

Trials & Tribulations: **Towards better design & practice** **in psychological therapy trials**

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Better by design...

- § RCTs in psychological therapies have generally adopted conventional methods from medical trials
- § Are there any unique features of psychological therapy trials?
 - can't be double-blind
 - can't use a credible 'placebo'
- § ... or issues that apply in medical trials but are more salient and likely to be problematic?
 - practitioner effects
 - patient preference
- § How to design better RCTs to underpin the evidence base for provision of psychological therapy
- § First session exploring these issues interactively
- § Second session designing a trial!

Maximising external validity

- § Every trial design is a trade-off between protecting against threats to internal & external validity e.g.
 - single diagnosis vs. complex co-morbidity
 - ‘manualisation’ & adherence checks vs. therapy as routinely practised
- § In one meta-analysis of 12 RCTs in depression, 68% of referred patients excluded at screening.
Westen & Morrison 2001
- § Important for applicability & translation to community & routine settings
- § Pragmatic trials address this by evaluating ‘black box’ interventions in real-world settings
- § The more routine the setting, the more difficult to conduct the trial?

Best of both worlds?

- § We explored how to maximise the yield from RCTs and practice-based evidence (Barkham & Parry 2008)
- § Is it possible to embed RCTs within a patient cohort for routinely collected outcomes?
- § Patients who are eligible and give consent are recruited to the RCT.
- § Patients declining randomization (or whose clinicians refuse to refer to a randomized trial) choose between the treatments being compared and are followed up for the duration of the study using the same outcome measures.

Therapy delivery

- § In drug trials, quality control is maintained in the laboratory & manufacturing process.
- § In psychological therapy trials, need to make sure that what is delivered is the intervention under study.
- § Number of ways to do this
 - Manual for the intervention
 - Training therapists in sticking to manual
 - Ongoing supervision
 - Treatment fidelity checks
- § BUT adherence is not competence.

Equipoise vs Allegiance

- § Psychological therapy world has strong 'tribal' allegiances to a school of practice.
 - good reasons for this,
 - but makes disinterested, fully objective research much more difficult.
- § Many (if not most) trials are conducted by people *not in equipoise*.
 - Those who designed the method
 - Enthusiasts for one approach
- § Evidence that it could matter
 - When allegiance is estimated & included as covariate in meta-analysis, removes specific treatment effects (Luborksky 1999)

Effective therapists

- § Trials are invariably designed to test a 'brand name' therapy (analogous to a drug)
- § But drug metaphor is wrong; A better medical metaphor is surgery
- § Each 'brand name' therapy has to be constructed anew in the consulting room by the patient & the therapist; responsive to individual needs.
- § Some therapists get consistently better results than others; confounding the results
- § Possible solutions:
 - Balancing therapists across treatment conditions (difficult & brings other problems)
 - Randomise to therapists not just treatments
 - Power the design to allow for non-independence within clusters & analysis of therapist effects in HLM (but N=big)

Measuring outcomes

- § Choice of measures influences results!
 - Global or specific
 - Reactive or robust
 - Patient-reported or observer rated
- § Specific symptom measures consistently give larger effect sizes than health utilities, global distress or quality of life
- § Reconciling different goals, e.g.
 - primary outcome on single measure at stated end point for planned analysis
 - broad range of measures across domains & statistical correction for multiple comparisons

