COMPARATIVE EFFECTIVENESS TRIALS:

THE IRB PERSPECTIVE

AGENDA: outline key concepts the IRB considers when evaluating a comparative effectiveness trial

Considerations for Protocol

- **Based on** the current state of the **literature**, **is it truly unknown** at this moment whether Treatment A or Treatment B is more effective?
- Does the institution **locally have the resources** to fully perform the study in a way that will generate meaningful data?

Considerations for ICFs

- Include a clear description of the **purpose** and what is currently unknown
- Outline that subjects must be **willing to be randomized**, as well as how that could alter care
- Describe all the **alternatives** to participation

PROTOCOL CONSIDERATIONS

WHAT DOESN'T THE LITERATURE PROVE THUS FAR

PROTOCOL DESIGN: **two core considerations** the IRB looks for when evaluating comparative trials

Show that There Isn't Enough Information to Prove A > B

Demonstrate that There is Enough to Assess & Prove A ~ B Locally

PROTOCOL NEED #1: background needs to **demonstrate** that it is **currently unknown** whether A is better or worse than B

Demonstrate that Interventions are "Usual Care"	• Outline how interventions align with standard practice both in literature and in the institution itself • Consider and note any differences in these interventions within the study
Outline How Design Elements Inform the Unknown	• Consider how the design choices impact the results of the protocol itself • Examples: whether physicians get to switch subjects to another option if not responding, whether randomization or blinding will occur, etc.
Show that the Question is Worth Asking!	• Clearly outline how literature was thoroughly reviewed and that even so it is still unknown which intervention is more effective • Demonstrate that there is a clear path to disseminate findings

PROTOCOL NEED #2: design needs to **demonstrate** that there are **locally adequate resources** to achieve this objective

Recruitment	Analysis/Monitoring
• Are there enough eligible patients who would be interested to get meaningful results? • For randomization, consider if there're enough patients to randomize to each group	• Consider whether an interim analysis to see potentially unexpected impacts may be necessary or feasible • If high risk, consider getting a Data Safety Monitoring Committee to review the study

CONSENT CONSIDERATIONS

OUTLINING WHAT IS UNKNOWN & HOW CARE VARIES IN PARTICIPATION

CONSENT TIP #1: Must include a clear description of the purpose of the study

State Why this is Being Studied

- Clarify **why the question is being asked** (i.e. determining which works better for their population)
- Explicitly note that they **could potentially receive** the **less-effective** option

Outline Necessary Procedures

- Only need **to specify the procedures related to** the **research** interventions (i.e. if studying two screw implants, only need to describe the screws & any components of the surgery that will be altered for research)
- Acceptable to include all procedures too, but need to delineate between clinical & research procedures (which can be hard for complex protocols)

CONSENT TIP #2: Must note that, in participating, subjects are **willing to be randomized** knowing that efficacy is unclear

- ***Essential Element***: participation involves the **elimination of patient-physician choice process**

- To **state this clearly**, you can use the following strategies:

Explain in Lay Language	Consider a Diagram	Describe Other Related Elements (e.g. "blinding")	Avoid Misleading Language (e.g. treatment, patients, study doctor)

CONSENT TIP #3: Must clearly state that an **alternative to participation** is **to receive either option** through standard clinical practice

Outline Alternatives, including the Accepted Practices

- Given nature of the study, each component should be available outside of participation at subject's discretion
- Participating also means **giving up patient-physician choice** in treatment

Outline the Risks & Benefits Accordingly

- *Risks*: be sure to include **any risks** to the standard procedures/options that are **outside what would be experienced otherwise**
- *Benefits*: update the potential benefits based on the different standard-of-care interventions

TAKEAWAYS: outline key concepts the IRB considers when evaluating a comparative effectiveness trial

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