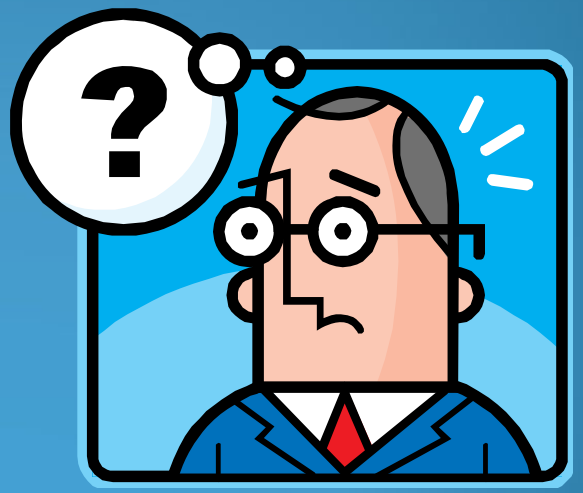
Writing a Pilot or Feasibility Study

"You never test the depth of a river with both feet"



Pilot and feasibility studies are not the same thing.

Why would you do either?

- An RCT is a big financial risk for a funder. Can they trust you will be successful?
- You may not be prepared to do an RCT – time, money
- You have a lot of questions on how to do this study in the best possible way

- Answer? Feasibility study to test your strategies, improve track record and odds of success

What is a pilot study?

- A miniature version of the main study run to determine if the components and processes can all work together to generate results
- A shake-down cruise of the main study
- Focused on procedures: recruitment, randomization, follow-up visits

What a pilot study is not

- It is not a study you undertake when you have no hypothesis.
- It is not a study that has a sample size that is too small to matter.
- It is not a small, underpowered clinical trial…"pilot" does not make it ethical.
- It is not a study that has no follow-up planned.
- Is it a good way to help generate sample size assumptions? Maybe, maybe not

Is a pilot study ethical to perform?

- Requirements for an RCT
  - Equipoise - True uncertainty which intervention will benefit the patient, hence random allocation
  - Balancing the potential to generate new knowledge with the protection of participants' welfare
  - Consider the burden placed on participants for the benefit of future populations, especially when participants are not receiving the standard of care.

So what if the sample size is too small to show important clinical benefit if it exists? A pilot study sample size is usually small, unrepresentative.

What is a feasibility study?

- Components of research done prior to the main study to answer the question, “Can this study be done?” Is it feasible?
- Undertaken ***before the planned study*** to determine whether to proceed with a project and to decide the best approaches to adopt
- Important in reducing uncertainties for the main study
- This work can provide reassurance to reviewers that the work has been thoroughly thought through

Thinking about feasibility…

- Should be one of the first steps in planning a trial
- Not conducting a thorough feasibility analysis increases your odds of failure and your own challenges
- Having data on feasibility will increase your odds of funding
- And your study will be more successful
  - You do not want to change the intervention, change the inclusion/exclusion criteria, need to add recruiting sites
- Do not forget the institutional costs of low enrolling studies – SPA, IRB, contracting, study start-up. In 2009, this cost OHSU almost $1M.

Feasibility Study

The endpoints for a feasibility study are factors that affect successful trial conduct, not measures of treatment effect or safety.

- What do we need to know that we currently don't in order to make the main study a success?
- What could go wrong in the main study?
- This is **not** a "study in miniature"

Writing a feasibility study

- What do you need to know to propose the "real" study you want to conduct? A feasibility study creates the pathway
  - Generate confidence about your ability to do this study
  - Generate data for sample size and power
- Describe how this feasibility study will lead to your next study
- Specific aims need to clearly delineate the steps you are undertaking, why, and what success means
- Can include hypothesis testing around feasibility
- Power calculations are usually unnecessary
  - However, sample size should be adequate to estimate parameters such as recruitment rate and sample variability

