
Introduction to Clinical Research
Boot Camp 2020
INVESTIGATOR TRACK
Day 2
Tuesday, July 28, 2020
ITHS
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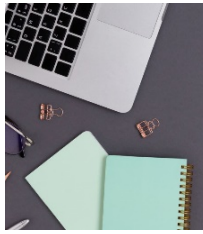
ACCELERATING RESEARCH. IMPROVING HEALTH.



Introduction to Clinical Research Boot Camp 2020

Protocol Design

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Professor of Medicine, University of Washington

Learning Objectives

By the end of this session you will be able to:

- Identify four critical questions that must be addressed in designing a clinical trial.
- Describe the problems that can occur if the trial design neglects any critical design elements.

STUDY PROTOCOL

What Are The Qualities Of A POORLY Designed Study?

Design Problems	Execution Issues
Unreasonable, unrealistic eligibility criteria	Slow (or no!) recruitment
Irrelevant data	Inadequate data
Vague language	Unreliable results
Errors and inconsistencies between protocol sections	Protocol deviations
Challenging procedures for participants and study staff	Safety issues


Identify the end goal

Critical Questions

- Who will be enrolled in the trial?
- How will participants be treated?
- How will results be evaluated?
- How will we protect participant safety?

Who Will Be Enrolled in the Trial?

Inclusion Criteria

Who Will Be Enrolled in the Trial?

Pitfalls:

- Too restrictive
  - Don't let the perfect interfere with the good
- Too 'generous'
  - Participants at specific risk of harm
  - Participant outcome likely to be uninformative
- Cherry picking
  - Match criteria to intended ***market*** population

Who Will Be Enrolled in the Trial?

Recommendations:

