Role of RWE and ICH-E17: A provocative perspective

Barbara E Bierer, MD
Faculty Director, MRCT Center
Professor of Medicine, Harvard Medical School
bbierer@bwh.harvard.edu
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Our Vision
Improve the integrity, safety, and rigor of global clinical trials.

Our Mission
Engage diverse stakeholders to define emerging issues in global clinical trials and to create and implement ethical, actionable, and practical solutions.

Addressing emerging issues of MRCTs
RWE and ICH-E17: Background

**Dictionary**

**pro-voc-a-tive**

/prəˈvɒkətɪv/

adjective

causing annoyance, anger, or another strong reaction, especially deliberately.

"a provocative article"

Similar: annoying, irritating, exasperating, infuriating, provoking, maddening
Real world data is defined as data that are collected outside the constraints of conventional randomised clinical trials.

Sources of RWD to consider

- **Electronic health records**
  - Primary care data, hospital records

- **Claims data**

- **Spontaneous Safety reporting**

- **Patient and caregiver surveys**

- **Patient Disease Registries**

- **Prescription databases**
  - Drug utilization data sources

- **Patient reported data**
  - Mobile Technologies

**Fit-for-purpose**

**Data quality known**
Real world data is not produced for research but rather clinical care delivery: subject to systematic and random error

Consistency, accuracy, completeness, and representativeness of the data, affected by clinical care setting, is unknown

The capture of demographic and non-demographic factors is variable among databases, missingness of data is significant

Patient population, exposure identification, and outcomes with sufficient sensitivity and specificity are difficult

Data integration across multiple datasets and the hierarchy of evidence are challenging; methodologies and assumptions variable

The absence of harmonization of data elements, transparency in data collection, and variability in settings creates additional problems in multi-regional settings
Challenges

In addition to data sources and data variability:

• Study design may differ
• Stringency and precision of data definition varies
• Methodology for definition of window of exposure window
• Disease stratification
• Comorbidities/medications, and medication adherence
• Methodology for matching
• Quality of measurement differs
• Outcome needs to be carefully defined
• Accuracy and completeness of data variable
Real World Data (RWD), Real World Evidence (RWE)

- RWD use in regulatory decision making is limited.
- When might RWE be used appropriately in a multi-national regulated research studies?
- What consideration would be needed?

- RWE study that captures and evaluates data derived from product utilization in real-world practice may be useful for:
  - Safety monitoring
  - Label revisions or extensions:
    - New indication for approved medicine (not new composition of matter)
    - Use in different populations than in original approval (e.g., pediatrics)
  - Confirmatory studies in real world settings
  - Hypothesis generation
  - Potentially accelerated approval based on surrogate endpoint (e.g., rare diseases)
  - RWD historical controls for single-arm studies of innovator product (rare and ultra-diseases, unmet medical need)
Evolution in the regulatory paradigm: RWE in MRCTs

Data:
- Structured
- Common data models
- Provenance
- Multiple sources
- Objective
- Standardized
- Federated
- Interoperable

Methods:
- Pre-registered
- Reproducible
- SAP shared

Governance:
- Deposition:
  - Data
  - Analytic methods
  - Algorithm
  - Analysis
  - Cooperative/shared
  - Transparent
  - Testable, Validated
  - HRAs independent, collaborative
  - Data subject privacy protections

Safety:
- Label revisions and extensions

First application

Later applications
Thank you
Questions and Discussion

Barbara E. Bierer, MD
bbierer@bwh.harvard.edu