Feasibility Study Questions

Intervention

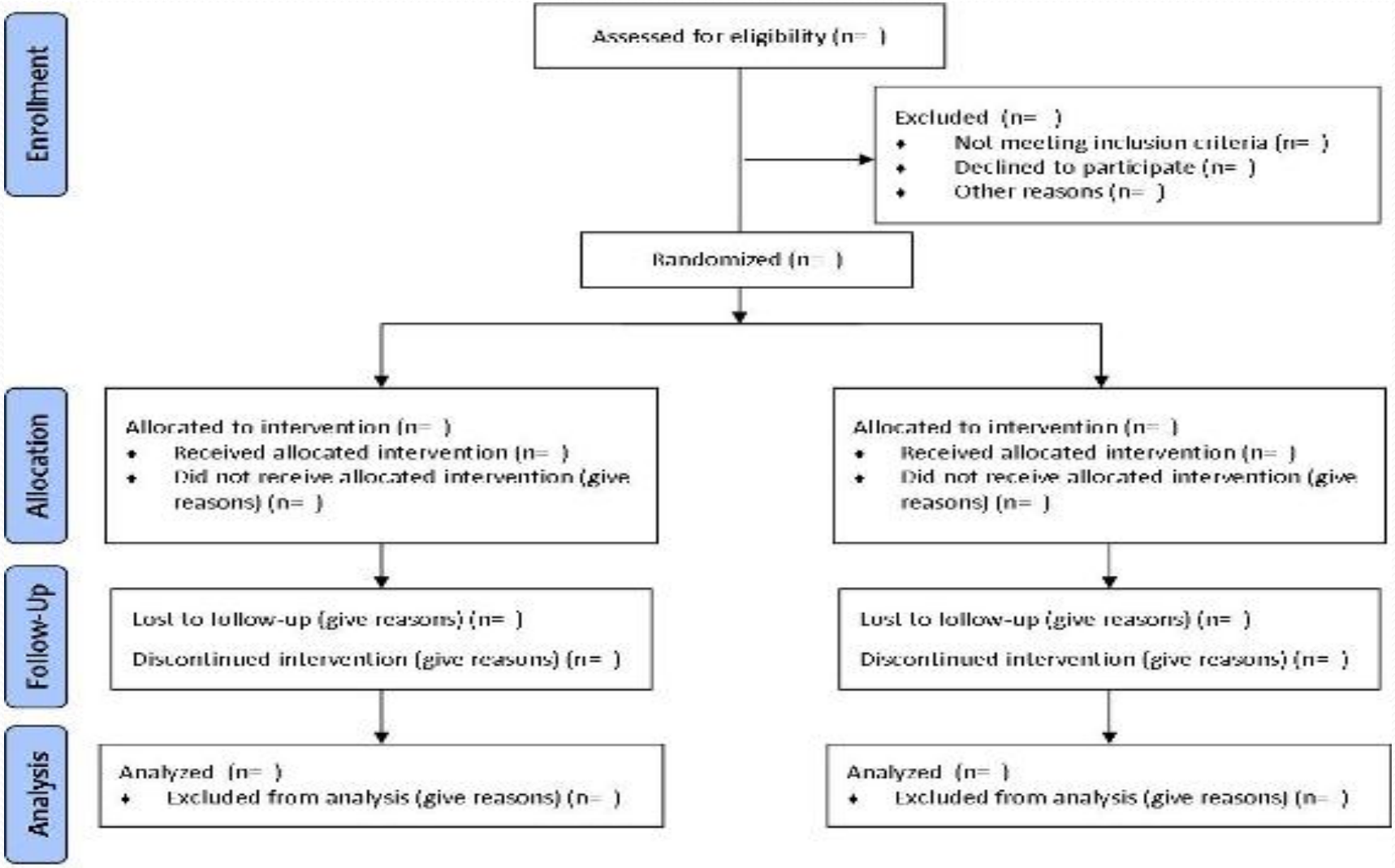
- Develop the exact way the intervention and control will be administered and by who
- Dose, duration, exact means of delivery
- Develop any patient-facing materials
- Develop any materials to encourage adherence
- What is adherence to the intervention?
- Is any modification needed?

Feasibility Study Questions

Study Participants

- How easy are they to identify?
- Can you demonstrate you have access to sufficient subjects?
- Proportion of the available population that are eligible
- How diverse/similar are the participants?
- How realistic are the eligibility criteria?
  - Is it obvious who meets and who does not meet the eligibility requirements? Do they need revision?
- How willing would they be to be recruited and/or randomized?
- What is the refusal rate?

