Real-World Evidence

What needs to happen for everyone to realize the potential value?

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Definitions & Scope

- **Big data** is an umbrella term describing large data sets from ANY source from Electronic Medical Records (EMRs) to unstructured non-health data such as social media postings.

- **Real-World Data (RWD)** is data collected from sources outside of traditional randomized controlled clinical trials, for example, patient registries, claims data, observational studies.

- **Real-World Evidence (RWE)** is the evidence derived from aggregation and analysis of RWD elements.
Key Messages
Greater Acceptance & Utilization of RWE is ongoing

Opportunities remain to ensure its full potential is realized

• Healthcare decision makers are increasingly open to using RWE to inform certain decisions

• Many fundamental components required for the greater utilization of RWE for healthcare decision making are already in place
  • Why? Because RWE isn't new, its simply the in vogue label for observational research

• Industry needs to ensure adherence to existing methodological and emerging behavioral standards to drive great acceptance and utilization of RWE by skeptical stakeholders

• Addressing the limitations of real-world data should be a priority for all stakeholders

• Organizations should focus on tackling any limitations in their RWE capabilities and challenge the notion that RWE is the new panacea
Opportunities for broadening the evidence base
Opportunity of Unprecedented Breadth and Scale

Common questions faced by internal & external stakeholders

Policy Makers
- Which diseases should be future healthcare priorities?
- How many people are impacted?
- What is the burden of disease?
- Is there a clear unmet medical need?

Regulators
- Does the drug work?
- How efficacious is the new drug?
- What is the risk / benefit?
- What are limitations of SOC?

Pharma
- How can we bring value to patients living with severe diseases?
- Does the new drug offer value for money?
- Is the drug effective?
- Is the drug cost-effective?
- What is the future drug impact?
- Which patients respond best?
- Will this replace SOC?
- Might other patient groups benefit?

Payers
- How does the new drug fit into clinical practice?
- Which investigational sites have eligible patients?

Prescribers
- Where should we focus our discovery efforts?
- Is this study feasible?
- Which investigational sites have eligible patients?

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Healthcare Decision Makers are Using RWE

Regulators (FDA)

- FDA committed to ‘robust policy development’ through consultation leading to published Guidance for Industry covering pre- and post-marketing regulatory requirements
  - Final guidance concerning Medical Devices was published on August 31, 2017
  - Public Workshop discussing ‘A Framework for Regulatory Use of Real-World Evidence’ in drug development was held September 13, 2017, 2017

- Insights on FDA concerns regarding RWE can be drawn from the 2016 NEJM sounding board publication
  - Suitability of EMR data (relevance, quality)
  - Analytical methods & risk of bias and confounding
  - Availability of expert researchers

Moving beyond the traditional hierarchy of evidence
Hierarchies of Evidence still act as a barrier

‘Because Cochrane reviews address questions about the effects of health care, they focus primarily on randomized trials.

Randomization is the only way to prevent systematic differences between baseline characteristics of participants in different intervention groups in terms of both known and unknown (or unmeasured) confounders.’

Influential voices challenging the supremacy of RCTs

NICE leads the way in its openness to NRS

‘Hierarchies attempt to replace judgment with an oversimplistic, pseudoquantitative, assessment of the quality of the available evidence. Decision makers have to incorporate judgments, as part of their appraisal of the evidence in reaching their conclusion. Such judgments relate to the extent to which each of the components of the evidence base is fit for purpose. Is it reliable? Is it generalisable? Do the intervention’s benefits outweigh its harms? And so on. …

Hierarchies of evidence should be replaced by accepting – indeed embracing – a diversity of approaches’

Professor Sir Michael Rawlins, NICE

Flexible Hierarchies to Reflect the Research Question

Example: Comparative Effectiveness Research

- Systematic Reviews
- Randomized Controlled Trials (RCTs)
- Pragmatic RCTs
- Cohort Studies
- Case-Controlled Studies
- Case Studies / Expert Opinion

- Systematic Reviews (pRCT / NRS)
- Pragmatic RCTs
- Cohort Studies
- Active-Controlled RCTs
- Case-Controlled Studies
- Case Studies / Expert Opinion
Addressing the comparative effectiveness question

Are Naturalistic (Pragmatic) RCTs the Solution? Example: SLS

- **Patient, problem or population**
  - 2799 patients with COPD

- **Intervention**
  - Randomly assigned to once-daily inhaled combination of fluticasone furovate (100µg) and vilanterol (25µg) or …

- **Comparison, control or comparator**
  - Usual care

- **Outcome**
  - Rate of moderate or severe exacerbations among patients who had had an exacerbation within 1 year before the trial.

