Realizing the Benefits of RWE

▶ The real-world evidence (RWE) market has grown significantly in recent years, supported by a favorable regulatory environment.

Increasingly, companies recognize that real-world evidence (RWE) presents an opportunity to improve efficiency and innovation. One of the biggest challenges for pharma companies is the time it takes to bring products to market. To shorten these timelines, companies need data on how their therapy works in wider population pools. As a result, more companies are looking to RWE to gain deeper insights, improve the drug development process, and reduce the cost of clinical research.

The FDA has placed growing emphasis on RWE and real-world data (RWD) to make regulatory decisions and to monitor a product's safety on the market, which has prompted more companies to place a greater focus on RWE's use in R&D. A 2020 survey from Deloitte found that companies with more mature RWE capabilities in place have seen an impact on areas such as regulatory submissions and building synthetic control arms. They are also starting to experience reduced clinical trial costs and trial failure rates. The survey also found that the vast majority (94%) of survey respondents believe using RWE in R&D will become important or very important to their organization by 2022. Most expect the highest impact of RWE to be on areas such as supporting regulatory submissions and supplementing clinical trials. RWE and RWD are also invaluable for important decision-making about clinical trials. For example, COVID-19 has had a negative impact on many clinical trials, but the Deloitte study found that by using RWD, companies could gain insights into which trials could become virtual, thereby helping to accelerate decision-making.

A Market for RWE Solutions

The increased focus on RWE has led to a growth in RWE solutions. Market research shows North America has the largest market share of RWE solutions. Meticulous Research predicts the RWE solutions market will grow at a CAGR of 15% between 2019 and 2024 and will reach $1.64 billion by 2024.

Companies in the RWE solutions space have sought to extend their presence through product developments, partnerships and collaborations, and expansion into new markets. These partnerships are particularly key to delivering research-quality data to pharmaceutical companies. Janssen has invested in several initiatives to find high-quality data sources, including HONEUR (Haematology Outcomes Network in Europe) and EHDEN (European Health Data & Evidence Network). HONEUR was established by Janssen as a collaborative network of partners — private hospitals, registries, medical societies, and

Driving Transparency in RWE

ISPOR has been at the forefront of working to improve standards and transparency with real-world evidence. The organization established a collaborative effort called "The Real-World Evidence Transparency Initiative Partnership" with the International Society for Pharmacoepidemiology, the Duke-Margolis Center for Health Policy, and the National Pharmaceutical Council. The objective of this initiative is to establish a culture of transparency for study analysis and reporting of hypothesis evaluating real-world evidence studies on treatment effects.

In addition, ISPOR has taken several steps to address concerns over RWE, such as biases due to lack of randomization, data quality, and the potential for spurious results due to data mining, including:

- Convened several RWD-related task forces and issued a number of Good Practices for Outcomes Research Reports on this issue.
- Assembled an International Digest of Databases with an associated special interest group.
- Collaborated with the Academy of Managed Care Pharmacy and the National Pharmaceutical Council to create a tool and related training for decision-makers in evaluating comparative-effectiveness research using RWD and other sources.
- Partnered with ISPE to form a joint Special Task Force on Real-World Evidence in Healthcare Decision Making. ISPOR and ISPE held a Summit in October 2017 that provided a forum to review these task force reports, consider the perspectives of key stakeholders, and discuss future steps that could help enable these recommendations.
- Leading a collaborative initiative regarding RWE transparency with about 35 different stakeholder organizations represented, related to a priori registration of hypothesis testing treatment effect evaluating studies, including a Summit in October 2019.

Source: ISPOR

Types and Sources of RWD

- **Medical records** — electronic health records, prescription data, lab, and imaging studies
- **Registries** — product and disease registries
- **Payers** — claims and billing activity
- **Regulatory** — government datasets, RWD used in regulatory approval process, safety, and adverse event data
- **Patient-sourced** — data gathered from patient wearables and mobile devices

other institutions — to improve how data is shared and analyzed with the objective of building knowledge of blood cancers. EHDEN is a federated data network that addresses the challenge of producing RWE from RWD. The network brings together 22 partners, including 11 public partners and 11 pharma companies, led by Janssen. The objective is to standardize research methodologies and RWD by harmonizing 100 million health records by 2024, which will help the broader healthcare community to improve patient outcomes.

