FASTER, BETTER, CHEAPER: THE INCREASING ROLE OF REAL-WORLD EVIDENCE IN DRUG DISCOVERY, DEVELOPMENT, AND COMMERCIALIZATION

The need to effectively utilize real-world evidence derived from big data sources to accelerate the discovery, development, and delivery of 21st century drug therapies in a post-COVID-19 world

Christopher P. Boone, PhD, FACHE, FHIMSS
Former Vice President, Global Head, Health Economics & Outcomes Research, AbbVie Inc.
Adjunct Assistant Professor, NYU Wagner Graduate School of Public Service
The speaker is an employee of NYU and serves on the Boards of PCORI and Global Medical Response -- the views expressed are the speaker’s personal views and do not represent those of any institution in which I’m affiliated with in any capacity.

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DIGITAL TRANSFORMATION IS YEARS AWAY. I DON’T SEE OUR COMPANY HAVING TO CHANGE ANY TIME SOON.
HELLO | A WORD ABOUT ME

• Spent the majority of my career in biopharma, health systems, nonprofits, and consulting firms
• Moonlight as a NYU Wagner School professor teaching health informatics, data analytics, and health policy courses
• Serves on several influential boards and committees, including the PCORI Board of Governors

• Dallas, TX native born and raised
• Husband & Father
• Dallas Cowboys Fan
• Patient Advocate, Social Scientist, Health Informaticist, Futurist
KEY TAKEAWAYS FOR TODAY

The ability to generate **compelling evidence** throughout the lifecycle of a drug or device therapy is increasingly important...

... as we move from a world where evidence generation is predominately generated from **randomized clinical trials** (RCT) prior to launch...

... to one where **ongoing generation of the right evidence** (Randomized Clinical Trials, Real-World Evidence, Patient Experience Data) is critical to delivering on the therapy’s **full potential**...

...whether that is measured in **safety and effectiveness of therapy**, or patient access to the therapy.
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Our clinical research (evidence generation) system is too slow and expensive, leading to a vast gap between what we need to know about health interventions and what we actually know.

[Link to article](journals.sagepub.com)
Now is the time to fix the evidence generation system - Robert M Califf, 2023
DRUG DISCOVERY AND DEVELOPMENT ARE EXPENSIVE AND HIGH-RISK INVESTMENTS

14 YEARS
$2.6 BILLION

AND LESS THAN 10%
OF THERAPIES THAT ENTER HUMAN TRIALS MAKE IT TO THE PHARMACY

Source 2: https://www.optum.com/business/resources/library/drug-approval-process.html
ONGOING CHALLENGES WITH CLINICAL TRIAL RECRUITMENT AND RETENTION

54% of clinical investigators participate in one research study and never participate in another.

<5% of patients participate in clinical research.

49% of patients drop out before study completion.

48% of trial sites miss enrollment targets.

50 mi Average distance patient lives from nearest site.

Rapid recruitment, Participant Diversity, Hard-to-recruit sub-populations, Patient retention, Speed to market, Cost efficiencies.

Source: IQVIA
Key Observations

• White males are the primary participants in trials, while women, people of color, and the elderly are generally underrepresented.

• People of color make up 39% of the U.S. population but represent between 2% and 16% of patients in clinical trials.

• African Americans alone are about 12% of the U.S. population but make up just 5% of trial participants.

• Hispanics are about 16% of the population but only 1% of trial participants.

Source: https://www.clinicalleader.com/doc/steps-to-address-diversity-in-clinical-trials-0001
Thumbs down on Lilly, Innovent China trial for lung cancer drug Tyvyt, says FDA AdComm

by Kevin Dunleavy | Feb 10, 2022 3:40pm

When is a clinical trial conducted exclusively in a foreign country enough to support FDA approval?

That was the question before the agency's Oncologic Drugs Advisory Committee (ODAC) on Thursday as it weighed whether to recommend Eli Lilly and Innovent Biologics’ application for its PD-1 lung cancer drug Tyvyt (sintilimab).

By a vote of 14-1, the independent panel ruled against the companies, declaring that another clinical trial, demonstrating that the drug works on U.S. patients, should be required before approval.

The decision might have been different had Tyvyt been destined for a market with no good options for patients—or if the trial had used the gold standard of cancer research, overall survival, as its primary endpoint. But it didn't, and Tyvyt was aiming to treat non-small cell lung cancer, a disease with multiple rival drugs that have proven they can extend patients' lives.

Plus, diversity in clinical trials has become more important than ever.

