Let’s Get Real: How Will the FDA Framework for Real-World Evidence Impact You?

January 30, 2019
Jennifer Graff
Vice President, Comparative Effectiveness Research
National Pharmaceutical Council
1. NPC’s engagement on real-world evidence
2. Overview of FDA’s use of RWE and Framework for FDA’s RWE Program
3. Patient community perspective on RWE (including new research)
4. Payer community perspective on RWE for payment and coverage
5. Industry perspective on RWE use throughout drug development and to address stakeholder needs
6. Panel discussion
7. Questions and answers
Speakers

Jennifer Graff, PharmD
Vice President, Comparative Effectiveness Research
National Pharmaceutical Council (Moderator)

Eleanor Perfetto, PhD, MS
Executive Vice President, Strategic Initiatives
National Health Council

Tricia Lee Wilkins, PharmD, MS, PhD
Director of Pharmacy Affairs
Academy of Managed Care Pharmacy

Brande Yaist, MHS
Senior Director, Center of Expertise in Global Patient Outcomes and Real-World Evidence
Eli Lilly and Company
Mr. Snuffleupagus and Use of RWE

- Real?
- Trusted?
- Routinely seen/used?
National Pharmaceutical Council (NPC) Focus on Evidence

High-quality evidence is available, accepted and used to drive decision-making

Raise awareness of **barriers that limit access to, and portability of, data** to support evidence-based decision-making, and **identify** potential solutions

Facilitate the adoption and communication of **high-quality evidence** as a critical component of decision-making
NPC’s Goal: Improve Generation and Adoption of High-Quality Evidence

Demand

Supply

Patients

Journal Editors

Payers

Clinical Guidelines

DEMAND

Supply Bodies?

Clinical Guidelines

Regulatory Bodies?

When no RCT data is available
- To understand heterogeneity of tx options
- To identify adverse events
- As a supplement to RCT data

Rationale for using RWE data
- 46% To understand data in available HIV care for adverse events to options
- 38% To identify adverse events
- 31% As a supplement to RCT data

CER Collaborative

Demand

Supply

Patient Perspectives on RealWorld Evidence: A Roundtable to Gather Views, Needs, and Recommendations

Demand

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Journal Editors

Payers

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Regulatory Bodies?

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Regulatory Bodies?
Sources of Real World Data: Electronic health records, insurance claims, patient registries, digital health applications.
FDA Use of RWE to Date

1. Monitor Safety:

2. Aid evaluation of drugs for rare disease
   - Blincyto (blinatumomab) used chart review for historical control in treatment of acute lymphoblastic leukemia

3. Contribute to post-market commitments
   - Kalydeco (ivacaftor) support indication expansion from 10 to 33 cystic fibrosis mutation subtypes
   - Zostavax assess long-term efficacy herpes zoster vaccine
Potential use of RWE to:
1) support approval of a new indication for a drug and
2) support or satisfy post-approval study requirements

- Legislation: 21st Century Cures Act December ‘16
- National Academies of Medicine (NAM): Workshop September ‘17
- NAM: Workshop #3 July ‘18
- FDA: Framework for RWE December ‘18
- FDA: Final Guidance 18 months from comment period
- Duke-Margolis: Public Meeting September ‘17
- NAM: Workshop #2 March ‘18
- Duke-Margolis: RWD and RWE October ‘18
- FDA: Draft guidance ‘21
“RWE provides us with a potential source of information that can complement, augment and expand our understanding of how best to use medical products -- improving what we know about our medical care.”
Putting $ To Action: FY2019 $100M Request for RWE Data Enterprise

Five Elements: Framework for FDA’s Real-World Evidence Program

1. Expands potential use of RWE from **safety** to drug and biologic **efficacy and effectiveness**
2. Broader types of RWD sources will be considered
3. Expands beyond traditional randomized clinical trials to consider pragmatic trials, hybrid trials, observational studies, control arms
5. FDA will review existing activities and guidance to identify gaps and engage groups.
FDA’s Three Part Approach

1. Is the RWD fit for Use?

2. Is the trial or study design used to generate RWE provide adequate scientific evidence to answer or help answer the regulatory question?

3. Does the study conduct meet FDA regulatory requirements?
For What Decisions?

• Safety monitoring

• Inform modeling/trial design

  ➢ Support changes to labeling about drug effectiveness
    • Adding or modifying an indication (e.g., dose, dose regimen, route of administration)

  ➢ Adding a new population

  ➢ Adding comparative effectiveness or safety information
What’s Next?

Demonstration Projects
- Informed Collaboration in Oncology
- Impact Afib
- HCV-TARGET
- RCT DUPLICATE

Guidance
- Pharmacoepidemiologic guidance to assess reliability and relevance of claims and EHRs
- Considerations for pragmatic trials and using pragmatic elements
- Use of RWD to generate external controls
- Observational study designs and reporting requirements
- Electronic signatures in clinical trials 21 CFR Part 11
- Potential gaps in RWD sources?
- RWD for effectiveness?

