CTTI REGISTRY TRIALS PROJECT
A Brave New World: Registry-Based Clinical Trials

Breakout Session Report-Outs

Data Quality
Registry Design
Regulatory Governance

MARCH 30, 2016
The expert interviewees identified Data Quality as one of the principle barriers to increasing adoption of registry-based trials. What actionable solutions/best practices do you recommend to address data quality concerns in registry-based trials?
DATA QUALITY (1)

The expert interviewees identified Data Quality as one of the principle barriers to increasing adoption of registry-based trials. What actionable solutions/best practices do you recommend to address data quality concerns in registry-based trials?

First, define “data quality”:

- “absence of errors that matter” – includes completeness of data
- Fit for purpose
- Reflects clinical reality
- What is the information upon which decisions are made?
- Data quality assessment recommendations for pragmatic trials – NIH group – reference this document…
DATA QUALITY (2)

Should the standards for registry-based trials’ quality be the same as pre-market trials?

- If yes, how would registries need to change to meet higher standards?
  - Software development:
    - Software: should it need to follow FDA clinical trial requirements? E.g. CFR-21 Part 11 compliant and CDRH guidance on software validation
    - Risk assessment based on what we need and don’t need
  - Data itself – should the data quality “rules” be different than clinical trials?
    - Depends on the question to answer or the purpose of the registry
    - Industry requirements for safety reporting from registry is similar to for clinical trials, however, more limited collection of AEs than in trials
    - Risks that lower quality data reported to FDA would delay approvals

- If no, what should the standards be? Or what trade-offs could be made?
  - Is this perception of FDA’s expectations misconceived? Red herring?
  - Do we need more guidance from FDA on data quality standards? Is it quality, or is it too much data collection? Any latitude for embedded RCTs in registries?
  - Define sensitivity analyses and key variables for analyses in initial SAP.
Who assesses data quality? Those conducting the trial? Regulators? Other?

- We do – registry study designer and analysts (statisticians) – but we could use guidance from customers, e.g., regulators, reviewers (journals) and payers, especially if it is for submission or publications
- Put quality report in the submission…

When are monitoring and adjudication important?

- “It depends” on risk assessment
- Consider any risk to patient and to study
DATA QUALITY

- Data Quality recommendations
  - Clearly define data quality
  - Risk assessment based on what we need and don’t need
  - Depends on the question to answer or the purpose of the registry
  - Data quality section in the SAP discusses degree and/or randomness of missingness, sensitivity analyses; Data Management Plans too?
  - Data quality is responsibility of registry study designer and analysts (statisticians) – but we could use guidance from our customers, e.g., regulators, reviewers (journals) and payers, especially if it is for submission or publications
Thank you.
What best practices/solutions do you recommend in Registry Design to increase value, acceptance, and success of registry-based clinical trials?
REGISTRY DESIGN

What best practices/solutions do you recommend in Registry Design to increase value, acceptance, and success of registry-based clinical trials?

- Can existing registries be adapted to conduct trials? For example, role of modular add-ons for trial specific data?

- Are we more likely to have success in therapy-based vs. disease-based registries?
  - If therapy, can multiple therapeutic options be tested within the registry?
  - How can a registry successfully incorporate both therapy and disease?
REGISTRY DESIGN

- Make it easier to look for existing data sources, such as by encouraging participation in AHRQ’s registry of registries.
- Disease-specific registries are more sustainable and valuable than therapy-specific registries.
- Partner with stakeholders from the start—not just doctors, but end users, patients, etc.
  - Stakeholders have different motivations for developing registries; need to develop collaborations and gather multi-stakeholder input to influence registry design.
- To have sustainable registries, need a business model framework; registries should not be designed for a single, narrow purpose.
REGISTRY DESIGN

- Keep registry design simple and add on as needed.
- Have the capacity to add adjudication but only when needed based on the research question.
- Need greater data standards.
- Need an overall culture change to incorporate learning into healthcare systems: physicians do experiments on patients everyday.
  - Demonstrate the value of using registries.
  - Stop doing pilots and move forward with doing registries. This will help develop the business model.
- Rethink how to do clinical trials through registries. Don’t try to apply the old ways of thinking.
- The real question is: how can trialists and registry owners collaborate?
Thank you.
Recommend best practices/solutions concerning regulatory factors
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- What are the regulatory issues around informed consent?
- What type and level of quality of data are necessary for regulatory purposes?
  - What would be reviewed during an inspection?
  - What is required to make regulators comfortable about data quality?
Informed Consent

Issue – Common Rule allows waiver of consent, FDA part 50 does not

If data being used for regulatory purposes need informed consent

Regulatory recommendation #1 – Obtain informed consent if intent is regulatory submission

Hope – harmonization of Common Rule and FDA regulation in progress
Data Quality

- CDRH – 3Rs – Reliable, Robust, Relevant
- Data is being audited for internal or external validity
- If following standards for well conducted RCTs - this data ok

Monitor internal validity through data monitoring
  - Should be risk-based
  - Data audit same as RCTs
    - Automatic queries for out of range values

External Validity through site audits – select % of sites participating in registry based on certain criteria
  - For example - audit poor performing sites
Best practices

- Pre-planning better than retrofitting
- If regulatory submission intended, set up registry
  - to obtain informed consent and/or obtain permission to contact patients
  - As part 11 compliant (electronic standards)
- Ability to add modular add-ons to existing registries
- Combine registry workflow with study work flow
- Ability to link to data registries
Thank you.
Recommend best practices/solutions around registry governance
GOVERNANCE

Recommend best practices/solutions around registry governance

- What are the governance issues around ownership and informed consent?
- What is the process for gaining access to the data? (Application, Advisory Committee, etc.)
- How can the need for immediate access to the data be addressed, if data ownership is shared?
The daydreams of cat herders

Finding the cache has got to be easier than this.
GOVERNANCE

- Governance recommendation #1:
  - Establishing the registry intent

- Governance recommendation #2:
  - Need a very prescribed process and structure

- Governance recommendation #3:
  - Develop a decision tree to decide if ICF is needed
Thank you.