“Over the past two to three years—especially since the pandemic—this country has experienced significant social change,” the FDA’s cancer drugs chief, Richard Pazdur, said during Thursday's virtual meeting. “And there has been a tremendous outcry for diversity and representation in clinical trials. We as a public agency have to adhere to what patients want in the United States.”
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RWE provides insight about how patients actually respond to treatments in typical care settings, which may differ from responses in the controlled environment of a randomized clinical trial. RWE can be used to show regulators, payers and physicians that a treatment is right for a specific condition and type of patient, and that it is better than available treatments in some way, such as effectiveness, safety or tolerability. RWE can also dash the hopes of once-promising treatments when benefits don’t translate to real-world settings.

LEADING SOURCES FOR CAPTURING REAL-WORLD DATA

Clinical
Demographics, EHR Data, Lab Test Results, Diagnoses, Procedures, Pathology/Histology Data, Radiology Images, Microbiology Data, Provider Notes, Admission/Discharge and Progress Reports, Performance Status

Medication
Medication Orders, Administration (Dose, Route, NDC/RxNorm codes), Concomitant Therapies, Point of Sale Data, (Prescription & OTC) Prescription Refill, Allergies

Claims
Medical Claims, Prescription Drug Claims, Other Drug and Treatment Use Data

Molecular Profiling
Genomic and Genetic Testing Data (SNPs/Panels), Multi-Omics Data (Proteomics, Transcriptomics, Metabolomics, Lipidomics), Other Biomarker Status

Family History
Historical Data on Health Conditions and Allergies Relating to Patient and Extended Family, Smoking Status, Alcohol Use

Mobile Health
Fitness Trackers, Wearable Devices, Other Health Apps Measuring Activity and Body Function

Environmental
Climate Factors, Pollutants, Infections, Lifestyle Factors (diets, stress), Other Environmental and Occupational Sources

Patient Reported
Patient Reported Outcomes, Surveys, Diaries (diets, habits), Personal Health Records, Adverse Event Reporting, Quality of Life Measures

Social Media
Patient Communities, Twitter, Facebook, Blogs

Literature
Disease Burden, Clinical Characteristics, Prevalence/Incidence, Rates of Treatment, Resource Use and Costs, Disease Control, Quality of Life Measures
EXAMPLE: USING AN EHR AS A MECHANISM FOR CLINICAL TREATMENT, THERAPY DEVELOPMENT, AND POPULATION STUDIES
WHY IS RWE ESPECIALLY APPEALING TODAY FOR BIG PHARMA?

- Pace of scientific innovation
- Rising development costs
- Increasing availability of data
- Importance of patient-centricity
- Emphasis on value
HOW DOES BIOPHARMA USE RWE TO SUPPORT THE LIFECYCLE OF DRUG DEVELOPMENT?

EXHIBIT 1 | Real-World Evidence Is Valuable Across the Product Life Cycle

Typical RWE applications

- **Research**
  - Support the understanding of diseases and unmet needs

- **Development**
  - Reduce clinical-development cycle time and costs

- **Launch**
  - Support pricing and demonstrate value

- **In market**
  - Improve commercial spending and effectiveness

- Support pharmacovigilance and label extension

Source: BCG.

**PRIMARY USE CASES FOR INFORMING REGULATORY DECISION-MAKING**

1. **Indication Prioritization**
   - *1st Indication*: RWE
   - *2nd Indication*: RWE

   - Explore indication landscape

2. **Primary Approval**
   - *Approval*: RWE

   - Create historical controls and synthetic comparison groups

3. **Secondary Indications**
   - *Initial Approval*: RWE
   - *2nd Indication*: RWE

   - Identify new uses and new populations

4. **Adaptive Pathways**
   - *Initial Approval*: RWE
   - *Full Approval*: Full Approval

   - Add biomarkers to clinical endpoints, broaden populations and learn what happens next

5. **Post-market studies**
   - *Approval*: RWE

   - Rapidly identify safety signals and understand comparative effectiveness in the real world

2020 FDA APPROVALS THAT INCLUDED RWE STUDIES SPAN TEN THERAPEUTIC AREAS

TODAY’S DISCUSSION

- Hello
- Why RWE is important?
- RWE in Big Pharma
- Regulators
- Future trends
- Tips & tricks
- Q&A
# The Evolving Global Policy Landscape for Leveraging RWE

## Food and Drug Administration (FDA)
- In 2018, FDA issued its 3-year plan on use of RWE in decision-making. Since then, it issued multiple draft guidelines encouraging submissions.

## European Medicines Agency (EMA)
- In 2019, the EMA issued its 5-year plan to promote the use of high-quality RWD in decision-making. In 2020, the EMA, HMA issued its joint 5-year strategy, which builds on EMA's plan. In 2021, the Big Data Steering Group released its 2021-2023 work plan, operationalizing these strategic goals.

