CLINICAL TRIALS TRANSFORMATION INITIATIVE

July 31, 2020

Using RWD to Plan Eligibility Criteria & Enhance Recruitment

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Disclaimer

- The views and opinions expressed in this presentation are those of the individual presenter and do not necessarily reflect the views of the Clinical Trials Transformation Initiative, Duke University, or Janssen Scientific Affairs.

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

Public-Private Partnership
Co-founded by Duke University & FDA

Involves all stakeholders
- Approx. 80+ members
- Participation of 400+ more orgs

MISSION: To develop and drive adoption of practices that will increase the quality and efficiency of clinical trials

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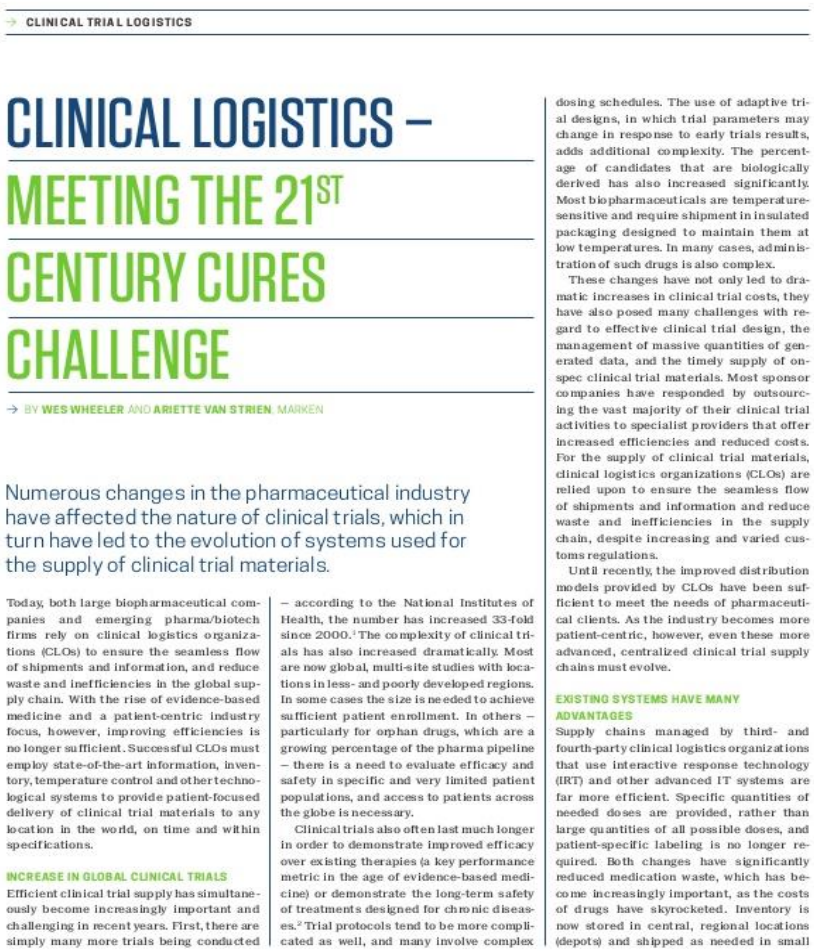
Meeting Recruitment Challenges



CLINICAL TRIAL LOGISTICS

CLINICAL LOGISTICS – MEETING THE 21ST CENTURY CURES CHALLENGE

BY WES WHEELER AND ARIETTE VAN STRIEN, MARKEN

Numerous changes in the pharmaceutical industry have affected the nature of clinical trials, which in turn have led to the evolution of systems used for the supply of clinical trial materials.

Today, both large biopharmaceutical companies and emerging pharma/biotech firms rely on clinical logistics organizations (CLOs) to ensure the seamless flow of shipments and information, and reduce waste and inefficiencies in the global supply chain. With the rise of evidence-based medicine and a patient-centric industry focus, however, improving efficiencies is no longer sufficient. Successful CLOs must employ state-of-the-art information, inventory, temperature control and other technological systems to provide patient-focused delivery of clinical trial materials to any location in the world, on time and within specifications.

