Real-world Evidence
What Does It Really Mean?

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VIEWPOINT

Real-world Evidence—What Does It Really Mean?

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Much has been written about real-world evidence (RWE) in scientific papers and the lay media. Although some researchers and journalists tout its value, opponents are vocal in challenging its validity, pointing out shortcomings and downplaying any potential benefits. Despite an emphasis on the importance of RWE in the 21st Century Cures Act, a standard definition of the term has not been uniformly embraced.[1] The US Food and Drug Administration defines RWE as "data regarding the usage, or the potential benefits or risks, of a drug derived from sources other than traditional clinical trials."[2,3] In addition, the agency's Real-world Evidence Program framework defines real-world data (RWD) as "data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources."[4(p4)] To maximize the potential of RWE and define its role moving forward, limitations must be balanced with merits when considering RWD sources

vice, and costs for each claim. When these claims are linked to a given patient over time, a longitudinal history that depicts his or her journey through the health care system can be created.

Electronic Health Records and Medical Record Reviews

Data are obtained from patients' paper and/or electronic medical records by manual abstraction, often by a clinical expert, and/or by automated abstraction using data feeds linked to structured and sometimes unstructured fields of electronic health records. Data abstracted from patient medical records typically contain greater clinical granularity than claims data, providing specific clinical elements, such as disease progression, biomarker results, scan results, and date of death. Electronic health record information is often limited to structured data fields, thereby missing external biomarker or imaging results within a patient's

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Outline

- Definitions
- RWD sources
- Strengths and Limitation of RWD
- A Path Forward

Definitions

- The US Food and Drug Administration defines RWE as:

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Definitions

- The agency's Real-world Evidence Program framework defines real-world data (RDW) as:

Data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources

Definitions

- Real-world evidence is obtained from RWD, which encompass data collected outside randomized clinical trials (RCTs).
- RWE can be derived through routine daily clinical practice or through patient interactions in their customary daily living environment.

Real-World Evidence (RWE)

- Because greater than 90% of patients with cancer are treated outside RCTs, RWE presents a unique avenue for obtaining data on patients with characteristic s outside those typically required for trial eligibility.

- RCTs that lead to Food and Drug Administration approval of drug therapies often enroll younger patients who lack comorbidities, have adequate organ functions, posses proper psychosocial support , are able to travel to study sites, and are white.
- Homegenous population

- Food and Drug Administration uses RWE and RWD to monitor post marketing safety and adverse events.

RWD Sources

- Administrative claims
- Electronic Health Records and Medical Record Reviews
- Patient-Generated Data
- Patient Registries
- Social Media

Strengths and Limitation of RWD

- **Administrative claims**

Strengths	Limitations
• Captures health care encounters across multiple places of service	• Important clinical end points often not available
• Large sample sizes	• Data not collected for research
• Typically, representative of the target population	• Do not capture services that are not billed and/or not submitted for reimbursement
• Contain patient demographics, diagnosis, procedures, medication as well as dates, place of service, and costs	• Loss to follow-up
• Longitudinal history of patient	

Strengths and Limitation of RWD

- **Electronic Health Records and Medical Record Reviews**

Strengths	Limitations
• Contain clinical data not available in claims	• Often limited to 1 place of service
• May contain the “why” when the abstraction is conducted by the treating provider	• Unstructured data not always available because of private health information or limitations in natural language processing
	• Unstructured data are not always available in EHRs and might not be scanned in a timely manner

Strengths and Limitation of RWD

- **Patient-Generated Data**

Strengths	Limitations
• Provide the perspective of the patient and do not rely on data reported by providers	• Lack a validated tool, which may limit interpretation and generalizability of the data
• Allow assessment of QoL not often captured elsewhere	• Often missing important patient characteristics and clinical data

Strengths and Limitation of RWD

- **Patient Registries**

Strengths	Limitations
• Source of uniformly collected and defined patient characteristics and clinical outcomes	• Missing data is common
• Often contain relatively long follow-up on patients	• Represent biased sample of enrolled patients
• May have elements tailored to research objectives at study initiation	• Costly to maintain

Strengths and Limitation of RWD

- **Patient Registries**

Strengths	Limitations
• Enhance understanding of the natural history of diseases, comparative effectiveness, and QoL	• Lack standardized therapy among enrolled patients
• Uncover adverse events in understudied patient population	• Lack uniform assessment for response and progression

Strengths and Limitation of RWD

- **Social Media**

Strengths	Limitations
• May enhance understanding of barriers to patient adherence	• Often limited to qualitative data
• Bring patient with rare diseases together despite geographic distances	• Data not uniformly reported by patients
• Provide unfiltered patient experiences	• Missing important patient characteristics
	• Clinical outcomes not confirmed
	• Verifying authenticity represents a challenge

The Path Forward

1. RWD should be meaningful, valid, timely, and transparent to justify decision making based on its analysis.
2. Favor using RWE to better clarify potential harms in understudied populations subsequent to marketing of novel therapies.
3. Analyzing RWE output to identify deficiencies that can guide future trials is critical, especially regarding rare diseases and groups that were excluded from the original studies.

The Path Forward

- Limitation of RWD is that therapies are selected in part on the basis of provider beliefs and expectations and in part on patient characteristics.
- This may lead to confounding by indication, whereby a causal relationship thought to be attributable to the intervention is driven by the patients to whom it was given.
- For this reason, RWE cannot substitute for RCT when assessing a new drug approvals.

The Path Forward

- RWE complement RCTs to help inform providers and patients of outcomes and safety concerns that may have gone unnoticed or unstudied when the trials were conducted.
- Costs of care, resource use, and to some extent patient-reported outcomes are absent from RCTs but are common in RWE research.

Thank You

Q&A