Role of RWE and ICH-E17: A provocative perspective

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The Multi-Regional Clinical Trials Center (MRCT Center)

MULTI-REGIONAL CLINICAL TRIALS

THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

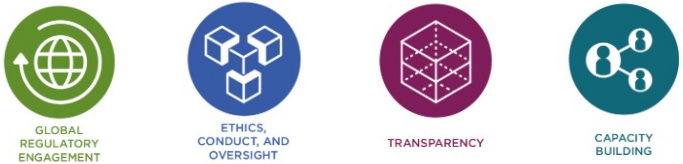
Our Vision

Improve the integrity, safety, and rigor of global clinical trials.

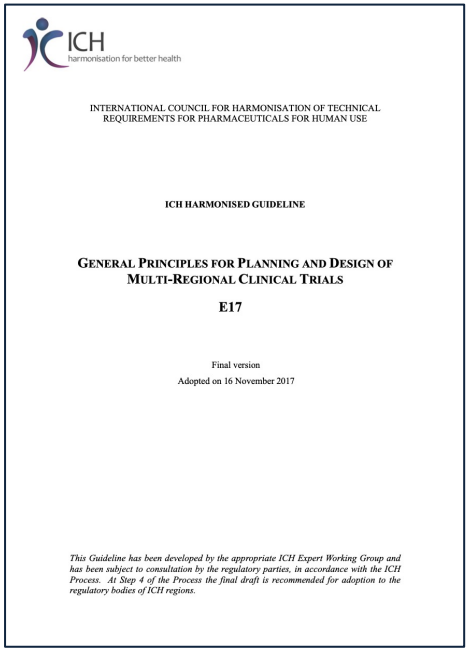
Our Mission

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



ICH
harmonisation for better health

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

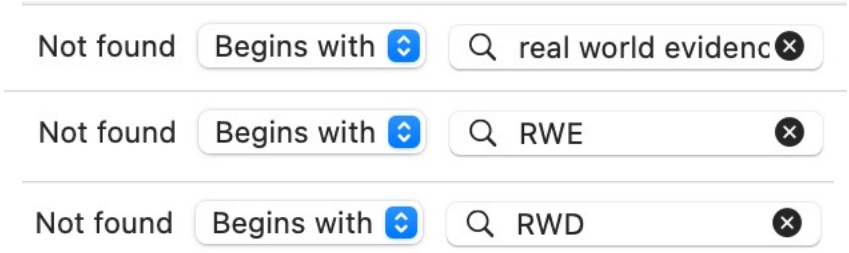
ICH HARMONISED GUIDELINE

GENERAL PRINCIPLES FOR PLANNING AND DESIGN OF MULTI-REGIONAL CLINICAL TRIALS

E17

Final version
Adopted on 16 November 2017

This Guideline has been developed by the appropriate ICH Expert Working Group and has been subject to consultation by the regulatory parties, in accordance with the ICH Process. At Step 4 of the Process the final draft is recommended for adoption to the regulatory bodies of ICH regions.



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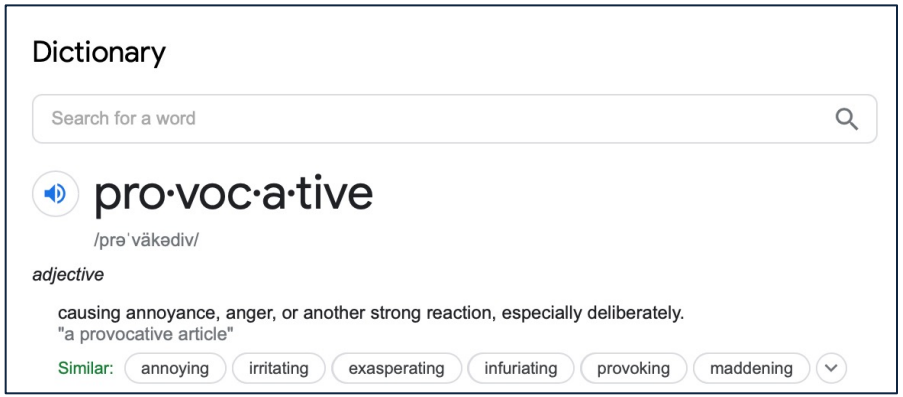