INCREASE IN GLOBAL CLINICAL TRIALS

Efficient clinical trial supply has simultaneously become increasingly important and challenging in recent years. First, there are simply many more trials being conducted – according to the National Institutes of Health, the number has increased 33-fold since 2000.[1] The complexity of clinical trials has also increased dramatically. Most are now global, multi-site studies with locations in less- and poorly developed regions. In some cases the size is needed to achieve sufficient patient enrollment. In others – particularly for orphan drugs, which are a growing percentage of the pharma pipeline – there is a need to evaluate efficacy and safety in specific and very limited patient populations, and access to patients across the globe is necessary.

Clinical trials also often last much longer in order to demonstrate improved efficacy over existing therapies (a key performance metric in the age of evidence-based medicine) or demonstrate the long-term safety of treatments designed for chronic diseases.[2] Trial protocols tend to be more complicated as well, and many involve complex dosing schedules. The use of adaptive trial designs, in which trial parameters may change in response to early trials results, adds additional complexity. The percentage of candidates that are biologically derived has also increased significantly. Most biopharmaceuticals are temperature-sensitive and require shipment in insulated packaging designed to maintain them at low temperatures. In many cases, administration of such drugs is also complex.

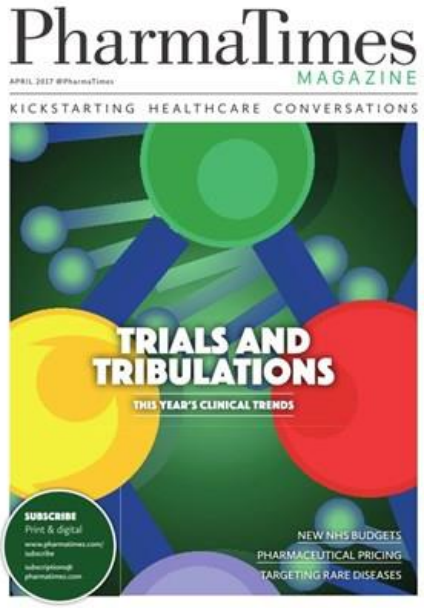
These changes have not only led to dramatic increases in clinical trial costs, they have also posed many challenges with regard to effective clinical trial design, the management of massive quantities of generated data, and the timely supply of on-spec clinical trial materials. Most sponsor companies have responded by outsourcing the vast majority of their clinical trial activities to specialist providers that offer increased efficiencies and reduced costs. For the supply of clinical trial materials, clinical logistics organizations (CLOs) are relied upon to ensure the seamless flow of shipments and information and reduce waste and inefficiencies in the supply chain, despite increasing and varied customs regulations.

Until recently, the improved distribution models provided by CLOs have been sufficient to meet the needs of pharmaceutical clients. As the industry becomes more patient-centric, however, even these more advanced, centralized clinical trial supply chains must evolve.

