Randomised Controlled Trials in Mental Health- AFFIRM Short Course

Key Design Elements 1

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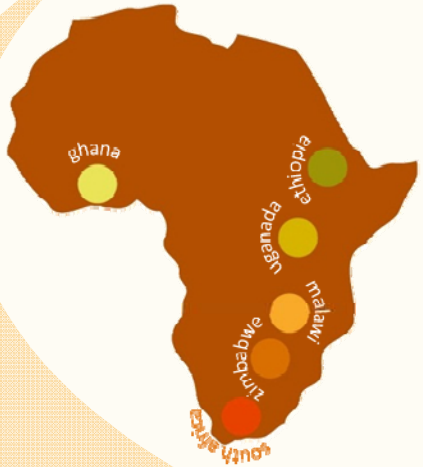

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AFFIRM
AFrica Focus on Intervention Research for Mental Health

Key Design Elements 1 Aims

Outline of key preparatory design elements

- Defining the Trial population
  - Inclusion / Exclusion criteria
  - Heterogeneous / homogenous Sample
- Characterising intervention and control conditions
- Participant adherence
- Outcome measures and endpoints

Defining the Trial population

Defining the Trial Population

- Defining the trial population (as defined by the eligibility criteria) is an integral part of defining the primary research question.

- The eligibility criteria (inclusion and exclusion criteria) should be specified in advance as precisely as possible in the trial protocol

Defining the Eligibility Criteria

General Rules:

Include:

- Patients who would potentially be treated with the intervention / who have the potential to benefit from the intervention
- Use a clinical measure for the inclusion criteria

Exclude:

- Patients who might be harmed by the intervention
- Patients who are unlikely to comply with the trial protocol
- Patients at high risk of developing conditions that preclude ascertainment of the primary outcome

Two Main Approaches

- **Homogeneous Trial Population**

  Use restrictive eligibility criteria

  – Participants suffering from no other conditions, no other medications etc

  – when asking efficacy questions

  – explanatory trials, Phase II trials

- **Heterogeneous Trial Population**

  Use inclusive eligibility criteria

  – when asking effectiveness questions

  – pragmatic trials, Phase III trials

Definitions

- Efficacy: is the capacity to produce a desired size of an effect under ideal or optimal conditions

- Effectiveness: is the capacity to produce a desired size of an effect under real life conditions

Homogeneous Samples

Advantages:

- Provides a cleaner comparison of experimental and control treatments
- Excludes complicated patients
- Reduces sample size required by

  i) Hypothesising larger treatment effect

  ii) Reducing variation within the sample

Disadvantages:

- Limits generalisability
- Limits recruitment rate

Heterogeneous Samples

Advantages:

- Increases generalisability of results
- Increases recruitment rate

Disadvantages:

- Dilutes the potential treatment effect and increases within sample variability and thereby increases the sample size required
- Necessitates reduced data collection per patient
- Results may be complicated by different treatment effects across subgroups of patients

ARC (Addiction Recover Clinic)

Inclusion criteria for the study are intended to be as close to clinical practice as possible. Each participant in the trial must meet all of the following criteria:

1. 18 years of age or older (no upper limit, but generally <60yrs);
2. In treatment at Lorraine Hewitt House for a minimum of 6 weeks by the date of randomisation;
3. Is able to comprehend English to the extent required by the study protocol;
4. Demonstrates verbal understanding of the study patient information material, is able to provide written consent, and can understand and confirm willingness to comply with the protocol;
5. Current diagnosis of opioid dependence;
6. Currently prescribed methadone or buprenorphine mono or combination therapy;
7. Voluntarily seeking treatment and able to attend the clinic as described in the protocol;
8. Lives in sufficiently stable accommodation in the community, with a personal phone;
9. Can nominate at least one locator individual (e.g. a family member, friend or recovery mentor) with a verifiable address and a telephone number which we can call to assist as necessary with the arrangement of follow-up appointments.

Exclusion criteria

1. Clinically significant medical conditions other than addiction that may compromise subject safety or study conduct; or any abnormality which, in the investigator's judgment, is clinically significant.
2. Current criminal justice involvement with legal proceedings and, in the opinion of the Chief Investigator, is expected to fail to complete the study protocol due to incarceration or relocation from the centre's catchment area.
3. Current (past 30 day) suicidal planning, or recent (past six months) suicidal ideation or suicide attempt.
4. Active, uncontrolled severe mental illness (e.g. psychosis, bipolar I disorder, schizoaffective disorder – addressed in routine admissions protocol) and/or a history or evidence of organic brain disease or dementia that would compromise the participant's ability to comply with the study protocol.
5. Has been in any research study in the past 30 days or an intervention research study in the past 6 months.