Know the product being tested

- Investigator's Brochure or package insert
- Toxicity profile

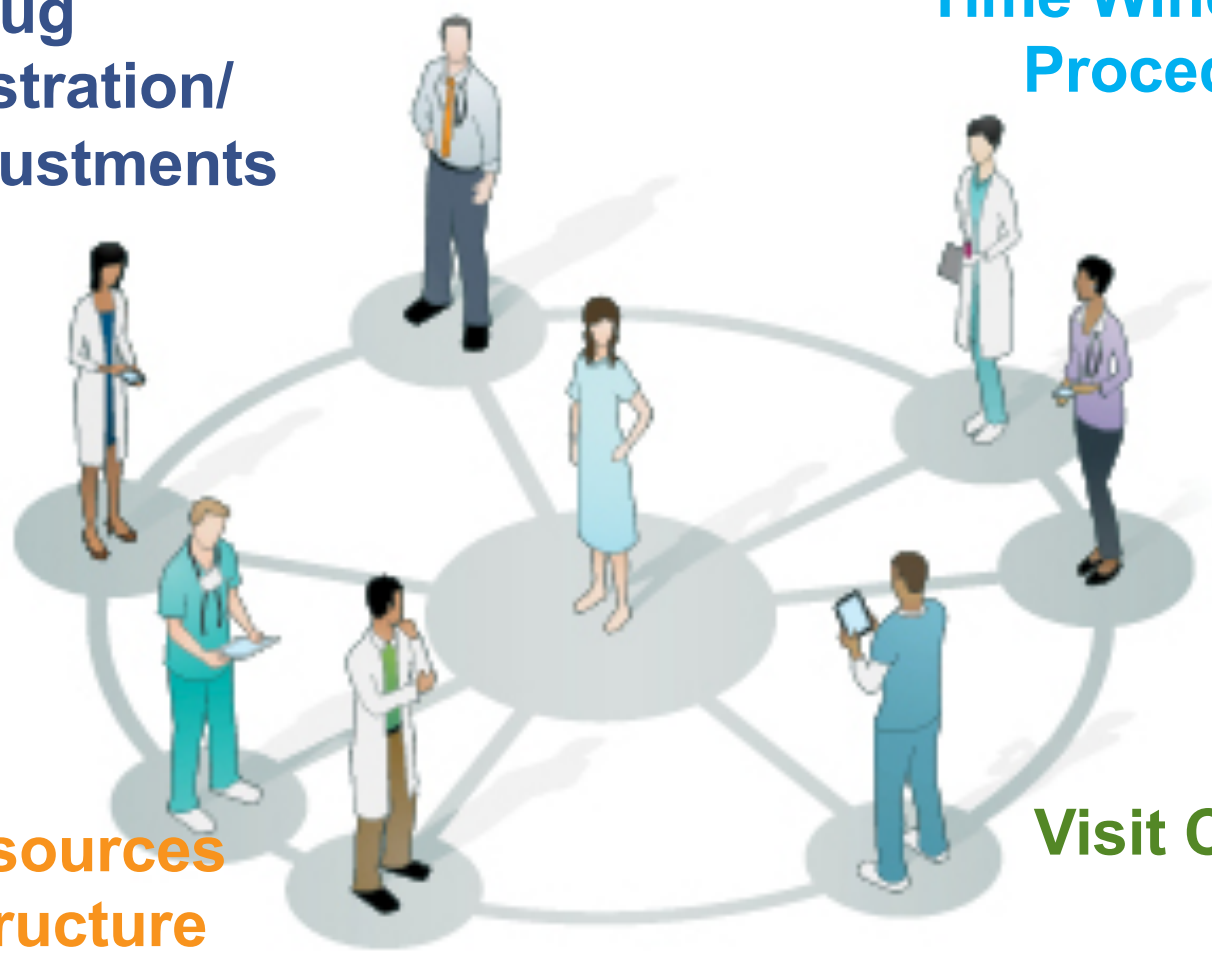
Understand the trial phase

Understand how results will affect the next step

How Will Participants Be Treated?

Drug Administration/ Dose Adjustments

Time Windows for Procedures



Clinic Resources & Infrastructure

Visit Calendar

How Will Participants Be Treated?

Pitfalls:

- Participant perspective
- Relationships with study/clinic staff
- Missing & unreliable data
- IRB, Institution, Sponsor, OHRP/FDA
- Future patients

How Will Participants Be Treated?

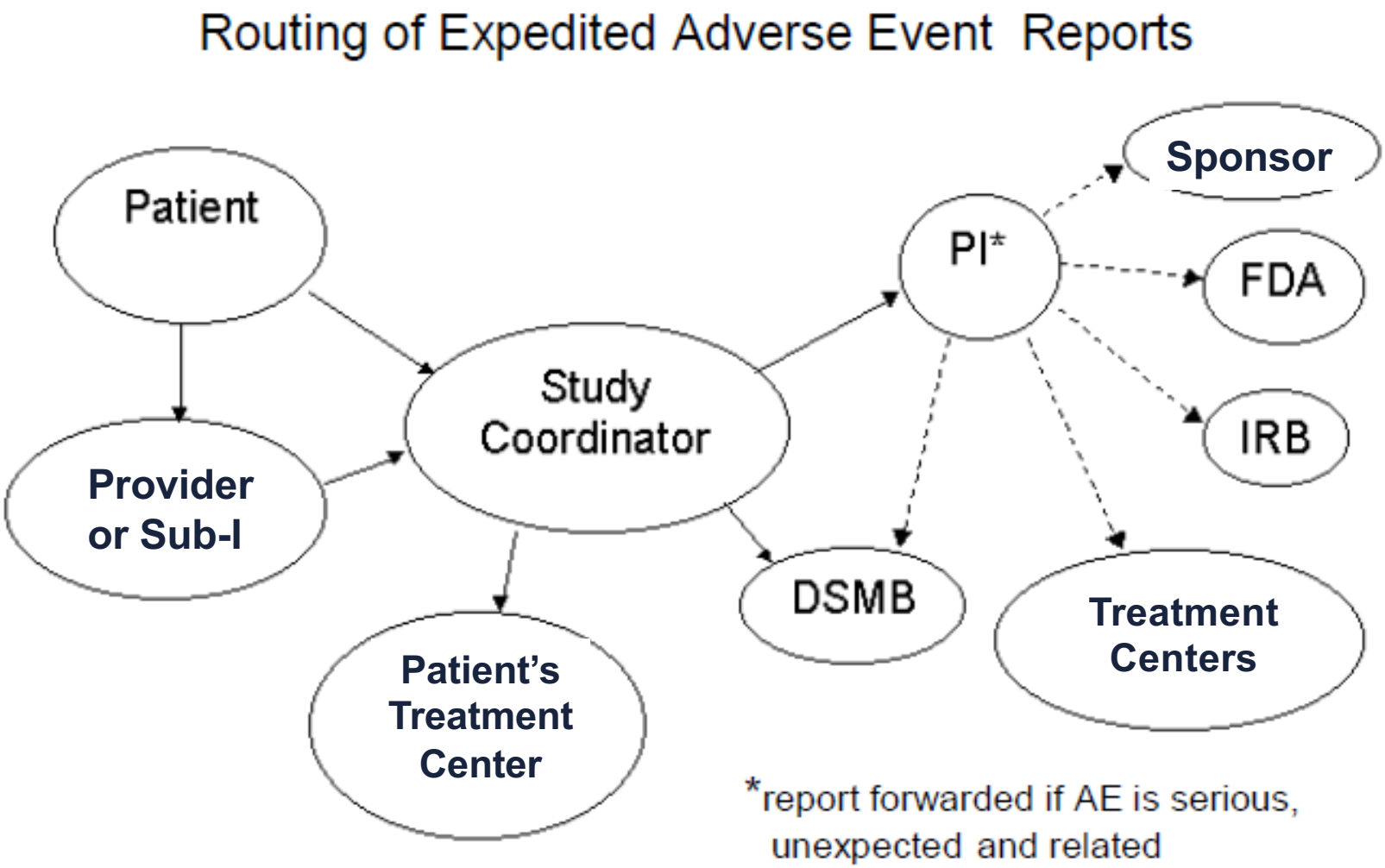
Recommendations:

- Consult with research & clinic staff for feasibility
- Create Data tools to minimize missed data
  - Fast Fact sheets
  - Visit checklists
- Look at the details
- Match protocol to practice (not vice-versa)

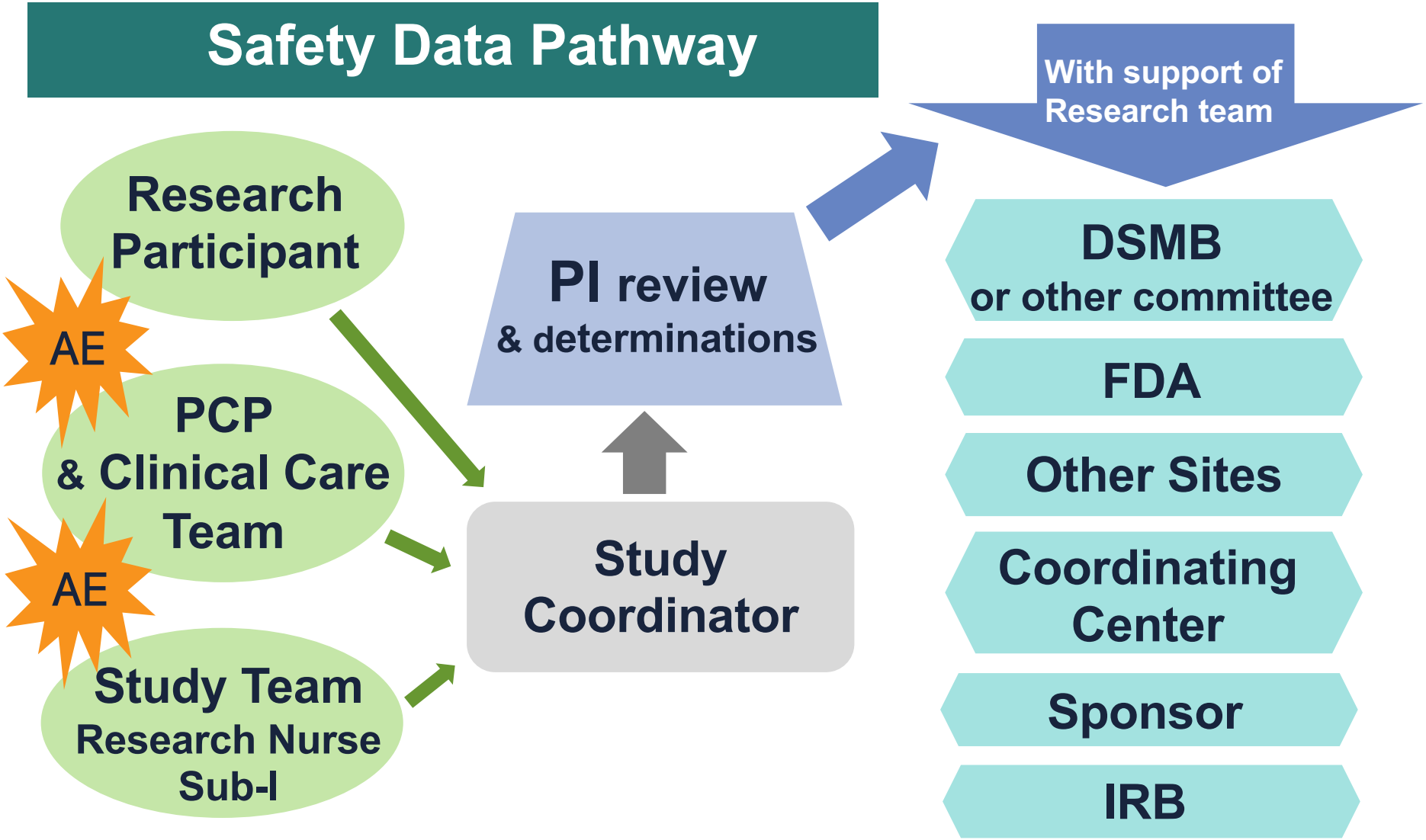
How Will Results Be Evaluated?