EXISTING SYSTEMS HAVE MANY ADVANTAGES

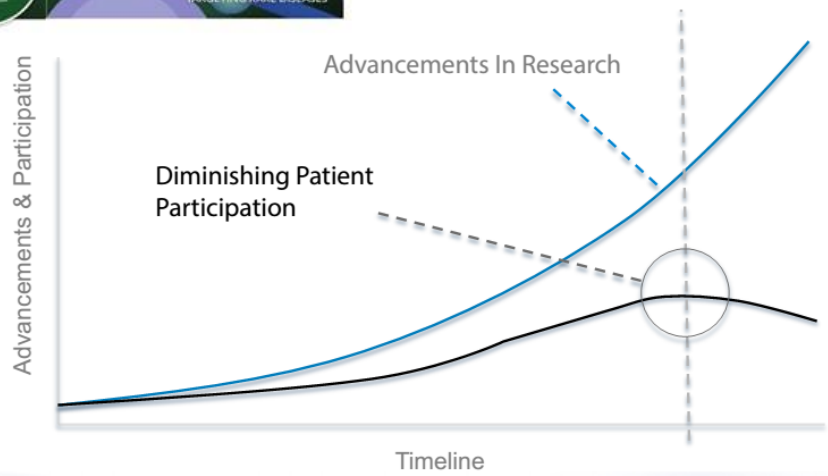
Supply chains managed by third- and fourth-party clinical logistics organizations that use interactive response technology (IRT) and other advanced IT systems are far more efficient. Specific quantities of needed doses are provided, rather than large quantities of all possible doses, and patient-specific labeling is no longer required. Both changes have significantly reduced medication waste, which has become increasingly important, as the costs of drugs have skyrocketed. Inventory is now stored in central, regional locations (depots) and shipped as needed in small

20 PHARMA'S ALMANAC GLOBAL PHARMACEUTICAL SUPPLY CHAIN LANDSCAPE | Q1 2016



Forbes

Discovery's 'First In Human' Calls Much-Needed Attention To Clinical Trials



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CTTI Real-World Data (RWD) Project Team

Executive Committee Champions:

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David Thompson, Syneos Health
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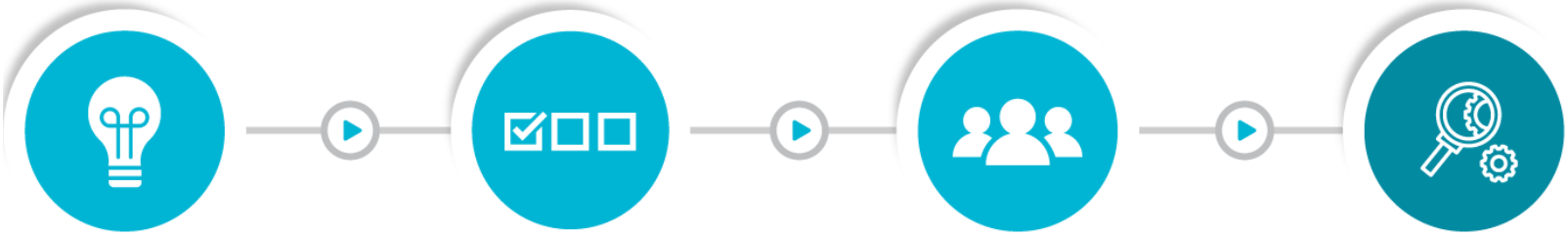
Guneet Walia, Genentech

Evolution of Gauging Public Opinion

Straw Poll

Telephone Poll

Real World Data (RWD) Recommendations



GENERAL
PRINCIPLES FOR USING RWD

RECS FOR
USING RWD TO PLAN FEASIBLE ELIGIBILITY CRITERIA

RECS FOR
USING RWD TO SUPPORT RECRUITMENT

RECS FOR
ENHANCING RWD CAPABILITIES FOR THE RESEARCH ENTERPRISE

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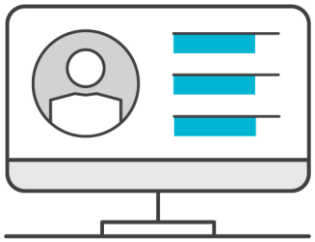
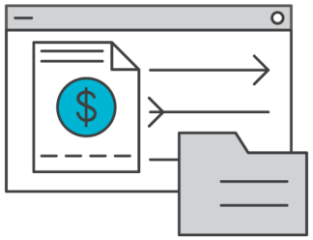
Data Sources



EHR

- Data richness / depth
- Clinical info
- Faster availability
- Integration with routine health care



Claims

- Fully structured
- Widespread availability
- Continuum of data capture

COMMON CHALLENGES

Data completeness, data accuracy, & generalizability

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- Start early in product lifecycle
- Engage patients & sites
  - *Data alone never tell whole story*
- Build cross-functional teams