Characterising intervention and control conditions

Intervention

- Research Question is ready, the investigators will have a class or type of intervention in mind.
- Such as
  - The precise drug to be tested
  - Procedure
  - Life style modification
- To decide on the intervention, consider several aspects
  - Potential benefit maximised , toxicity minimised
  - Dose of drug / intensity of rehabilitation / route of administration
  - Dose titration / stability of intervention over study
  - Single drug / device / combination

Intervention Arms

- Therapy
  - CBT
  - Individual or group
- Intervention
  - Exercise program
  - Diet
- Change in Dose
  - Vitamin
  - Poly pharmacy combination
- Drug

Choice of Trial Arms: Purpose of the Control Group

"To allow discrimination of patient outcomes caused by the test treatment from outcomes caused by other factors, such as the natural progression of the disease, observer or patient expectations, or other treatment"

(ICH E10, 2001)

Types of Control Group

- Placebo
- No Treatment / Waiting-List
- Different Dose / Regimen
- Different Active Treatment
- Treatment as Usual (TAU)

Choice of Control Group

The choice of control group affects:

- The inferences that can be drawn from the trial
- The ethical acceptability of the trial
- The degree to which bias in conducting and analysing the trial can be minimised
- The types of subjects that can be recruited
- The pace of recruitment
- The kinds of endpoints/outcomes that can be studied
- The public and scientific credibility of the results

MENOS 1

INTERVENTION

A treatment manual was produced in advance of the study, which contained detailed session content, presentation slides and handouts, and notes for facilitators. A clinical psychologist was trained to deliver the sessions with the help of an assistant (five assistants took part over the course of the study). All sessions were audio taped, then 10% were randomly selected (with a computer-generated random number sequence) and a psychologist (MSH) experienced in cognitive behavioural therapy for HFNS, rated them for adherence to the treatment manual, by indicating on coding sheets the extent to which the group leader covered each topic. Coding sheets included specific components of the intervention (eg, reviewing home work, providing information about the role of stress, demonstrating paced breathing in the session, group discussion of behaviours relating to HFNS) developed for the trial (appendix).

CONTROL

All participants received usual care—they had access to clinical specialists and cancer support services, either through routine follow-up appointments or as part of a breast cancer survivorship programme in southeast London.

Mann E et al. The Lancet Oncology. 2012: 13(3); 309 - 318

Participant Adherence

Participant adherence

- Compliance – the extent to which a person's behaviour (in terms of taking medicine , attending therapy) coincides with medical or health advice
- Adherence –similar – implies active participant involvement
- Standards of adherence
  - Taking 80% of protocol dose
  - Attendance at 60% of therapy sessions
- Before enrolment adherence should be considered.
- Plan to
  - Main good adherence
  - Monitor adherence
  - Deal with low adherence

Considerations before participant enrollment

- Many potential adherence problems can be prevented or minimized before participant enrollment.
- Once a participant is enrolled, taking measures to enhance and monitor adherence is essential
- Three major considerations
  - 1) when selecting the study population, steps should be taken to avoid, to the extent possible, enrollment of study participants who are likely to have low adherence
  - 2) efforts should be made to limit the impact of design features that may adversely influence adherence
  - 3) research setting influences adherence over a long term. Have realistic estimates of adherence and adjust the sample size accordingly

Adherence monitoring and low adherence

- Monitoring adherence is important:
  - 1) to identify any problems so steps can be taken to address them and enhance adherence
  - 2) to be able to relate trial findings to level of adherence
  - 3) as part of CONSORT the level of adherence that occurred can also be compared with what was expected when the trial was design

- Dealing with low adherence
  - 1) low adherence should be discussed openly and sympathetically
  - 2) given example of reasons for low adherence
  - 3) complete ascertainment of response variables in participants who are no longer involved in the trial
  - 4) Prevent lost to trial (complete withdrawal)
  - 5) Maintain secondary contact

Outcome Measures and Endpoints

Outcomes

- Design a simple trial to answer one question well rather than try to answer every question

- Debate in complex interventions in particular
  - More than one primary may be consistent with disease
  - May want to address explanatory (mediation) questions
  - Moderators to treatment effect