Embedding Clinical Trials within Registries: How Feasible?

A project of the Clinical Trials Transformation Initiative (CTTI)

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Background

Well-controlled clinical trials are necessary to assure the safety and efficacy of drugs, biologics, and devices that enter the marketplace.

- Costs and efficiencies have led many to suggest that the clinical trials enterprise needs to be modified and modernized. 1,11
- Registries may be designed to serve several purposes (Fig. 1).

- Embedding clinical trials within registries offers opportunities to evaluate an intervention in a population broader than the typical randomized clinical trial, increase operational efficiencies, and potentially decrease clinical trial costs.3,4

- Examinations of Thrombus Aspiration in ST-Elevation myocardial infarction (TASTE)5 and Study of Access Site for Enhancement of PCI for Women (SAFE-PCI for Women)6 present examples of this strategy.

- The U.S. Food and Drug Administration (FDA) has signaled its commitment to developing policies regarding the use of what is being called “real-world evidence” (e.g. registries, electronic health records, and claims databases) across a wide spectrum of research including interventional trials.11

Objectives

- Identify the essential characteristics and capabilities of registries needed for the conduct of high quality clinical trials.
- Provide a conceptual framework for assessment and design of embedded clinical trials within registries that would be acceptable to regulatory authorities.

Methods

Figure 2: Registry Trials Project Methods
- A multidisciplinary group of DCRI and CTTI subject matter experts worked to identify clinical needs and develop metrics for registry-based trials.
- The CTTI Registry Trials Project Team14 created a conceptual framework for registry trials, developed tools for assessing registry trials, and designed a set of methods for conducting registry trials.
- The methods were tested through application to a real-world example: the TASTE (Thrombus Aspiration in ST-Elevation myocardial infarction) registry trial.

Results

- Registries can be more widely used for clinical trials
- Key factors to consider suitability for regulatory purposes:
  - “Relevance,” “Reliability,” “Robustness”
  - Assurance of patient protections
  - Interoperability and/or ability to reconcile
- Recommendations for three registry frameworks:
  1. Can an EXISTING REGISTRY be appropriate for embedding clinical trials (Table 2)?
  2. What elements must be present for an EXISTING REGISTRY to support embedded clinical trials (Table 2)?
  3. What are the requirements for a NEW REGISTRY to be suitable for embedding clinical trials (Table 3)?

Table 1: Existing Registry—Historical Evaluation

<table>
<thead>
<tr>
<th>RELEVANCE AND ROBUSTNESS</th>
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<tr>
<td>Data are relevant:</td>
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<tr>
<td>Adequate in scope and</td>
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<tr>
<td>Generalizable:</td>
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<tr>
<td>High site- and patient-</td>
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<tr>
<td>Participation rates</td>
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<td>Compared with total population</td>
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Data are robust—acceptable for use in one or more of the following:
- Validated risk predictions
- Quality assurance
- Performance improvement
- Benchmarking
- Informing practice guidelines
- Post-market surveillance
- Generating peer-reviewed publications
- Comparative effectiveness research

Table 2: Existing Registry—Suitability Assessment

<table>
<thead>
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<th>RECOMMENDATIONS</th>
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<tr>
<td>1. Registry focused on patient population, disease and intervention of interest</td>
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<tr>
<td>2. Evaluate if historical data in registry are robust and reliable</td>
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<td>(See Table 1)</td>
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Table 3: Designing a New Registry

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<th>RECOMMENDATIONS</th>
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<td>1. Publication of data dictionary</td>
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<td>2. Use standard data element definitions and nomenclature</td>
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<tr>
<td>3. Allow for disparate treatment modalities, including drugs, biologics, devices</td>
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Table 4: Registry Generate the Information/Evidence Needed to Answer the Question at Hand

- Establish necessary associations to other data sources
- Ensure availability of line-item data to regulators

Funding Statement

CTTI developed a conceptual framework and created tools to assist in 1) EVALUATING AN EXISTING REGISTRY’s suitability for conducting clinical trials, and 2) DESIGNING A NEW REGISTRY in which to conduct clinical trials.

- Project recommendations will be released on May 18, 2017 during a CTTI webinar: www.ctti-clinicaltranslational.org/reference-webinar.
- CTTI encourages researchers and those engaged with registry development to interact with regulators to ensure that data generated from a registry trial are acceptable for regulatory purposes.