Dictionary

Search for a word

pro·voc·a·tive

/prəˈväkədiv/

adjective

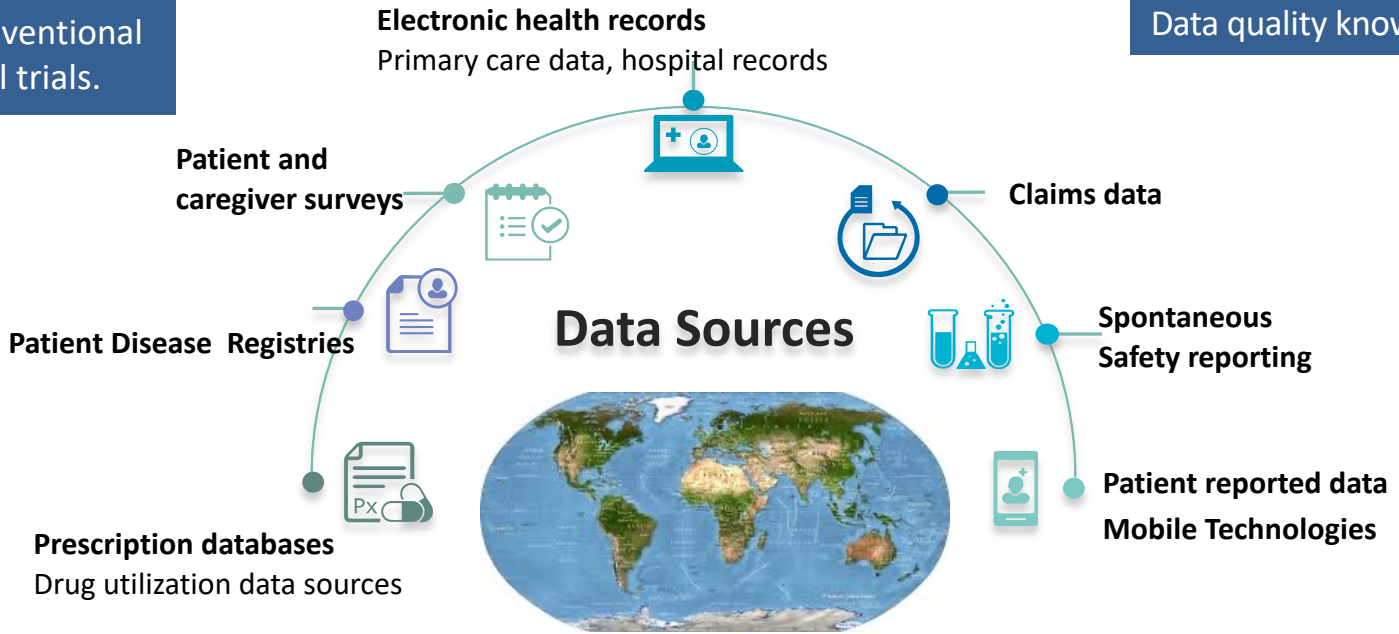
causing annoyance, anger, or another strong reaction, especially deliberately.
"a provocative article"

Similar: annoying | irritating | exasperating | infuriating | provoking | maddening

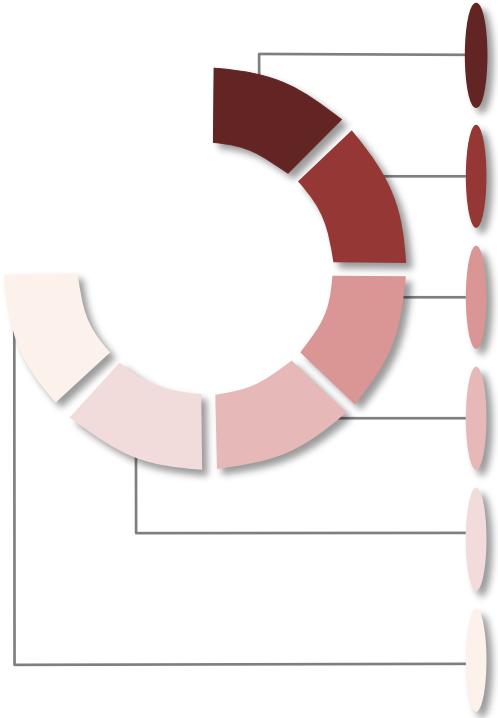
Sources of RWD to consider

Real world data is defined as data that are collected outside the constraints of conventional randomised clinical trials.

Fit-for-purpose
Data quality known



Multiple Uncertainties



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

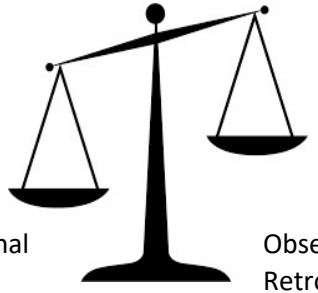
In addition to data sources and data variability:

- 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

Goal: Substantial Evidence

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?



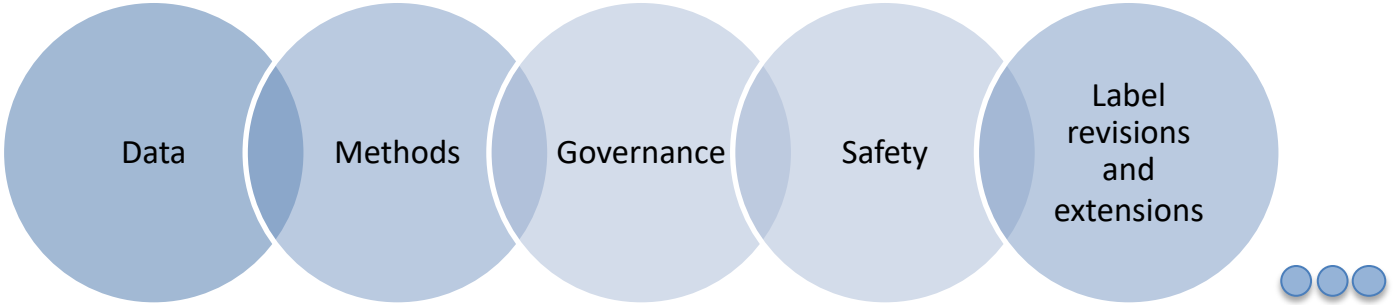
Interventional
Prospective
Data sources validated
Data quality known
Confounders understood
Minimal missingness
Methodology robust

Observational
Retrospective
…

- 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

First application



Data:
- Structured
- Common data models
- Provenance
- Multiple sources

Objective

Standardized

Federated

Interoperable

Pre-registered

Reproducible

SAP shared

Deposition:
- Data
- Analytic methods
- Algorithm

Analysis
- Cooperative/shared
- Transparent
- Testable, Validated

HRAs independent, collaborative

Data subject privacy protections

Later applications

Thank you

Questions and Discussion

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