Think about the CONSORT diagram….



Feasibility Study Questions

Study Sites

- In recruiting sites, what makes the site useful? Number of patients available? Do sites bring a different perspective?
- How suitable are the investigators in terms of qualifications, experience, probity?
- What facilities and staff are present? Experience?
- How well did they recruit patients as an indicator of what might happen in the main study?
- How willing are they to recruit or randomize patients when faced with alternatives?

Feasibility Study Questions

Study Processes

- Retention rates
- (Non)compliance or adherence rates
- Test exactly how you will measure outcomes
- Use of study questionnaires or data collection tools:
  - Do subjects provide no answer, multiple answers, qualified answers, or unanticipated answers to study questions
  - Run a cognitive test of selected instruments

A chance to involve the community

- Stakeholder engagement!
- Community of clinics/practices
- Community of similar patients and their families
- Can help to determine:
  - How the intervention will be implemented
  - How frequently patients complete the study
  - How best to collect information…internet, SMS, mail
  - Are participants willing and able to answer the questions and complete the procedures?

Feasibility Study Questions

Power and Sample Size

- How frequently does the outcome occur in the population you expect to recruit from? (baseline)
- Expected range of the outcome, sample variance
- What is the variability of other important variables?

Questions more specific to pilot studies

- Determining capacity:
  - Staffing….how many people, how to recruit
- Determining process time
  - How much time does a study visit take?
  - Is the equipment readily available?
  - What backup is available?
- Are there problems collecting and entering data?
- Determining center willingness and capacity
  - Do the centers do what they committed to doing?
  - Do investigators have the time to perform the tasks they committed to doing?
  - Are there any capacity issues at each participating centre?

Critical points that will not come from pilot or feasibility

Scientific:

- Is it safe to use the study drug/intervention?
- What is the safe dose level?
- Do patients respond to the drug? (maybe not best question)
- What is the estimate of the treatment effect?
- What is the estimate of the variance of the treatment effect?

Feasibility Specific Aims

- Determine the willingness of women over 60 with T2DM to participate in a daily anaerobic walking program.
  - Hypothesis: This program is feasible if >70% agree to participate.
- What is the most efficient and effective means to recruit eligible patients in a community practice to participate in a research study?
  - Hypothesis: Online consent using an iPad in the waiting room enables a significantly higher proportion of successful recruiting (to participate in a questionnaire study?) as compared to distributing a recruitment card with QR code.
  - Using participant interviews, explore the attitudes toward being asked to consent.
- In an unselected population, determine the proportion that meet all inclusion and exclusion variables criteria.
  - Hypothesis: If at least 50% of the sample meet inclusion/exclusion criteria, the study will be deemed generalizable and feasible.

Feasibility Specific Aims

- Identify, recruit, and consent an eligible cohort and determine the proportion who are adherent to the study protocol over a short period of time.
  - Hypothesis: Of those participants who provide consent, at least 80% will complete anaerobic exercise for at least 45 minutes duration at least 3 days a week.
- Determine the reliability and validity of measurement of the primary outcome comparing 3 different survey instruments.
  - The XYZ questionnaire will demonstrate criterion validity of at least 80% and test-retest reliability

Writing the study outcomes

- State the criteria for success *a priori* – benchmarks for success
  - Stop
  - Continue but modify protocol
  - Continue but monitor
  - Continue, no change

How to apply for a feasibility study

- Relatively common for K awardees (K12, K01, K23)
- NIH has a series of awards for this:
  - R03
  - R21
  - R34
  - R61/R33
  - UG3/UH3

  - NIH has tightened policies around clinical trial implementation and now requires considerable documentation that clearly reflects your preparation for a clinical center and data center if multicenter.

Perhaps the best reference?

- Teresi JA, Yu X, Stewart AL, Hays RD. Guidelines for Designing and Evaluating Feasibility Pilot Studies. Med Care. 2022 Jan 1;60(1):95-103. doi: 10.1097/MLR.0000000000001664. PMID: 34812790; PMCID: PMC8849521.