External Stakeholder Engagement
- Duke-Margolis conference
- National Academies of Medicine Workshop series
- Others

Internal Engagement
- Internal website
- RWE subcommittee
- Additional resources
Mr. Snuffleupagus and Use of RWE

- Real!
- Trusted!
- Routinely used by all stakeholders!
Panelist Discussion

1. How are you and others like you using RWE today?
2. How does the FDA’s use of RWE impact your work?
3. What are the unique considerations for stakeholders like you?
Eleanor Perfetto, PhD, MS
Executive Vice President, Strategic Initiatives
National Health Council
The Patient Perspective on Real-World Evidence

Eleanor Perfetto, PhD, MS

JANUARY 30, 2019 1:00-2:00 P.M.
Real-World Evidence Roundtable

NHC and NPC convened a day-long multi-stakeholder roundtable discussion in July 2017 to gather:

- Patient community views on RWE
- Areas of greatest concern
- Information and tools most needed to understand, trust, and use RWE

Emerging themes

- Raising Patient-Community Awareness
- Enhancing Patient-Community Capacity
- Patient-Specific Uses of RWE
- Consider Context
Raising Patient-Community Awareness

• Most patients have little understanding of RWE

• Patient organizations can play an important role in disseminating important insights from RWE
Enhancing Patient-Community Capacity

- Common definitions of RWD & RWE are vital

- Skills and tools are needed by patient organizations to facilitate uptake of RWE

- Partnerships with the scientific community
  - Scientific advisory boards can help patients interpret study findings

Patient-Specific Uses of RWE

• RWE should support informed decision making

• Clinicians must be champions for dissemination and use

• Communications to patient should be balanced and empowering
  o Keep it simple
  o Openly address limitations of RWE
Consider Context

- Acceptable uses of RWE must be linked to the context of its use
- Privacy must be protected and data ownership clear to promote trust
- RWE should include “authentic” sources of patient data
Future Directions

• Investments in capacity building and tools

• Develop research-methods, good-practice principles on *how* and at which study-design stage, patient-provided information can be used by researchers
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Tricia Lee Wilkins, PharmD, MS, PhD
Director of Pharmacy Affairs
Academy of Managed Care Pharmacy
AMCP: Who We Are and Why We Care About RWE
The AMCP Format for Formulary Submissions
Version 4.0
Is Real-World Evidence Used in P&T Monographs and Therapeutic Class Reviews?

Jason T. Hurwitz, PhD; Mary Brown, PhD; Jennifer S. Graff, PharmD; Loretta Peters, MBA; and Daniel C. Malone, PhD, RPh
Will Standards for Coverage and Payment Differ for Regulatory Decisions?

How Standards Proliferate:

SITUATION: THERE ARE 14 COMPETING STANDARDS.

14?! RIDICULOUS! WE NEED TO DEVELOP ONE UNIVERSAL STANDARD THAT COVERS EVERYONE'S USE CASES. YEAH!

SOON:

SITUATION: THERE ARE 15 COMPETING STANDARDS.

https://imgs.xkcd.com/comics/standards.png
Will Standards for Coverage and Payment Differ for Regulatory Decisions?

SITUATION: There are 14 competing standards.

14?! RIDICULOUS! We need to develop one universal standard that covers everyone's use cases. YEAH!

SITUATION: There are 15 competing standards.

(Soon:) one really thick standard with 14 independent chapters.

https://blog.viewpoint.com/wp-content/uploads/2016/01/BimBlog5-3-600x221.png
The Learning Health System
The Learning Health System: Using RWE to Connect Health and Care for the Nation

Connecting Health and Care for the Nation A Shared Nationwide Interoperability Roadmap Version 1.0
AMCP Initiatives

AMCP Partnership Forum Series
Brande Yaist, MHS
Senior Director, Center of Expertise in Global Patient Outcomes and Real-World Evidence
*Eli Lilly and Company*
Framework for FDA’s RWE Program

An Industry Perspective

Brande Yaist
Senior Director - Global Patient Outcomes and Real World Evidence
Eli Lilly and Company
Industry uses RWE to support the **entire lifecycle** of drug development.
Many possibilities for RWE to add value

RWE has a long history of applications for Value and Access and Safety/Risk Management. More can be done with RWE to improve outcomes while lowering costs.

- Personalized medicine
- Clinical decision support
- Tailoring diagnostic and treatment decisions
- Support desired patient behaviors
- Population health
- Documentation/traceability
- Regulatory product labeling, safety monitoring

FDA and industry recognize common opportunities for RWD/RWE in clinical studies

Our Goal: Make life better for people around the world

Real World Evidence involves data and insights related to people’s health outside of a clinical trial.

We must promote practices that

♦ protect people
♦ provide reliable results
♦ and address the questions of interest with speed and value
Diverse stakeholder expectations drive multiple paths to deliver RWE

There is no broadly accepted standard for defining what makes insights from real world data broadly acceptable and scientifically reliable for healthcare decision making.

FDA-approved standards for data collection, analysis and dissemination do not apply to other stakeholders, such as health care delivery systems and health insurers.

What the RWE landscape lacks today is a widely shared framework that defines what good and appropriate collection, integration, analysis and use of data means.¹


Image Adapted from "road currently under construction at several levels to increase traffic" by Lev Kropotov. Accessed from https://www.123rf.com/stock-photo/road_construction.html?orSearch=road+constructions&st=lau5rza5r2za54j&mediapopup=39790087
Wider acceptance of RWE by the FDA (and other stakeholders) depends on:

- Establishing causal inference of treatment effectiveness in observational studies
- Development of data standards for RWD
- Reliability and relevance of RWD, particularly EHR data
- Transparency of study design and analysis (research integrity)
Industry will continue to apply and advance real world data and design/analytics

FDA’s RWE Framework *amplifies* the need for stakeholders to work together.
The *common expectations* for reliable and valuable RWE establish guardrails. Diversity in the application and acceptance of strengths in limitations of the evidence determines the path.

- Focus on a specific question
- Examine using standard criteria
- Recommended by experts
- Discuss strengths, limitations and value

Implement a learning system
Questions & Answers

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Thank you!

Your feedback is appreciated. Please complete the forthcoming evaluation survey.