RWE Applied

Already RWE has been used to support decision-making, including product approval. For example, Pfizer's Ibrance breast cancer treatment gained extended approval, for both post-menopausal women and for men, based at least in part on RWE. Using RWD from EHRs, Pfizer was able to show how Ibrance used with endocrine therapy benefited male patients with breast cancer based on observed tumor responses. Pfizer used Flatiron's longitudinal database to explore baseline characteristics, treatment patterns, and clinical outcomes from de-identified data of male patients with metastatic breast cancer.

Roche, which acquired Flatiron in 2018, has been working on a shareable global RWD set with the goal of accelerating R&D by providing insights on the effectiveness of personalized cancer treatments, to assist clinical decision-making, and to support reimbursement discussions. The company carried out a RWE-based control arm to support the clinical benefits of Alecensa for anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer. The RWD study used U.S. EHR data from Flatiron Health. Treatment patterns and outcomes, including real-world progression-free survival and overall survival were extracted for first- or second-line therapy.

RWE can also help patients become more active participants in their own care and push the industry toward personalized medicine. At a clinical research level, RWE can help companies to design more patient-centric trials by offering different insights about their products' safety and efficacy.

In addition, some research suggests that RWE can be used to enhance diversity in clinical studies. Often, the exclusion/inclusion criteria of clinical trials result in patient subgroups being underrepresented. By supplementing this with RWE, companies and regulators can gain deeper insights into outcomes on subgroups. PV

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Scott Swain, Ph.D., MPH
Director of Regulatory Sciences and Real-World Evidence, Cardinal Health

RWE and RWD Positive Impact on Clinical Trials

RWD and RWE can generate market research and patient preference information to inform drug development at any point in the process, including before clinical trials are initiated. RWD can be used for patient recruitment or to supplement trial data (such as patient reported outcomes), or as a primary source of data. Similarly, post-marketing RWD and RWE can inform long-term safety and efficacy, utilization patterns, market penetration, and can be incorporated into label expansions.

RWD can be generated from multiple sources (insurance claims, medical records, manufacturer data, social media, etc.) to estimate trends in utilization and perception of specific products and the overall market. Thus, RWE can drive market research to describe past or current market conditions or to target specific audiences who may benefit from a product. Identifying treatment gaps, including social disparities, can inform manufacturer development of patient support programs and physician engagement strategies with the goal of reducing barriers to treatment.

RWE At Every Phase of the Drug Life Cycle

With the passing of the 21st Century Cures Act, RWD and RWE can be used to facilitate drug development and generate information to demonstrate drug safety and efficacy at every phase of the drug life cycle. The Cures Act paved the way to utilize observational data to incorporate evidence for drug efficacy into the regulatory decision-making process. Noting that the standard of evidence required for regulatory approval remains unchanged, the ability to incorporate RWD and RWE to generate information to demonstrate drug efficacy gives the industry a new time- and cost-efficient method for evidence generation.

Thus far, RWE has been incorporated into regulatory decisions primarily in the form of historical control arms, typically as a comparison arm for accelerated approval or to inform safety issues post-marketing. The potential for prospective RWD and RWE, via pragmatic and decentralized trials, to improve and accelerate drug development and approval is nearly limitless. With many upcoming cell and gene therapies, the expected efficacy is high enough that randomization to placebo or standard of care may be unethical. In these circumstances, RWD may be the best alternative source for study controls.

Melissa Thompson, BSc., MBA
Senior VP, Value & Evidence Division, Marketing and Market Access, EVERSANA

Telling a Holistic Patient Story

Product value and effectiveness are increasingly becoming dependent on RWE derived from high-quality RWD. From early-stage strategic planning through launch and post-launch marketing, RWD and RWE are the building blocks that can inform a product's unique value proposition

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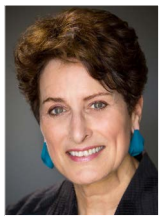
▶ and drive go-to-market and commercialization strategies. RWE from datasets across the healthcare ecosystem offer a representative view of the diverse populations that tell a holistic story of the patient journey, leading to better decision-making and ultimately improving patient outcomes.

