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** $A \sim B$ 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

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

<table>
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<tr>
<th>Outline Alternatives, including the Accepted Practices</th>
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<td>• Given nature of the study, each component should be available outside of participation at subject’s discretion</td>
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<td>• Participating also means <strong>giving up patient-physician choice</strong> in treatment</td>
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<th>Outline the Risks &amp; Benefits Accordingly</th>
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<tr>
<td>• <strong>Risks</strong>: be sure to include <em>any risks</em> to the standard procedures/options that are <em>outside what would be experienced otherwise</em></td>
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<tr>
<td>• <strong>Benefits</strong>: update the potential benefits based on the different standard-of-care interventions</td>
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TAKEAWAYS: outline key concepts the IRB considers when evaluating a comparative effectiveness trial

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