More Questions Than Answers-
Toward Efficient Generation of High-Quality Evidence

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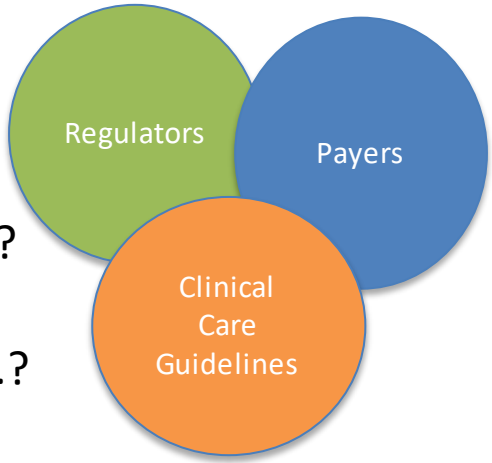
- I have no financial relationships to disclose

Many Important Questions

- Does an investigational treatment's efficacy outweigh its risks?
- Is a new treatment better than an existing treatment?
- What is the best sequence of approved drugs in a disease?
- Is it equally effective to de-escalate a treatment?
- Is it more effective to escalate treatment for high-risk groups?
- What is the safety and effectiveness of a drug in older adults, racial/ethnic subgroups, patients with organ dysfunction, etc.?
- What is the optimal dose and schedule?

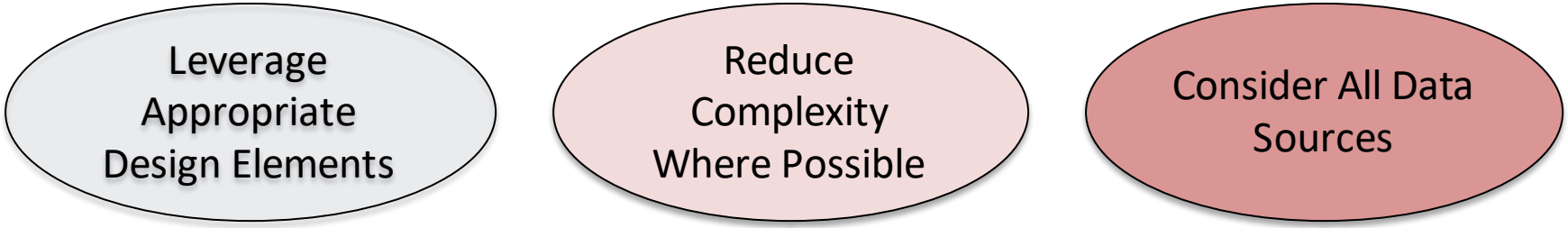


Answers to these questions can impact clinical decisions and patient access to important cancer therapies- **Evidence must be high quality**

Every Question Cannot be Answered by Traditional Centralized Complex Explanatory Randomized Trials

- $ Lengthy, expensive process
- Extraordinary pressure on research staff including:
  - Nurses, research assistants, investigators
- Significant burden on patients

Consider a Range of Design and Data Source Options Depending on Context



Master Protocols

Adaptive Designs

Common Controls

Decentralized Trial Elements

Focused objectives

Reduced collection

Pragmatic Trial Elements

Trial Data

Patient-Generated Data (ePRO, etc.)

Electronic Health Records

Registries

Take Home Points

- High quality evidence is needed more than ever
- We can be more thoughtful about **what, how** and **where** we obtain evidence- considering all appropriate design and data source options
- Ongoing trials are deploying various decentralized and pragmatic design elements- it can be done
- Appropriate design elements and data sources depend on the regulatory objective, disease and treatment context. Meet with FDA review Division.