‘In patients with COPD and a history of exacerbations, a once-daily treatment regimen of fluticasone furoate and vilanterol was associated with a lower rate of exacerbations than usual care’

Pragmatic RCTs are not always feasible or affordable

Non-randomized studies are required to supplement RCTs

‘ASCO believes that high quality observational studies can advance evidence-based practice for cancer care and are complementary to randomized controlled trials (RCTs).’

1. Improve the quality of electronic health data available for research
2. Improve interoperability and the exchange of electronic health information
3. Ensure the use of rigorous observational research methodologies
4. Promote transparent reporting of observational research studies
5. Protect patient privacy

Transparency and reproducibility are the ‘now’ frontier

Industry and professional guidelines call for full disclosure

**Joint ISPE-ISPOR Special Task Force on RWE in Healthcare Decision-making**

- Draft recommendations for good procedural practices¹ include:
  - A priori determination and declaration that a study is an exploratory hypothesis-generating or hypothesis-testing (so called Hypothesis Evaluation Treatment Effectiveness -HETE study)
  - Posting hypothesis-testing study protocols and analysis plans on a public study registration site prior to conducting the study analysis; such as ENCePP
  - Published results with attestation regarding conformance and/or deviation from the protocol and original SAP.
  - Perform hypothesis-generating studies on a different data set than hypotheses-testing study feasible

**WHO Statement on Improving Availability and Transparency of Observational Studies on Influenza Vaccine Effectiveness²**

- Draft recommendations include:
  - Study registration and making the study protocol publicly available
  - Reporting results within 12 months including registry identifier code/number

Source: (1) http://www.who.int/immunization/research/meetings_workshops/Draft_WHO_statement_Influenza_VE_Transparency_9jun17.pdf
Even cautious consumers of RWE are opening up

Cochrane NRS Methods Group checklist for systematic reviewers

- **Study Design**
  - Identify issues relating to study design and the risk of bias
  - Determine selection of NRS for inclusion in terms of study design features; risk of residual confounding vis a vis meta-analysis

- **Confounding**
  - Establish an expert panel to identify likely domains of confounding for each outcome
  - Assess validity of approach to control for confounding such as propensity score matching

- **Selective Reporting**

- **Directness (relevance > PICO)**

Tackling the limitations of real-world data
Improving the Quality of EHRs more holistically

Standardization, Breadth and Relevance

- Government to create an environment that drives a change to existing data collection standards, including
  - introduction of unique anonymous patient identifier to aid more effective record linkage

- Professional societies need to work together with data owners / generators to define new standards that specifically address the level of content and quality required for research purposes
  - Agreed common data elements
  - Streamlined codes and standardized coding processes
  - Routine capture of standardized disease-specific outcomes including PROs and quality of life; eg. ICHOM standard sets

Ensure Continued Access is Essential

As a revenue generator, RWD is at risk of commoditization

- EHR and Claims data owners are part of the solution, however ASCO important raises concerns about interoperability (“the ability of systems to exchange electronic health information with other systems and process the information without special effort by the user”) and exchange

- ‘Information blocking (ie. the practice of knowingly and unreasonably interfering with the exchange or use of electronic information) is common.’

Table 3. Types of Information Blocking

- Adding per transaction fees with contracts for each import or export of information to a different platform for electronic health information.
- Refusal to establish connections to permit information exchange with systems developed by competitors, or charging unreasonably high fees to establish such connections.
- Establishing technological limits to the amount of historical health information that can be exported to a recipient using a different electronic health record platform.
- Developing proprietary standards for communicating clinical information documents that are inconsistent with established industry standards. (Thus, customized translation features are necessary for parties to effectively communicate).
- Requiring that a provider contractually agree to give the electronic health record company an exclusive license to use the provider’s data.

Preparing for Success
UCB’s Approach & Vision
UCB’s Vision & Mission

**Vision**
ONE DAY, RWD WILL BE THE MOST INFLUENTIAL SOURCE OF EVIDENCE IN HEALTHCARE, ENSURING EVERY PATIENT GETS THE RIGHT CARE

**Mission**
WE DELIVER ROBUST RWE TO DRIVE BETTER DECISION MAKING and IMPROVE PATIENTS’ LIVES THROUGH DIFFERENTIATED MEDICINES
Thanks!