Pilot & Feasibility Randomized Controlled Trials

Department of Evaluation and Research Services

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Content Overview

- Definitions: RCT, pilot & feasibility studies
- Objectives for conducting pilot/feasibility studies
- Differences between internal & external pilot studies
- Designing a pilot RCT
- Sample size calculation
- Analyses and interpretation of results
- Publication of results from pilot studies

Definitions

Randomized Control Trial (RCT)

- A type of research design that involves:
  - Participants assigned to groups (control & intervention)
  - The assignment of groups is at random
  - Study conditions are controlled/manipulated by researcher
- Goal is to establish cause-effect (causal) relationships: to determine the effectiveness of the intervention while controlling for all factors
- Considered the gold standard for a clinical trial

Pilot & feasibility studies

United Kingdom's National Institute for Health Research Evaluation, Trials and Studies Coordination Centre (NETSCC; 2012):

- "***Feasibility*** studies are pieces of research done before a main study in order to answer the question 'Can this study be done?'. They are used to estimate important parameters that are needed to design the main study" http://www.nets.nihr.ac.uk/glossary?result_1655_result_page=F
- "***Pilot studies*** are smaller version of the main study used to test whether the components of the main study can all work together. It is focused on the processes of the main study…. all run smoothly. It resembles the main study in many respects, including an assessment of the primary outcome" http://www.nets.nihr.ac.uk/glossary?result_1655_result_page=P

Feasibility RCT Studies

- Completed before main study: build foundation for the planned study
- Done by testing pieces/components of main study
- Do not evaluate the outcome of interest
- Examples: participants' willingness to participate and be randomized, # of eligible participants

Pilot RCT Studies

- A smaller version of the main RCT study to test if all the components work together.
  - tests the entirety of the RCT but at a smaller scale
- Pilot studies have different objectives to RCTs and these should be clearly described
- Debate about the appropriateness of estimating treatment effect size or the size of the difference between groups in the context of a pilot study
  - **Remember: not powered to test a hypothesis of the outcome** (e.g., examine efficacy of a drug or an intervention)

Pilot Studies

Types of pilot studies:

1. **External**
   - Stand alone study implemented independent to the main study
2. **Internal**
   - Incorporated into the main study design as the first phase
   - Data from first stage may contribute to the final analyses
   - May lead to changes in the study protocol, should not substantive
   - Larger sample size

Objectives for conducting RCTs, pilot and feasibility RCTs

RCT, Pilot & Feasibility Studies

- The aim of a true RCT is to determine the efficacy/effectiveness of an intervention(s) compared with a comparison group
- The terms feasibility & pilot studies are used interchangeably, some however draw clear distinction between the two types
  - Both conducted to assess if the proposed plan can be successfully carried out
  - Guide in the design, planning and implementation of the larger scale study
  - Criteria to evaluate the success of the Pilot & Feasibility studies should be specified a priori

Reasons for conducting pilot & feasibility studies

Based on Thabane et al. (2010), reasons for pilot/feasibility studies are to evaluate the:

1. Process: steps needed to complete study: practicality & restrictiveness of the inclusion/exclusion criteria and the effects on recruitment & retention rates;
2. Resources & management: time and resources; identify challenges, barriers and facilitators
3. Scientific: treatment safety, determine dose levels & responses, effects of treatment, answer methodological questions (e.g., data entry & management; collecting data needed)

Objectives for external pilot

1. Obtain effect size to calculate a sample size for a full RCT
   - ❖ Only if data is not available from previous studies to provide estimates needed for sample size calculations

Caution should be taken when relying on **effect size** derived from pilot studies because of the

- high likelihood of imbalances at baseline to calculate a sample size for a full RCT
- Sample variance will be lower than true variance in over 50% of the time
- Questionable validity of estimates of event rates

Objectives for external pilot

2. Testing the study integrity & procedures “dummy run”
   - inclusion/exclusion criteria
   - recruitment & consent: rates of consent, time to recruit and consent, barriers & facilitators to recruitment
   - randomization procedures: preparation of the assignment, the allocation of the interventions, the acceptance of randomization to patients, the success of blinding of treatment codes for participants and assessors
   - standardization of procedures

Objectives for external pilot

2. Testing the study integrity & procedures “dummy run” (cont.)
   - ❖ training of staff in administering the intervention
   - ❖ number of research assistance needed
   - ❖ completeness time
   - ❖ missing data
   - ❖ follow up rates
   - ❖ safety of intervention
   - ❖ acceptability of intervention to participants
   - ❖ adherence to intervention plan

Examples of Objectives and Outcomes for Feasibility, Pilot & RCT studies: Adapted from Abbott (2014)