Patient preference

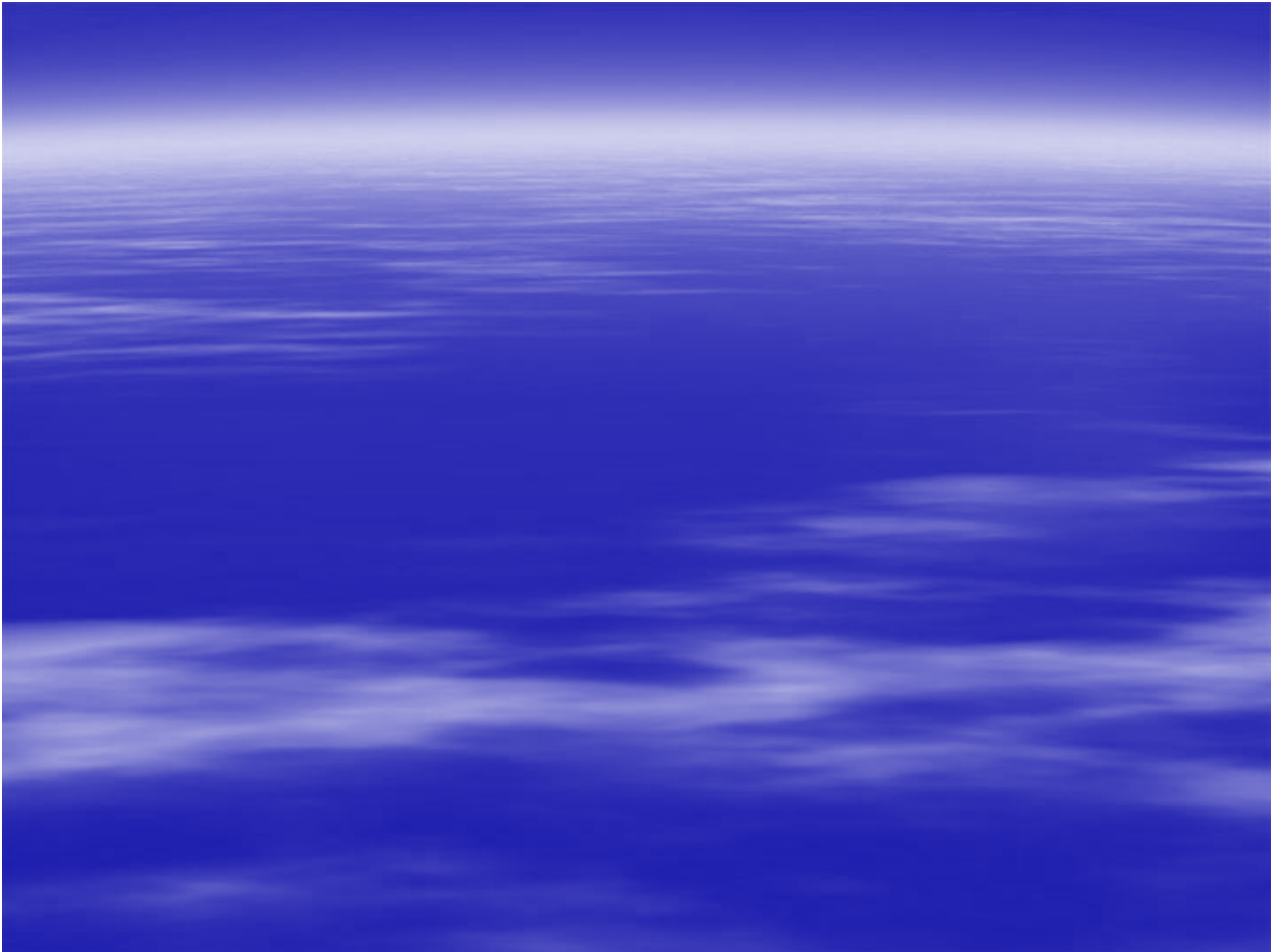
- § Psychological therapies require major investment & commitment from the patient
 - Much more than ‘taking the tablets’
- § Randomisation away from preferred therapy can undermine purpose
 - Differential attrition introduces systematic bias
 - More subtle effects are possible
- § Possible solutions
 - Intention-to-treat is good but often differential drop out means true outcomes are not obtained
 - Patient preference partial randomisation designs, but practical difficulties
 - Leave RCT intact but ensure alternatives are equally credible and monitor initial preference for later analysis

Learning from the patient

- § Given large investment in RCTs, great added value from small investment in qualitative study alongside
- § Mixed methods designs give opportunities
 - Understanding drop out
 - Patients' experience of therapy & the research process itself
 - RCT data give a good sampling frame for specific purposes, e.g. impact of randomisation away from preference, gender- or ethnic-matching, etc.

References

- § Westen, D., & Morrison, K. (2001). A multidimensional meta-analysis of treatments for depression, panic, and generalized anxiety disorder: An empirical examination of the status of empirically supported therapies. *Journal of Consulting and Clinical Psychology*, 69, 875–899.
- § Barkham, M. & Parry, G. (2008) Balancing rigour and relevance in guideline development for depression: The case for comprehensive cohort studies. *Psychology and Psychotherapy: Theory, Research and Practice*, 81, 399–417
- § Luborsky, L. et al (1999) The researcher's own therapy allegiances: A "wild card" in comparisons of treatment efficacy. *Clinical Psychology – Science & Practice*. 6, 95-106.



Design a trial!

- § Small groups consider two of the issues each; focus on trial design in relation to these.
- § Mindfulness-based Cognitive Therapy vs. Person-centred counselling vs. Treatment as Usual for loss-related depression.
- § Phase III trial, can cost as much as you like!
- § Assume best practice in aspects of trial design not covered by your group

Issues to consider

§ Group 1

- External validity
- ‘Blinding’
- Therapy delivery

§ Group 2

- ‘Blinding’
- Therapy delivery
- Equipoise

§ Group 3

- Equipoise
- Patient experience
- Therapist effects

§ Group 4

- External validity
- Outcome measurement
- Patient preference

§ Group 5

- ‘Blinding’
- Outcome measurement
- Therapist effects