## National Medical Products Administration (NMPA)
- In 2019, NMPA released a draft/final guidance on its guiding principles for RWE for development/review.

## Health Canada
- In 2019, Health Canada issued reports on protocol elements and data quality and optimizing use of RWE. It is also inviting manufacturers to submit high-quality RWE for evaluation. We're awaiting its guidance.

## Pharmaceuticals and Medical Devices Agency (PMDA)
- In 2021, PMDA researchers published a manuscript discussing seven guidance documents published since 2019 and the increasing use of RWE for regulatory decision-making.

## Medicines and Healthcare Products Regulatory Agency (MHRA)
- In 2020, the MHRA issued the first in a series of guidances discussing RWE trial designs.

## Taiwan Food and Drugs Administration (TFDA)
- In 2020, the TFDA published RWE guidance use on label changes, premarketing safety profile evaluations, and premarketing effectiveness assessments.
Regulators across the globe are offering guidelines and frameworks for expanded use of real-world evidence.

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| FDA  | Staff and experts | Conduct workshops and meetings | Industry | Publications and reports | Decision-making: 
  ● New drugs approved |
|      | Financial          | Provide project findings | Academic institutions | Regulatory guidelines | Awareness |
|      | Technology         | Together stakeholders | Domestic government institutions | Database and data sharing platforms | Knowledge |
|      | Equipment and platform | Develop reports, curricula, resources | Overseas institutions |        | Skills |
|      | Domestic and international partners | Facilitate access to information | Work with partners |        | Motivations |
|      |                   |                        |                      |        | Behavior |
|      |                   |                        |                      |        | Health |
|      |                   |                        |                      |        | Social |
|      |                   |                        |                      |        | Economic |
| EMA  | Staff and experts | Conduct workshops and meetings | Industry | Publications and reports | Decision-making: 
  ● New drugs approved and indications added, |
|      | Financial          | Organize initiatives | Agencies and community | Centers and committees | Communications |
|      | Committee          | Together stakeholders | Decision-makers | Tools developed by activities. | |
|      | Technology         | Facilitate access to information | EU country health institutions | Annual conference reports | Motivations |
|      | Resources and organization | Work with partners from different countries | Overseas institutions | Database and data sharing platforms | Behavior |
|      |                   |                        |                      |        | Health |
|      |                   |                        |                      |        | Social |
|      |                   |                        |                      |        | Economic |
| NMPA | Financial          | Conduct workshops and meetings | Industry | Publications and reports | Decision-making: 
  ● New devices approved and indications added, |
|      | Technology         | Organize projects | Academia | Regulatory guidelines | RWE platform |
|      | Domestic partners  | Together stakeholders | Local institutions | Regulatory Science Action Plan | Motivations |
|      |                   | Facilitate access to information | Leadership in local institutions |        | Health |
|      |                   |                        |                      |        | Social |
|      |                   |                        |                      |        | Economic |
BIG DATA IN CLINICAL RESEARCH ALLOWS FOR MORE PRECISION BUT RAISES ETHICAL ISSUES

Privacy
Bias
Transparency
Consent
Accountability
Fairness
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SOME KEY ADVANCES IN CLINICAL RESEARCH OVER THE LAST 25 YEARS

Human Genome Project

Targeted Cancer Therapies

Precision Medicine Revolution

Patient Products Achieved with 3D Printing

Ubiquity of Digital Health and Health Data

Artificial Intelligence in Healthcare
AI Model Enables Alzheimer’s Disease Detection from Brain MRIs

A research team at Massachusetts General Hospital developed an artificial intelligence model that uses routinely collected clinical brain images to detect Alzheimer's disease.

By Mark Melchionna

March 09, 2023 - Published in PLOS ONE, a recent study described how a team of researchers at Massachusetts General Hospital (MGH) developed and validated an artificial intelligence (AI) model, specifically a deep-learning model, to analyze data from brain magnetic resonance images (MRIs) to detect Alzheimer's disease.
The healthcare industry is faced with the challenge of incorporating simultaneous advances in physical, biological, and digital technologies, as the development of new diagnostic approaches and therapies coincides with a push to digitize patient records and capitalize on the wealth of information that can be gathered from wearable devices and implantable technologies.

