Fundamentals of real world evidence

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Questions for you

What is RWE?

Do we need RWE if we have good RCT data?

RCT, randomized controlled trial; RWE, real world evidence
Types of evidence

RCTs provide evidence on efficacy and safety, and remain crucial for securing regulatory approval.

RWE is the product of studies that use data collected through observation of current clinical practice and/or patient-reported experience.

RWE can complement evidence acquired in RCTs by assessing a wide range of outcomes that are representative of an everyday clinical setting.

**Efficacy** is the intrinsic effect of an intervention measured under pre-specified conditions.

**Effectiveness** measures the beneficial effect in routine clinical practice.
Efficacy versus effectiveness: an analogy

Standing quarter mile: 12.5 seconds

Standing quarter mile: > 12.5 seconds!
Steps to success

Disease insights and burden of disease

Unmet need

Efficacy and safety

RCT

Effectiveness

Safety

Cost-effectiveness

Effectiveness

Safety

Cost-effectiveness

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Safety
RWE complements data from RCTs

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<thead>
<tr>
<th>Objective</th>
<th>RCT</th>
<th>RWE study</th>
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<tbody>
<tr>
<td>Can it work?</td>
<td></td>
<td>Does it work?</td>
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<tr>
<td>Purpose</td>
<td>To gain regulatory approval</td>
<td>To influence clinical practice</td>
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<tr>
<td>Setting/design</td>
<td>Ideal conditions</td>
<td>Real world conditions</td>
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<tr>
<td>Intervention</td>
<td>Fixed regimen</td>
<td>Flexible regimen</td>
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<tr>
<td>Compliance</td>
<td>High</td>
<td>Low to high</td>
</tr>
<tr>
<td>External validity</td>
<td>Low to medium: homogeneous populations</td>
<td>High: heterogeneous populations</td>
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<tr>
<td>Internal validity</td>
<td>High</td>
<td>Variable</td>
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**Objective**
- RCT: Can it work?
- RWE study: Does it work?

**Purpose**
- RCT: To gain regulatory approval
- RWE study: To influence clinical practice

**Setting/design**
- RCT: Ideal conditions
- RWE study: Real world conditions

**Intervention**
- RCT: Fixed regimen
- RWE study: Flexible regimen

**Compliance**
- RCT: High
- RWE study: Low to high

**External validity**
- RCT: Low to medium: homogeneous populations
- RWE study: High: heterogeneous populations

**Internal validity**
- RCT: High
- RWE study: Variable
A question for you

Where does RWE come from?
Evidence can be generated from primary or secondary data sources

- Primary data are newly generated by an investigator during a study
- Secondary data refer to patient-level data that were collected for other purposes and are being used again to answer another research question or hypothesis

<table>
<thead>
<tr>
<th>Primary data sources</th>
<th>Secondary data sources</th>
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<tbody>
<tr>
<td>RCTs</td>
<td>Administrative claims databases</td>
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<tr>
<td>Pragmatic clinical trials</td>
<td>Electronic medical records</td>
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<td>Prospective cohort studies</td>
<td>Disease registries</td>
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<td>National and regional registries</td>
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Validity of evidence

- Some types of studies are typically perceived as being more scientifically rigorous than others.
Evidence can be generated prospectively or retrospectively.
A question for you

How important do you think RWE is?
1. It is a critical element of evidence-based medicine
2. It is helpful for informing clinical decisions but it is not essential
3. It is not important at all, RCTs give us all the evidence we need

Please use the app to respond!
A question for you

What is RWE used for?
Healthcare decision-makers need evidence

- Healthcare decision-makers are interested in clinical decisions and the evidence that supports those decisions
- There are a variety of healthcare decision-makers

Understanding their different perspectives is key to generating the right evidence

- Does this treatment work? How safe is it?
- How much does this treatment cost? Is it worth it?
- How are other healthcare professionals using this treatment? What results are they seeing?
- Is this the best treatment for me?
Payer evidence needs

- Which patients should receive this treatment and how can it be targeted to appropriate patients?
- What is the unmet need for me and my patients?
- What are the consequences of not funding this treatment?
- Is this treatment affordable and what part of my budget will I use to fund it?
- What am I currently paying for treating this disease?
- Is this treatment more effective than alternatives?
- How much does this treatment cost and is it worth it?
- What are the consequences of not funding this treatment?
Healthcare professional evidence needs

What is the unmet need for me and my patients?

Which patients should receive this treatment and how can it be targeted to appropriate patients?

How do I monitor the effectiveness of this treatment?

How are my colleagues using this treatment and what results are they seeing?

What do I need to understand about how this treatment works?

Is this treatment more effective than alternatives?

Will my patients tolerate this treatment and how do I manage side effects?
Patient evidence needs

- Why do I need this treatment?
- Can I afford this treatment?
- What support will I be offered to manage my illness more effectively?
- For how long will I receive this treatment?
- What do I need to understand about how this treatment works?
- Is this treatment more effective than alternatives?
- What side effects might I experience and how will these be managed?
- Can I afford this treatment?
Evidence is needed throughout the product life cycle

1. What is the disease epidemiology and unmet medical need?
2. What is the patient pathway from diagnosis to treatment?
3. What are the characteristics of the patient population?
4. How feasible is the clinical protocol?
5. What is the safety and effectiveness in the real world?
6. How is the product used in the real world?

Phases:
- Preclinical phase
- Phase 1
- Phase 2
- Phase 3 and launch
- Phase 4 and commercialization

Teams:
- Research and Development, and Safety teams
- Medical and Payer teams
- Commercial and Marketing Companies
Summary: what is RWE?

Where does RWE come from?
• Observational studies
• Current clinical practice
• Patient-reported experiences

What does RWE do?
• Complements evidence from RCTs
• Describes outcomes representative of an everyday clinical setting

What information can RWE provide?
• Burden of disease and unmet medical need
• Treatment reality
• Comparative clinical effectiveness and safety
Summary: why is RWE important?

RWE demonstrates ...

- Unmet needs
- Effectiveness
- Safety

in patients in the real world

- Payers
- Regulators
- Patients
- Politicians
- Clinicians
- Industry

- Patient access