- Define the primary & secondary endpoints
- Stats questions
  - sample size, type 1 & 2 errors
- Data collection tools
- Data cleaning methods
- Interim analysis plan
- Data Safety Monitoring Plan
  - information flow

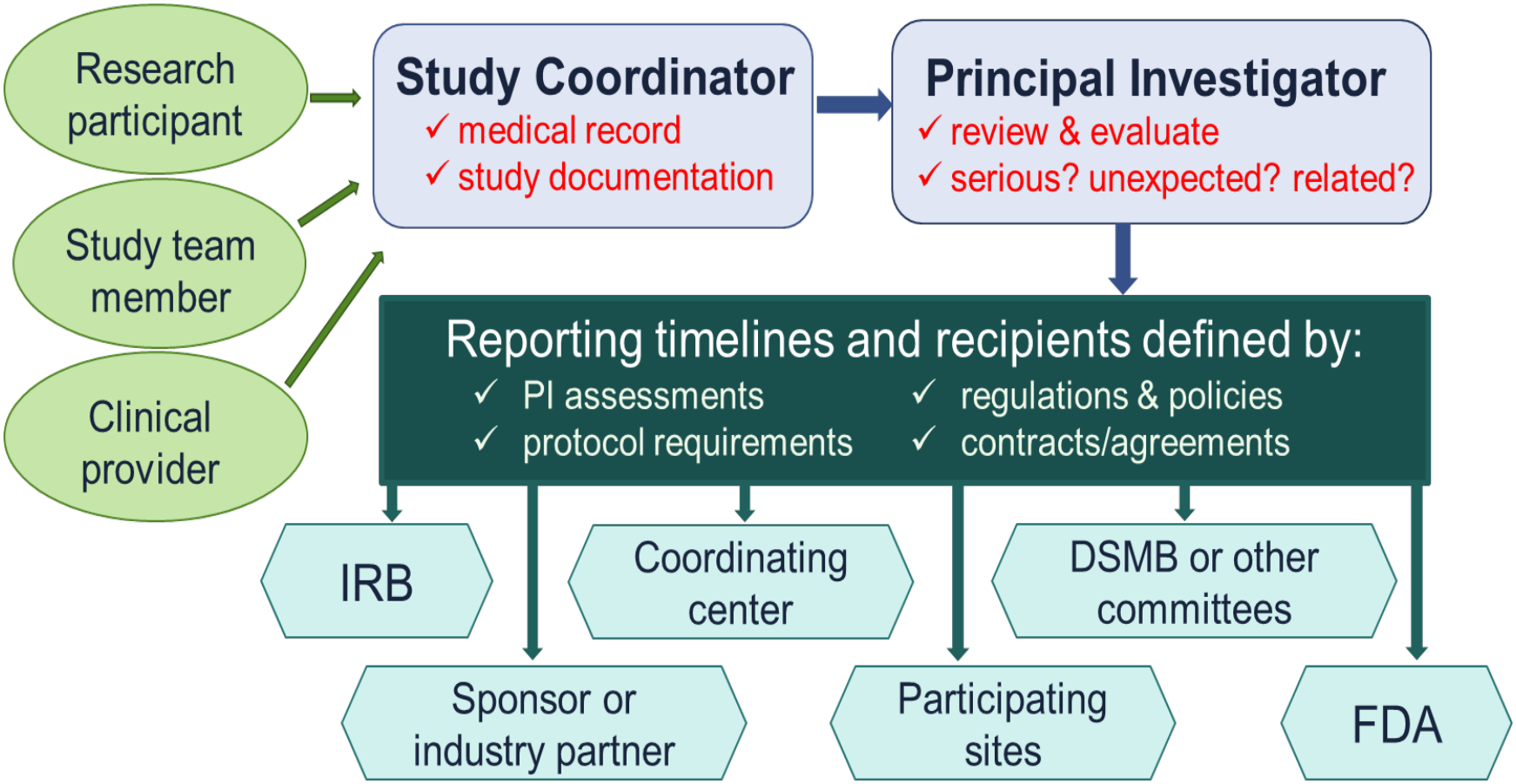
How Will Results Be Evaluated?