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Resource: Establishing Use of RWD as Standard Process in Study Planning & Recruitment

Early Stages

- Engage study teams as early as possible
- Demonstrate value (e.g., case studies)
- Pilot with early phase / feasibility trials

Standard Process

- Leadership understanding & support
- Identify and maintain data sources (consider budgets, priorities, & responsibilities)
- Support cross-functional teams

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- Evaluate RWD against particular needs of study
- Use RWD to test important assumptions
- Plan iterative team discussions
  - *Starting early in study design*

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Tool: Is the Data Fit-for-Purpose?

Important eligibility criteria identifiable?

- Directly or via proxy measures
- Structured and unstructured data

Data of sufficient relevance & quality?

- Acceptability of errors in data
- Recency relative to study needs
- Generalizability

Analysis cost-effective?

- Number of databases
- Challenges in pooling data

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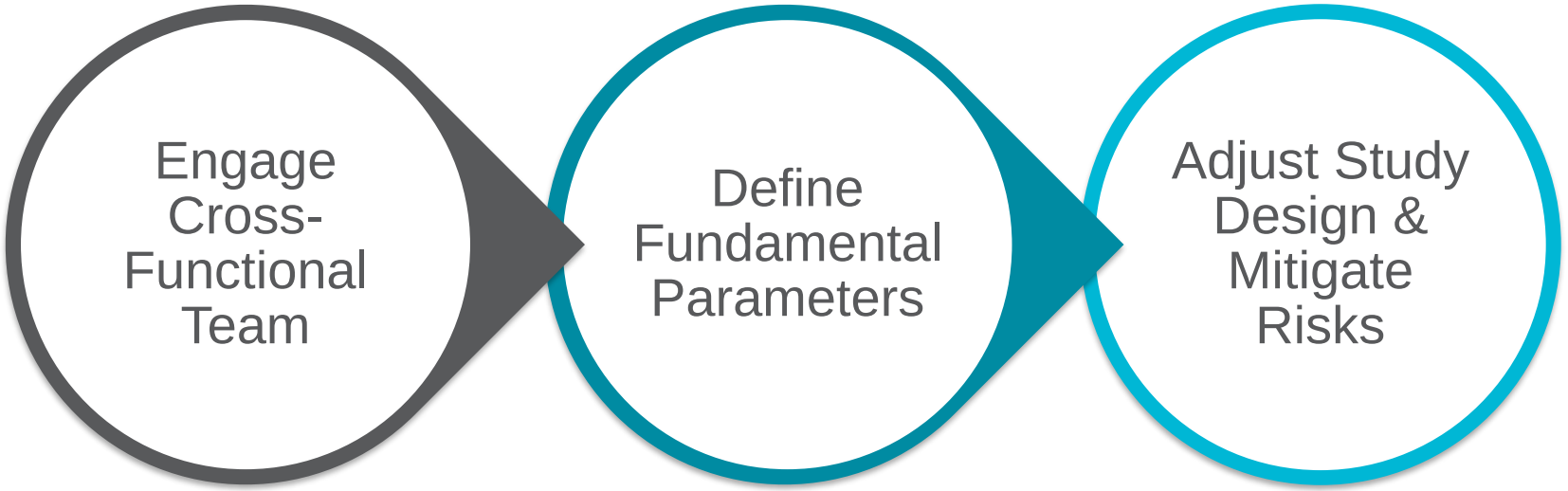
Tool: Effective RWD-Supported Discussions



For example…

- Clinical
- Operations
- Informatics
- Epidemiology
- Patients
- Investigators

Including…

- Study objectives
- Key endpoints
- High-level eligibility criteria
- Likely operational challenges

Identify and plan for…

- Risks associated with non-negotiable eligibility criteria
- Impact of changing other proposed eligibility criteria
- Outside factors impacting feasibility

Case Study: Using RWD to Expand Eligibility Criteria for Phase III Endocrinology Study

