>
</tr>
<tr>
<td>Single handed</td>
<td>0.83</td>
<td>-5.89</td>
</tr>
<tr>
<td>Dispensing</td>
<td>0.85</td>
<td>-4.43</td>
</tr>
<tr>
<td>Lincolnshire South West</td>
<td>6.08</td>
<td>0.08</td>
</tr>
<tr>
<td>West Lincolnshire</td>
<td>9.78</td>
<td>3.89</td>
</tr>
<tr>
<td>Nurse attended</td>
<td>9.61</td>
<td>3.11</td>
</tr>
<tr>
<td>(Warwick) diabetes course</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Key issues

• Pre-experimental and quasi-experimental vs. RCT designs
• Importance as potential applications for assessing and evaluating health technologies, interventions and services
• Modelling prior to RCTs, particularly of complex interventions.
Summary

- Experiments in health research
- Non-randomised experimental designs
- Applications, advantages and disadvantages of non-randomised designs
Reading

Thank you