How Will Results Be Evaluated?



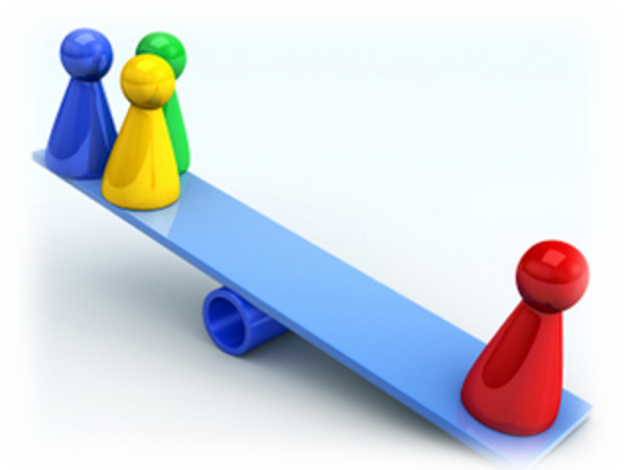
Adverse Event Communication Pathway



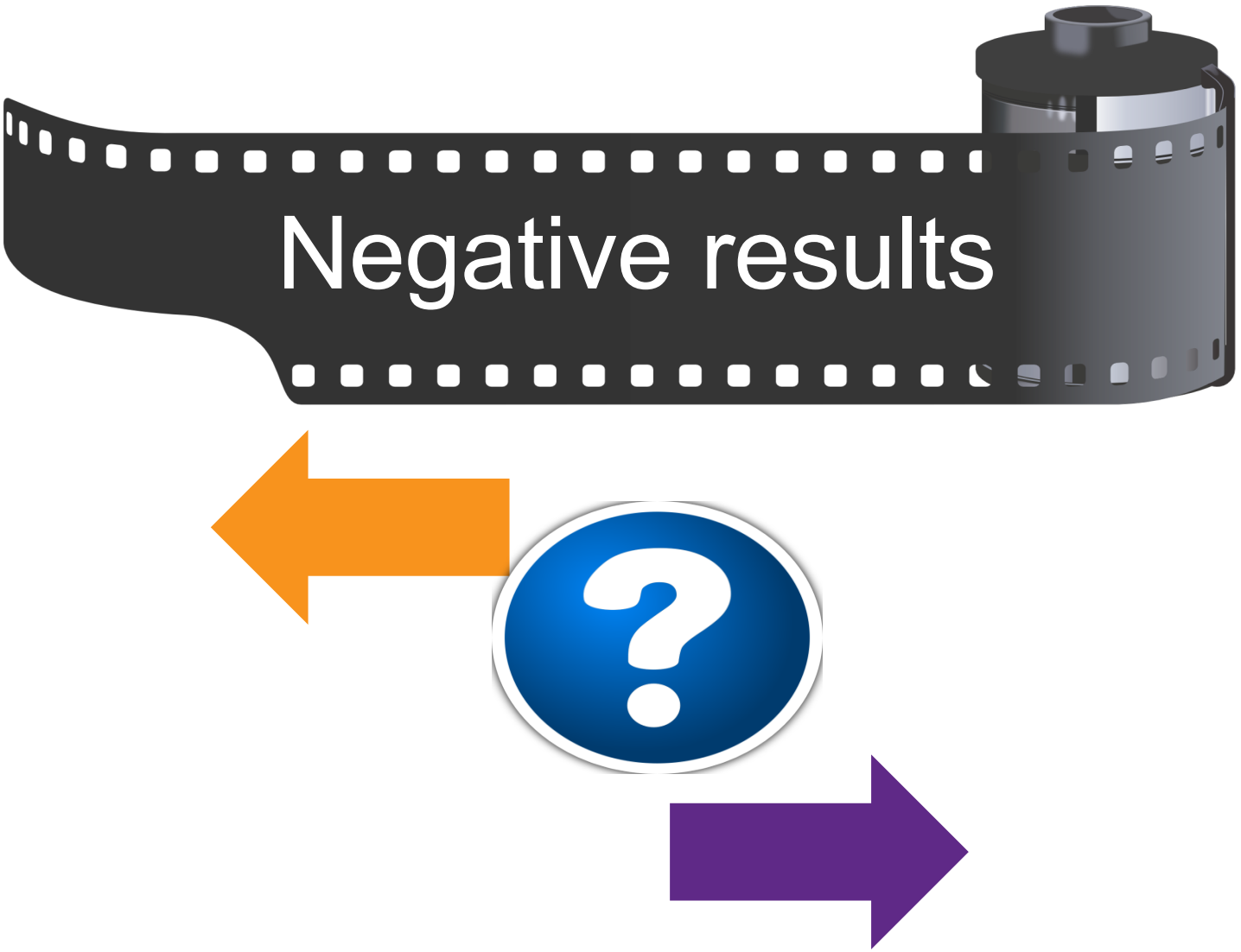
How Will Results Be Evaluated?

