

Pilot Study Design Issues

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Outline

- Pilot Study Definition
- External Pilot Study Objectives
- Internal Pilot Studies
- General Principles
- Examples
- Concluding Remarks
- Discussion

Starters

How many statisticians does it take to light a gas stove?

I don't know because we haven't run the pilot study yet.

Pilot Study Definition

- Definition One
A small experiment designed to test logistics and gather information prior to a larger study, in order to improve the latter's quality and efficiency.
- Definition Two
A pilot study is a model of the full research study but on a smaller scale performed whose results will affect the design of the larger study.

Pilot Study Definition

- | | | |
|---|---|---|
| Pilot Study | ≠ | Exploratory Study |
| <ul style="list-style-type: none">• objective something other than hypothesis generation• prelude larger study of same type• no explicit justification of the sample size | | <ul style="list-style-type: none">• generate hypotheses• stands on its own• explicit justification of sample size |

Pilot Study Types

- External
 - stand-alone studies
 - carried out independently to the main study
- Internal
 - incorporated into the main study design
 - carried out a initial part of main study

Pilot Study Types

- **Examples of published pilot studies**
 - preparation for a trial
 - new treatment or technique (phase I and II studies)
 - screening program
 - guidelines, education package, patient care strategy
 - survey / questionnaire
 - laboratory test of activity of compounds

Pilot Study Objectives

- To obtain data to help plan full study
- To see where Murphy's Law will strike
 - *anything that can go wrong, will go wrong*
- Familiarize research team with protocol
- Selection of key study components

Data for Planning

- **Estimate of variability of outcome measure**
 - **continuous measure**
 - variability of control group
 - assume same variability in experimental group
 - **scour the literature**
 - standard deviation
 - standard error
 - coefficient of variation
 - confidence interval

Data for Planning

- **Estimate of variability of outcome measure**
 - **study design**
 - control treatment
 - at least 30 subjects*
 - **analysis**
 - estimate the standard deviation of measurements
 - use the 80% upper one-sided confidence limit of standard deviation estimate
 - use this to power main study

Data for Planning

- **Estimate of probability of some event**
 - categorical outcome measure
 - scour the literature
 - **study design**
 - control treatment
 - at least 30 subjects*
 - **analysis**
 - determine the sample proportion
 - use the 80% upper one-sided confidence limit of estimate
 - use this to power main study

Data for Planning

- **Participation rates**
 - How many eligible subjects can be recruited per month?
 - What is the compliance rate?
- **Resource requirements**
 - How much time is required per subject?
 - What is the cost per subject?

Murphy's Law

- Integrity of study protocol
 - prep for large trial
 - dummy run
 - trouble shoot
 - inclusion/exclusion criteria
 - drug preparation
 - storage and testing of equipment and materials
 - training of staff in administration and assessment of intervention

Murphy's Law

- Recruitment and retention
 - Do you get the types of subjects you think you will get?
 - Do people turn down opportunity to participate in study? If so, why?
 - Do people fail to finish study? If so, why?
 - Do people fail to comply with study protocol? If so, why?

Murphy's Law

- Randomization procedure
 - How well does the randomization procedure work?
 - How acceptable is the concept of randomization to the patient?
 - What is the best way to provide an explanation of randomization to subjects?

Murphy's Law

- Acceptability of intervention
 - Does it have unacceptable side effects?
 - Is it difficult to administer?

Murphy's Law

- Data collection: questionnaires
 - Do the study subjects provide no answers, multiple answers, qualified answers, or unanticipated answers in a questionnaire?
 - Does it take too long for subjects to fill out questionnaire?
 - Does everyone give identical answers to a question?

Murphy's Law

- Data collection: general
 - Is there enough room on data collection form for all possible situations?
 - Can you match data that comes from different sources?
 - Were any important data values forgotten?
 - Does your data show too little / too much variability?
 - Are most of your lab results below the limit of detection?
 - Do different study personnel fill the form out identically for same patient?

Familiarize research team with protocol

- Assure standardization and consistency
- Identify any areas of ambiguity
- Get study team “buy-in”
- Ramp up to main study

Selection of key study components

- Decide between competing approaches
 - **interview vs self-administered survey**
- Choice of most appropriate primary outcome measure
 - reliability of outcome
 - feasibility of measurement

Internal Pilot Studies

- Main study is planned
 - sample size determined on best available data
 - study started
- Internal pilot mechanics
 - uses first XX number of subjects
 - sample size recalculated
 - if larger sample size needed, this is new sample size
 - if smaller sample size needed, retain original sample size

Internal Pilot Study

- Other characteristics
 - more accurate sample size without increasing time to conduct full trial
 - does not allow pre-testing feasibility of other trial factors
 - Type I error will be slightly inflated
 - needs to be specified as part of study protocol

General Principles of Pilot Studies

- Requires well-designed set of aims and objectives
- Participants in external pilot should NOT be included in main study
- Analysis should be mainly descriptive or focus on estimation
- Hypothesis testing is discouraged
- Need to proceed to main study, even if pilot has significant differences

Example of Well-Designed Pilot

- Phase I clinical trial
 - **objective:** find the maximum tolerated dose, if one exists
 - specific criteria
 - know how it will be incorporated in next study
 - subjects typically are not included in next study

Example of Well-Designed Pilot

- **Phase I clinical trial**
 - **descriptive analysis**
 - adverse events
 - outcomes
 - **no hypothesis testing**
 - **proceed to Phase II, if MTD found**

Pilot Study Example 2

- **Quality of life intervention in patients with primary brain tumors**
- **Primary objective**
 - to determine the feasibility of implementing a cognitive rehabilitation and problem-solving therapy intervention
 - successful implementation and tolerability will be operationalized as at least 75% of patients completing all stages of the intervention

Pilot Study Example 2

- **Secondary objectives**
 - to provide support that a brief, structured rehabilitation intervention for patients with primary brain tumors can affect quality of life
 - to investigate the variance in the brain tumor patient population on the primary quality of life measures, which will allow the researchers to adequately power future studies of the efficacy of the intervention

Pilot Study Example 2

- **Analysis**
 - determine the observed complete rate
 - descriptive statistics on the scores of the cognitive and quality of life instruments used
 - trends toward better scores on these measures in the intervention group than in the control group will be considered supportive; better score is defined as a 10% difference between the intervention group and the control group

Concluding Remarks

- **Design pilot with specific objective in context of the larger study**
 - conclusion of pilot should affect future study
 - cite specific information that pilot would provide
 - place pilot in context of main study
 - no rationale need for sample size, other than large enough to be useful

Concluding Remarks

- **Analysis of pilot**
 - descriptive
 - estimation
- **Pilot is not an exploratory study**
 - both useful for preliminary data
 - have different objectives
 - need more attention to sample size in exploratory study

Concluding Remarks

- Do not use pilot data in main study
 - never for external pilot
 - only for internal pilot if pre-specified

Pilot study helps by providing data needed to plan larger study and by identifying areas where Murphy's Law will strike.

Discussion and Questions