THE NEXT 25 YEARS: THE CONVERGENCE OF BIOTECH AND HUMAN DATA

SCIENCE BENEFITS HUMAN LIFE

- DNA sequencing of an increasingly representative and diverse slice of the world’s population will be sequenced – approximately 60 million genomes are projected by 2025
- Expanded use of digital technologies will enable the use of mass phenotyping – enabling longitudinal data that provides deeper understanding of the effects of nutrition, health, and disease
- Digitization and virtualization will allow for the storage and democratization of larger datasets globally
- Precision therapy will increase significantly in importance and utility – driven by patients

Source: “The Next 25 Years.” Nature Biotechnology, Volume 39, March 2021, Published online at: www.nature.com/naturebiotechnology
THE ERA OF PRECISION IN HEALTHCARE AND LIFE SCIENCES IS UPON US

**Precision Medicine**

*Tailoring prevention and treatment to individuals*
Requires taking into account individual differences in genes, environments, and lifestyles when developing a treatment plan and/or drug therapy

**Precision Reimbursement**

*Informing decision-making to specific patient clusters*
Integrates economic and clinical value assessment by explicitly discovering distinct clinical and health care utilization phenotypes among patients

**Precision Public Health**

*Targeting interventions for populations*
Requires rapid and iterative collection, analysis, and visualization of genomic, epidemiologic, geospatial, and contact tracing data
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HOW THE ROLE OF THE RWE FUNCTION IS EVOLVING

PAST
In the early days, the RWE group was all about...

- Data sourcing / the identification and procurement of real world data assets
- Portfolio management / tracking RWE projects and identifying synergies for better collaboration and resource utilization
- Best practices / trying to reduce duplication of effort and eliminate process roadblocks
- Pilots and proof cases / demonstrating the actual value of RWD/E

PRESENT
But, increasingly, it involves...

- Talent and community development / attracting, developing, and retaining talent
- Enterprise operating models / designing and implementing a platform and operating model that are grounded in an enterprise strategy
- Technology enhancements / Deployment of central analytics platforms
- High-value use cases /

FUTURE
The future resides in its ability to incorporate...

- Novel partnerships / Developing a data strategy and organizational capability to engage in external partnerships with health care system stakeholders to gain access to the right data
- Advanced RWE capabilities / applying advanced analytics to RWE generation to deliver impact at scale
RWE FUNCTIONS COME IN DIFFERENT SHAPES AND SIZES

Individual RWE groups are spread across different functions in the organization, reporting to and serving business/function-specific teams. Provides stronger alignment with business priorities and processes.

A core RWE organization providing services to the entire enterprise as a center of excellence. Offers greater consistency and knowledge sharing when under one roof.

A core RWE organization that serves as a center of excellence, while specific functions / business units have their own RWE teams – often referred to as hub-and-spoke. Offers the best of both worlds.
Leaders are actively deploying strategies to elevate understanding, accessibility, and communication of RWE’s value drivers to the enterprise with high-value use cases.

Leaders are establishing agile operating models that drive adoption and integration of RWE across the pipeline, while developing risk mitigation plans.

Leaders are deploying rapid, cost-effective data analytical platforms that can democratize the use of data and analytics at scale.

Leaders are focused on developing and/or expanding robust partnership ecosystems.

Leaders are thinking about ways to shift to the expanded use of advanced RWE capabilities and the recruitment of high-performing diverse talent to achieve success.
NEXT STEPS FOR BIOPHARMA TO ACCELERATE THE USE OF RWE

1. INCREASE UNDERSTANDING AND COMMUNICATION OF RELEVANT ENDPOINTS USING RWE
   Elevation of frontline capabilities across medical affairs, commercial, development, market access, and HEOR/RWE will be required to identify novel data sources that generate evidence for regulators and other stakeholders.

2. CREATE AN ORGANIZATION, OPERATING MODEL, AND CULTURE THAT DRIVES INTEGRATION OF RWE
   This should include (1) an enterprise RWE strategy focused on the organizational culture and role of RWE; (2) structure, processes, and resourcing to make it repeatable and sustainable; (3) approach to governance and interface with the other functions within the organization.

3. BUILDING SCALABLE PLATFORMS TO MANAGE AND ANALYZE DATA IN A RAPID, LOW-COST FASHION
   Building platforms and capabilities—including data infrastructure and storage—to increase the turnaround time and decrease the cost of RWE studies is critical to being able to utilize this data for internal business decisions.

4. ADVOCATING FOR GLOBAL HARMONIZATION OF REGULATORY GUIDANCES FOR RWE ACCEPTABILITY
   Standardization of regulatory submission processes and availability of clear guidance on submission of evidence packages that include RWE.
THE FUTURE OF EVIDENCE IN PHARMA-shifts to strategic cross-sector partnerships.
Every company has big data in its future and every company will eventually be in the data business.

— Thomas H. Davenport
THANK YOU

Scan me!