As part of a broader strategic initiative, the sponsor saw:

33%

Increase in **PATIENT ELIGIBILITY**

71%

Increase in **ENROLLMENT RATES**

2.1 month

Reduction in **RECRUITMENT TIMELINES**

Additional case studies available at https://www.ctti-clinicaltrials.org/projects/real-world-data

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- Start with realistic eligibility criteria
- Incorporate RWD-supported recruitment whenever feasible
- Understand needs of patients & sites

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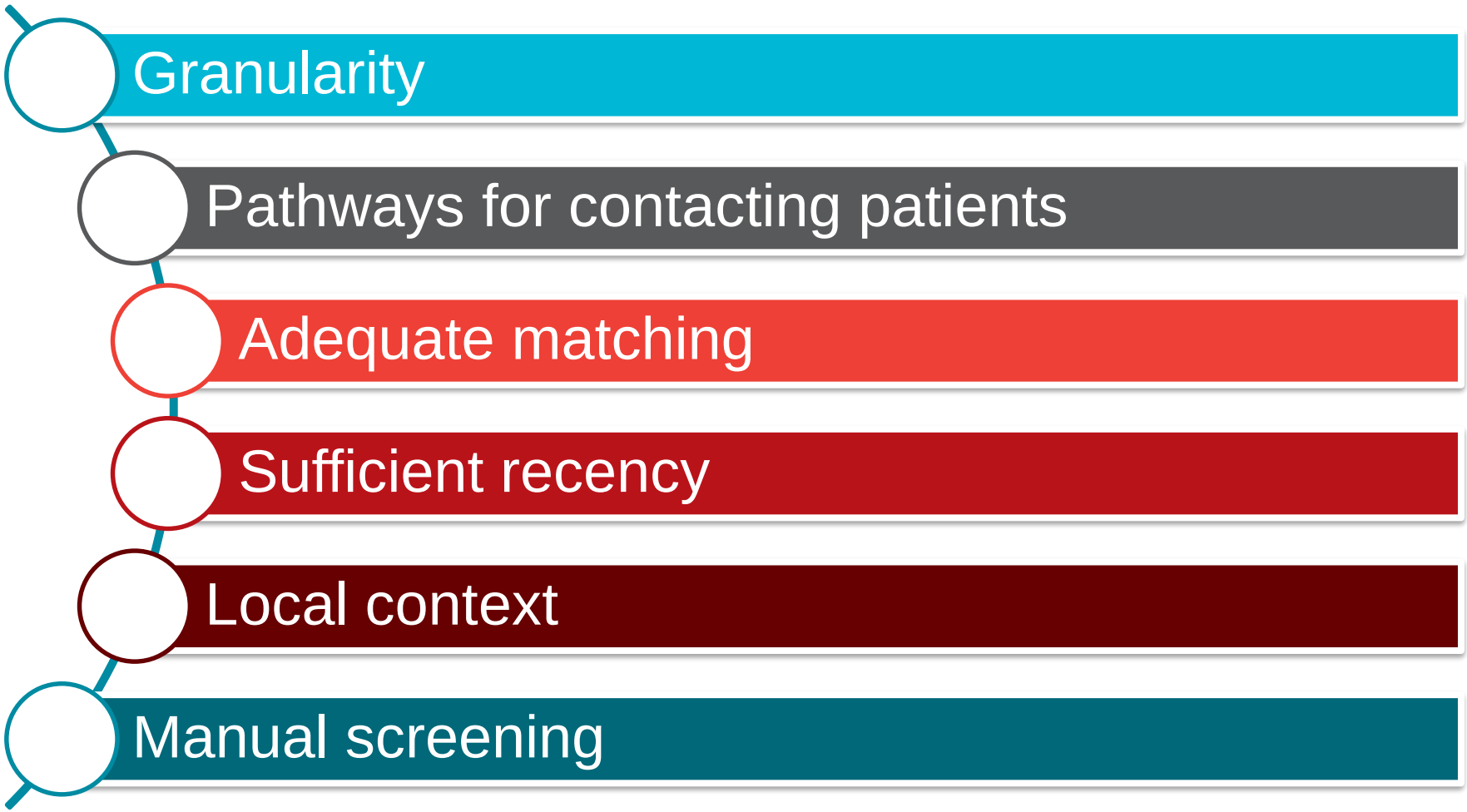
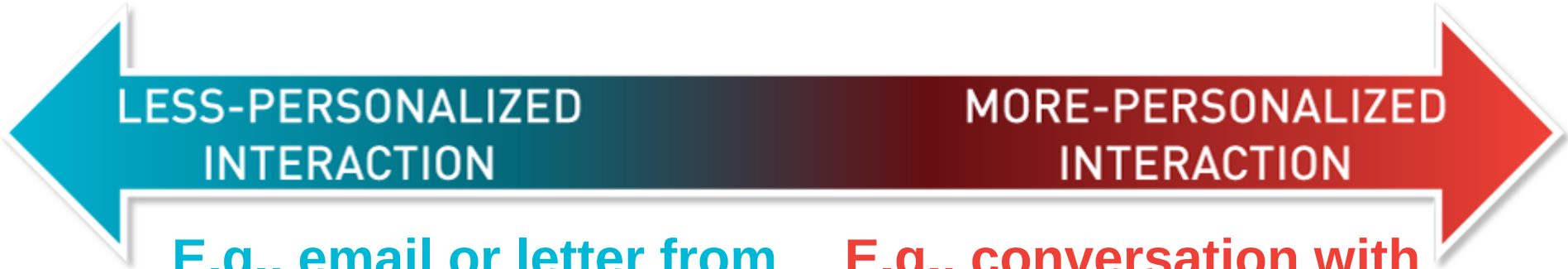
Tool: Evaluating RWD for Recruitment