Pitfalls:

- Introduction of bias
  - unblinding practices
  - unbalanced protocol arms
  - unspecified endpoints



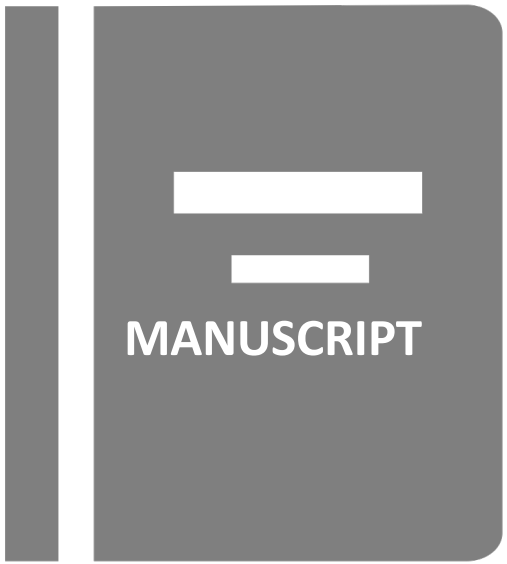
How Will Results Be Evaluated?



How Will Results Be Evaluated?

Recommendations:

- Consult with statistician
- Understand the question
- Maintain blinding
- Balance between arms
- Pre-specified endpoints



Sample of Study Protocol Elements

- Background information and rationale
- Objectives and endpoints
- Eligibility criteria
- Enrollment and withdrawal
- Investigational product/Intervention
- Study Schedule
- Study Procedures/Evaluations
- Risk/Benefit Assessment

Further details:

ICH GCP
Section 6

21 CFR 312.23 (6iii)

Eight benchmarks for ethical research

Collaborative partnership
Social value
Scientific validity
Fair participant selection
Favorable risk/benefit ratio
Independent review
Informed consent
Respect for participants and communities

Emanuel et al. What makes clinical research ethical? *JAMA* 2000;283:2701-11; *JID* 2004;189:930-37.

Poll: Who will be enrolled in the trial?

- Collaborative partnership
- Social value
- Scientific validity
- Fair participant selection
- Favorable risk/benefit ratio
- Independent review
- Informed consent
- Respect for participants and communities

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Poll: How will participants be treated?

Collaborative partnership
Social value
Scientific validity
Fair participant selection
Favorable risk/benefit ratio
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Respect for participants and communities

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Poll: How will results be evaluated?

- Collaborative partnership
- Social value
- Scientific validity
- Fair participant selection
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- Independent review
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Poll: How will we protect participants safety?

Collaborative partnership
Social value
Scientific validity
Fair participant selection
Favorable risk/benefit ratio
Independent review
Informed consent
Respect for participants and communities

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QUESTIONS?
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