	Feasibility	Pilot	RCT
Objectives	▪ Determine: access to participants, barriers to participation, time & resources to complete assessment, need for stratification, adherence to protocol, training needs	▪ Assess: # of potential participants per week & # who fit the inclusion criteria, access to time $ resources to complete the entire study	▪ Investigate: null hypothesis (H_0): treatment A is more effective compared to treatment B
Outcomes	▪ whether recruitment & screening are working well ▪ Effectiveness of blindness, ▪ Access to space and personnel, data completeness & variability	▪ # of potential participants per week & # who fit the inclusion criteria, ▪ % of participants who complete the study to their allocated group	▪ p <= alpha reject H_0 ▪ p >= alpha accept H_0

Abbott, J. H. (2014). The Distinction Between Randomized Clinical Trials (RCTs) and Preliminary Feasibility and Pilot Studies: What They Are and Are Not. Journal of Orthopaedic & Sports Physical Therapy, 44(8), 555-558. *doi:10.2519/jospt.2014.0110*

Internal pilot

- Proceeds in two stages
- Main study is planned
- The first stage: pilot stage (internal pilot) is started with **n** based on best available estimates
- Sample size is recalculated from pilot stage estimates
- If a larger sample is required, then additional participants are recruited into the study
- If less is required, maintain original number
- Allows for more accurate sample size calculations
- Does not allow for additional testing (re external pilot)

Designing pilot RCT

Designing Pilot RCT

Design while keeping the larger study in mind & align with the aims of the pilot study

- Identify aim
  - at least one of the reasons for conducting a pilot should apply
  - decide if aim is to determine the processes/logistics (attrition rate) or the outcome (effectiveness)
- Draft specific, measurable & achievable objectives
  - Evaluate adequacy of eligibility criteria
  - Determine adequacy of blinding procedures
- Define the end points/outcomes (e.g., proportion of participants retained until the end of the study)

Source: Johanson & Brooks (2009)

Designing Pilot RCT

- Include a sample size and its justification with appropriate references
- Ensure that the study is designed to answer the larger study questions
- Determine as a priori the criteria that will be used in the decision to pursue a larger study, e.g.,
  - Consent rate of 80% or higher
  - Recruitment of the study sample within 6 months
- Arnold et al. (2009) recommends public registration of the study protocol to minimize publication biases

Source: Johanson & Brooks (2009)

Sample size for pilot studies

Sample size for pilot studies

- Not designed or powered to evaluate the effectiveness of an intervention
- However, sample size justification/rational is required
  - Clear rational linked to the study-specific objectives
- Avoid statement such as: “no sample size justification is required for pilot studies”
- Impacted by costs and time limitations, number of sites, variability in the population
- A smaller sample needed for objectives investigating processes & resources

Sample size for pilot studies

Different guidelines & rules of thumbs:

- Julious (2005) and van Belle (2002): for continuous variables n=12 per group
- Hill (1998): n=10 to 30 participants for pilots in survey research
- Browne 1995: n>=30 participants to estimate a parameter
- Lackey & Wingate (1998): n=10% of the sample projected for the larger study

Note. Small ***n*** will not be adequate for providing estimates for larger studies

Sample size for pilot studies

Different guidelines & rules of thumbs (cont.):

- Sim & Lewis (2012): at least 50 participants per group
- Stallard (2013): approximately 0.03 times that the sample size planned to be included in the largre study
- Estimating rate: width of the 95% confidence interval for the rate

Note. Small ***n*** will not be adequate for providing estimates for larger studies

Sample size for internal pilot

- Initial sample size calculation: estimate sample size as usual
  - Significance level alpha
  - Desired power
  - Effect size (based on best estimates)
  - Select proportion to include in the pilot phase (n1)
- Adjust sample size: after recruitment of initial n
  - Estimate variances and other important parameters
  - Recalculate the sample size using the new parameters (n2)
  - If new parameter<= initial parameters, continue with initial plan
  - Otherwise, adjust sample size based on new parameter
- Final stage: hypothesis testing using initial and adjusted samples

Source: Wittes & Brittain 1990

Analyses

Statistical Analysis Plan

- Plan the analyses following the same standards for a larger study
- Include complete & specific analyses plan for each aim
- Depends on type of pilot: external is stand alone, not typically used to test hypothesis or treatment effectiveness
- Depending on sample size and data distribution, the analyses may be descriptive: calculating point and interval estimates (limited hypothesis testing)

Reporting results from pilot studies

Publication & reporting

- Some journals have publication policies/guidelines for publishing pilot studies
- Some have case by case consideration
- Some do not publish or encourage the publications of results from pilot studies
- CONSORT is in the process of developing new guidelines for pilot and feasibility studies
- Ask a FH librarian to help you identify a journal with history of publishing results from pilot studies

Publication & reporting internal pilot studies

- Refer to the specific journal's guidelines while writing the manuscript
- Cochran warned of over-interpretation of results from small pilot studies, positive or negative
- Results are limited to descriptive statistics (means, SD and 95% CI)
- Can provide preliminary estimates of the effect size, however it is recommended that statements regarding treatment efficacy be avoided
- Transparency in reporting results on efficacy with emphasis on the limitation of the statistical power

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