Tool: Planning RWD-Support Recruitment

Identify Communication Channels



E.g., email or letter from insurance company or research hospital

- Casts widest possible net
- Main challenge is finding enough participants
- Appropriate intermediary not available

E.g., conversation with physician prompted by EHR pop-up

- Complex eligibility criteria
- Highly sensitive discussions (e.g., mortality)
- Narrow window of eligibility
- Patients have strong connection to care provider

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Evolution of Gauging Public Opinion

Straw Poll → Telephone Poll → Robocalls

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- Data linkage
- Global data sets
- Technology development
- Best practices
- Transparency & data usage
- Communication channels
- Participant diversity

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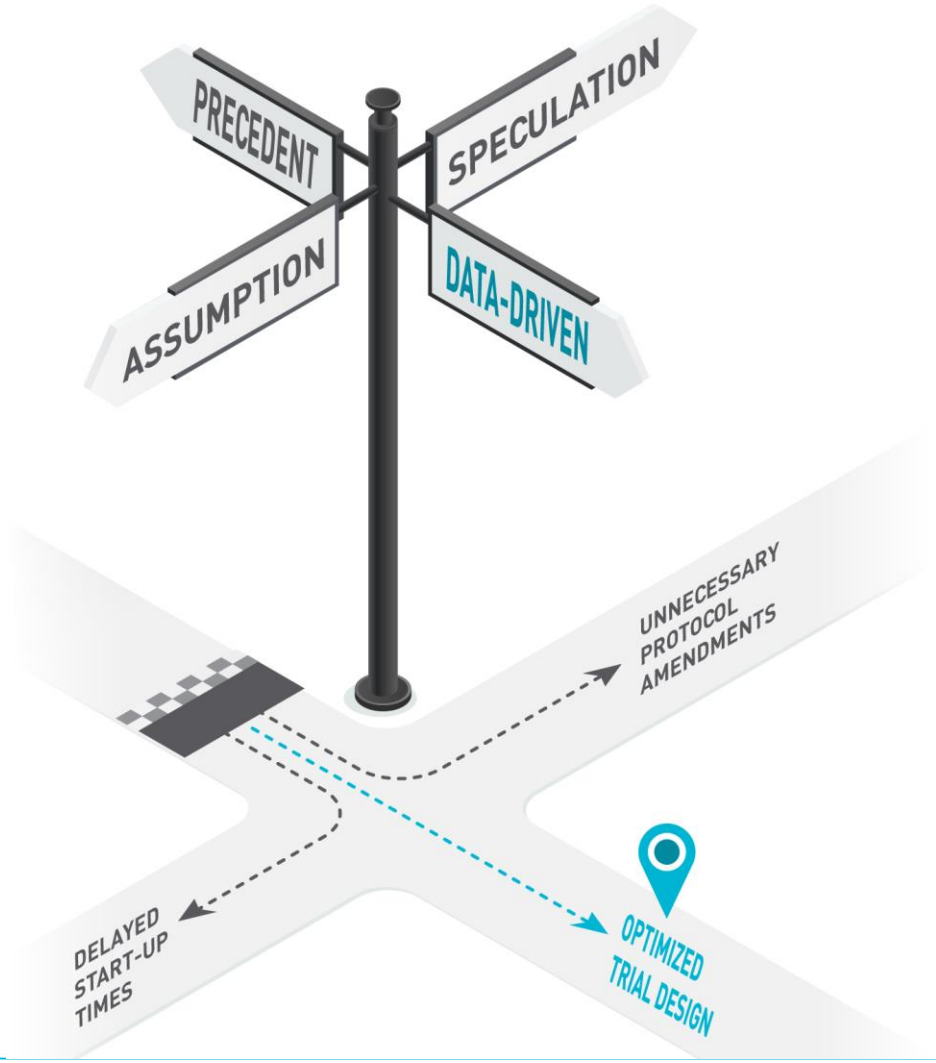
Now Available

- Full Recommendations
- 5 Actionable Tools
  - Establishing Use of RWD as a Standard Process in Study Planning and Recruitment
  - Evaluating Whether RWD Is Suitable for Planning Eligibility Criteria and Supporting Recruitment
  - Effective RWD-Supported Discussions of Eligibility Criteria
  - Evaluating Feasibility of RWD-Supported Recruitment
  - Planning RWD-Supported Recruitment Strategies
- 3 Case Studies



Download at www.ctti-clinicaltrials.org/projects/real-world-data

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THANK YOU.

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www.ctti-clinicaltrials.org