Mission Possible: Improving the Patient Experience

Regulatory-grade RWE is driving safety and efficacy insights, accelerating regulatory approvals, and getting products to market sooner. Leveraging RWE opens the door for the expedition of traditionally sluggish processes, like assessing gaps in clinical care, monitoring key performance metrics relevant for reimbursement or assessing comparative effectiveness. Improving the patient experience across the entire care continuum is the mission, and RWD and RWE are critical components to moving that needle forward.



Nancy Dreyer, Ph.D., MPH, FISPE, Fellow DIA
Chief Scientific Officer and Senior VP, Head, Center for Advanced Evidence Generation, IQVIA Real World Solutions

Optimizing Protocols and Site Selection

RWE is being used to optimize protocols and site selection. Clinical trials are more likely to succeed when RWD is used to test the protocols to identify which, if any, criteria lead to a large loss of eligible patients. Testing the inclusion and exclusion criteria that are assessable in RWD gives the opportunity to reconsider the criteria before launch. Also, RWE is being used to locate and size-eligible patient pools, allowing smarter site selection.

RWE Driving innovation?

RWE is driving innovation through its use in accelerated product approval, providing context for single-arm trials; augmenting trial data with information about the path to diagnosis; long-term post-trial follow-up; benefits, risks and costs of current treatment paradigms, etc. RWE is also providing robust and timely intelligence to guide decision-making. For example, RWD will help build comfort and confidence in COVID-19 vaccines through near-real time and other timely insights about their benefits and risks.

Iyiola Obayomi
Marketing Analytics, Ogilvy Health

Creatively Using RWD to Change Behavior

As a marketing analytics professional with a keen interest in the intersection of data, creativity, and behavior change, the biggest trend I'm tracking is the creative use of RWD in changing HCP and patient behaviors. For instance, the record-setting COVID-19 vaccine development and the incredible logistical accomplishments of getting vaccines to recipients are mere potentials until shots are delivered into arms. I'm following how data and information are being used to overcome vaccination resistance.

Using RWE and RWD for Product Positioning

Locating a differentiating, sizeable, valuable, and defensible location on the competitive spatial map requires a good understanding of that space. RWD now generates enough data to evaluate different variables or factors that can help dimensionalize this competitive space. Companies can prioritize the development of a product into a value space and can shift existing products into new valuable spaces based on clinical or nonclinical attributes.

Leanne Larson
Senior VP, Worldwide Head Real-World Evidence & Access, Parexel

Applying Totality of Real-World Evidence

With an increasing recognition of the insights that RWE can bring to stakeholders' decisions for regulators, payers, clinicians, and patients alike, we've seen the emergence of new and integrated datasets, and innovative data technologies and analytics. Together, these innovations are influencing the ways in which RWE can be applied alongside clinical-trial data to ensure we are applying a totality of evidence in our critical decisions. It is truly transforming our clinical-development and treatment models today.

David Brown, Ph.D.
VP, Epidemiology, Parexel

Informing Better Decisions

We've recently seen an emerging focus on utilizing RWE to optimize the clinical-development process. No longer solely a late-phase application, RWD is increasingly used to form external controls to clinical trials, and

to better inform trial design and operations. Particularly in rare and complex diseases, these external controls can accelerate patient recruitment, obviating the need to randomize patients to placebo in some trials, offering all patients the hope of receiving a promising new therapy.

David Thompson, Ph.D.
Senior VP, Real World and Late Phase, Syneos Health

Combining RCTs and EHRs

There are many ways RWD can be used to positively impact clinical trials, but a novel use-case I've been working on is to embed a randomized controlled trial (RCT) within a clinical practice setting and leverage the existing electronic health records (EHR) system for data capture. EHRs are usually tapped as a source of RWD but in this context data for trial endpoints are available either as part of practice workflows or from supplemental data forms inserted into the EHR. This saves time and money.

RWE and Commercialization

We continue to see the growing use of RWE to support product commercialization. For example, manufacturers and payers see a critical role for RWE in the design and execution of value-based contracting agreements. These agreements generally involve rebates or other measures to adjust product price based on patient outcomes of care using it — careful collection of RWE on patient outcomes is critical as these measures are the yardstick on which the rebate decisions are made.