

Therapist effects in randomised trials

An issue for supportive and palliative care?

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What is a “therapist effect”?

- Individually randomised trials provide the gold-standard for the evaluation of interventions
- If interventions are delivered by therapists, some variation in outcomes between therapists can be expected
- Outcomes for different participants are no longer independent (i.e. clustering of outcomes)

Some similarities with cluster randomised trials, where groups of patients are randomised together

Examples of therapist effects / clustering

Likely clustering

- Therapist-led interventions (psycho, physio)
- Surgical interventions
- GP-led, nurse-led, facilitator-led interventions
- Educational interventions, self-help groups

Therapist effect = Health professional variation

Possible clustering

- Centres in a multicentre trial
- Geographical area

Consequences of clustering

- Design
- Analysis
- Interpretation

Issues are not new

- Psychotherapy literature (1970s)
- Re-emergence more generally (1990s)
- CONSORT Statement extension (2008)

Nested and crossed clustering

1. Nested clustering in one arm of trial

e.g. Therapists deliver intervention vs. no-intervention control

2. Nested clustering in both arms of trial

e.g. Therapists deliver intervention 1 vs. **other** therapists deliver intervention 2

3. Crossed clustering

e.g. Therapists deliver intervention 1 vs. **same** therapists deliver intervention 2

How common are therapist effects / clustering?

Review of all individually randomised trials published in the BMJ 2002

Aim: To investigate the extent of clustering, and whether it was recognised

Any clustering	38 / 42
Crossed clustering (usually centre / GP):	31 / 38 (82%)
Nested clustering (usually therapist):	17 / 38 (45%)
Issue recognised	6 / 38 (16%)

Also shown to be common in psychology / psychotherapy research in 1970-80s, but largely ignored

Telemedicine trial (Wallace *et al*, Lancet 2002)

Trial of video-conferencing between consultant, GP and patient to improve the effectiveness of hospital referral

2094 patients randomised to tele-consultation (with GP and consultant) or standard outpatient visit (with consultant)

20 consultants involved (each in both arms of the trial)
– crossed clustering

Primary outcome: Whether patients were offered a further follow-up hospital appointment

Telemedicine trial – results

Odds ratio of being offered a further hospital appointment
(tele-consultation vs. control)

	Odds ratio (95% CI)
Ignoring consultant effects	1.52 (1.27 to 1.82)
Accounting for variability between consultants (hierarchical model)	1.36 (0.85 to 2.13)

Telemedicine trial – comments

Different consultants react differently to initial tele-consultation

Confidence interval for treatment effect now wider (and includes 1)

No longer convincing evidence of treatment effect

Ignoring clustering leads to spurious claim of statistical significance

Design of ALCO-HELP (Murray *et al*, UCL)

Trial of motivational enhancement therapy (MET)
(delivered by alcohol worker) vs. access to interactive
website (facilitated by nurse) for patients in general
practice with moderate alcohol problems

1 alcohol worker per practice

1 nurse per practice

30 patients per practice (15 in each group)

How many patients in total?

Nested clustering – in both arms of trial

ALCO-HELP – sample size

Intraclass correlation coefficient (ICC) describes how much of the total variation in outcome is due to differences between therapists

But ICC is unknown before trial

In a previous related trial of alcohol workers, the ICC was 0.02 – we used this in the sample size calculation

To maintain power, sample size must be multiplied by:

$$1 + (\text{cluster size} - 1) \times \text{ICC} = 1 + 14 \times 0.02 = 1.28$$

So need total sample size of 1800 rather than 1400 patients

Inflation of sample size is worse if:

ICC is larger

Cluster size is larger

Examples from randomised trials in supportive or palliative care

- Thanks to Irene Higginson
- Apologies if misrepresented
- Simplified for sake of presentation
- Focus on therapist / clustering effects

Schnur *et al* (J Clin Psych 2009)

Trial of cognitive behavioural therapy and hypnosis (CBTH) on positive and negative affect in women receiving breast cancer radiotherapy

Design

- 40 women randomised to either CBTH or standard care
- CBTH delivered individually by a therapist (psychologist)
- 2 therapists involved in the trial

Results: Showed reduced levels of negative affect and increased levels of positive affect during radiotherapy

Issues

- Results may be specific to these 2 therapists?
- Not a generalisable test of CBTH?
- Differences between therapists not investigated

Wilkinson *et al* (J Clin Oncol 2007)

Trial of aromatherapy for anxiety and depression in cancer patients

Design

- 288 patients randomised to either course of aromatherapy or usual supportive care alone
- Aromatherapy delivered individually by therapists
- 12 therapists involved

Results: Aromatherapy improved clinical anxiety and depression in the short-term but not in the long-term

Issues

- Therapists were "allowed a degree of autonomy", but the variability between therapists not investigated
- Therapists not described, so difficult to generalise?
- But using several therapists tests "the intervention rather than its application by a particular therapist"

Fallowfield *et al* (Lancet 2002)

Trial of communication skills training for oncologists

Design

- 160 oncologists randomised to attend a communication skills course, or not
- Course participants worked in groups of 3-5 led by a facilitator

Results: Course attendance improved key outcomes (e.g. use of focused questions, expressions of empathy)

Issues

- Not clear how many facilitators?
- Would the trial generalise to other facilitators?
- Was there variation between groups of participants

Velikova *et al* (J Clin Oncol 2004)

Trial of effect of measuring QoL + feedback to physician on wellbeing of cancer patients and physician-patient communication

Design

- 286 patients randomised to (i) completing QoL questionnaires + feedback to physician, (ii) completing QoL questionnaires, or (iii) not completing QoL questionnaires
- 28 physicians involved (each in all arms of the trial)

Results: Recording QoL + feedback improved patients' emotional wellbeing, and led to more frequent discussion of non-specific symptoms

Issues

- Possible randomisation of physicians considered, but rejected as impractical
- Analysis of 'physician effects' planned at design stage
- Paper describes characteristics of the 28 physicians (gender, age, seniority, experience)
- Physician effects found to be non-significant, and reported that this did not affect the intervention estimates

Considerations for design

Think about therapist effects / potential clustering in advance

Define eligibility criteria for therapists (e.g. training, experience)

Consider randomly allocating therapists to treatments

Consider randomly allocating patients to therapists

Record which therapist each patient is allocated to !!

Use many therapists

Increase sample size

Considerations for analysis & interpretation

Describe therapists (e.g. age, qualifications, experience) as well as patients

Investigate variability in results between therapists (e.g. using hierarchical models)

Answer: can one generalise outside of the trial?

See CONSORT extension on reporting trials of non-pharmacological treatments (Ann Intern Med 2008):

- Eligibility criteria for care providers
- Standardisation of the intervention across care providers
- Procedure for tailoring the intervention to individual participants
- Number of care providers, and number of participants per care provider

Summary: consequences of therapist effects

Design

- Reduced precision of treatment effect estimates
- May not be able to distinguish effect of the treatment from the effect of the therapist

Analysis

- Need to address variability in outcomes between therapists

Interpretation

- Generalisability of treatment effects observed

References

Lee & Thompson: BMJ 2005; 330: 142-4

Lee & Thompson: Clin Trials 2005; 2: 163-73

CONSORT extension: Ann Intern Med 2008; 148: 295-309