Sign up to receive CTTI's monthly e-newsletter for updates.

Summary of Recommendations

GENERAL PRINCIPLES FOR USING RWD	RECOMMENDATIONS FOR USING RWD TO PLAN FEASIBLE ELIGIBILITY CRITERIA	RECOMMENDATIONS FOR USING RWD TO SUPPORT RECRUITMENT	RECOMMENDATIONS FOR ENHANCING RWD CAPABILITIES FOR THE RESEARCH ENTERPRISE
1. Begin seeking insights from RWD as early as possible.	1. Evaluate available RWD sources against the particular needs of the study being planned.	1. Start by designing realistic eligibility criteria.	1. Identify opportunities and risks of enhanced data linkage.
2. Use RWD to complement and support collaborative study design.	2. Use RWD to identify and test important assumptions about the impact of potential eligibility criteria on trial feasibility.	2. Incorporate RWD-supported recruitment strategies whenever feasible.	2. Support continued development of underlying technology.
	3. Plan for iterative, targeted team discussions starting early in protocol design.	3. Understand and address the needs of patients and sites with respect to RWD-supported recruitment.	3. Evaluate RWD-supported recruitment strategies and identify best practices.
			4. Explore transparency of secondary data use to the patient community and opportunities to enhance patient agency with respect to usage of their data.
			5. Enhance communication channels for RWD-supported recruitment.
			6. Identify opportunities to increase diversity of study participants.
			7. Identify and support approaches for creating global data sets.

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