

EBOOK

USING PATIENT GENERATED REAL-WORLD DATA TO DRIVE BETTER INFORMED HEALTHCARE DECISIONS

INTRODUCTION

Imagine a new wonder drug has become available. Its release to the market has taken years of carefully controlled clinical development and regulatory compliance that ensures it is both safe and effective. Patients prescribed the medication feel new hope as they start showing signs of improved health. But, there's a catch: not all patients seem to be responding to treatment and few patients respond to the same magnitude reported in the clinical publications of the pivotal trials. The drug has not stopped working, but many patients are struggling with the treatment paradigm and cannot integrate treatment into their daily lives. Not to mention that they don't really like taking it, the combined effect leading to low compliance as treatment adherence begins to waver. The reality is becoming clear: evidence of efficacy within the controlled environment of the clinical trial setting is not generalizable to the real-world setting.

Fortunately, the healthcare industry is moving towards a new way of thinking. Healthcare decision-makers, such as regulators, physicians and patients themselves, are increasingly questioning the extent to which new products are helping patients outside of a controlled clinical trial setting. In response, companies are starting to not only assess products in traditional randomized controlled trials (RCTs), but also in real-world programs in which patients take the medicine in real-life environments and report back about their experiences.

These real-world initiatives present an exciting opportunity to gather patient generated Real-World Data (RWD) to contribute to Real-World Evidence (RWE), which is seen by many as the industry's valuable new currency. Healthcare decision-makers are increasingly adopting RWD to complement the evidence obtained from traditional RCTs, to inform decisions about the cost effectiveness and patient value of a new product to the healthcare system.

In this ebook, we describe what RWD is, as well as exploring why it is becoming increasingly important in driving forward RWE-informed healthcare decisions. We also consider the growing influence of patient voice in RWD programs and how it can provide richer insights into the effectiveness of new drugs than traditional RCTs can alone. In the second ebook of this series, we will focus on the challenges of capturing patient generated RWD, which threaten to constrain the great potential of RWE-informed healthcare, and how technological advances provide a new way to combat these challenges. REAL-WORLD EVIDENCE IS SEEN BY MANY AS THE INDUSTRY'S VALUABLE NEW CURRENCY

WHAT IS RWD AND HOW DOES IT SUPPORT RWE?

As new, often life-changing, drugs are developed, RCTs have long been considered the gold standard of establishing safety and efficacy. However, as part of the continual evolution of the pharmaceutical industry to best serve patients, there is a drive to further evaluate drugs in real-world settings. Some key concerns that are helping to push this development are that RCTs operate in an idealized environment for a short duration and only measure efficacy in limited groups of patients. This means they do not reveal how medicines will fare in real life settings among the general population.

KEY DIFFERENCES BETWEEN RANDOMIZED CONTROLLED TRIALS AND REAL-WORLD DATA PROGRAMS

RANDOMIZED CONTROLLED TRIALS	REAL-WORLD DATA PROGRAMS
Is the drug effective and safe?	Is the drug effective in real-life settings? No direct
	assessment of safety
Experimental, interventional	Observational, non-interventional methodology
Narrow, restricted patient population	Wide, unrestricted patient population
Intense monitoring, enforced compliance	Low-level monitoring, real-world adherence
Controlled setting, short-term outcomes	Clinical practice, long-term outcomes

Consequently, healthcare decision-makers are calling for additional real-life information to indicate elements of efficacy and patient voice that RCTs do not always provide. In response, it is becoming increasingly common for pharmaceutical companies running RCTs to assess the same product in real-world settings. Patients self-manage their treatment as they live their normal lives, such as while they are at work or at home interacting with family, friends and colleagues, while conveying information back about their treatment journeys.

These real-life patient observations and outcomes generate a rich source of RWD, which in turn contributes to the RWE base. RWD generating programs can therefore provide healthcare decision-makers with valuable information not just about the effectiveness of a medicine in the real world, but also about what matters to the patient.

REAL-WORLD DATA

Data that are collected outside the controlled constraints of conventional randomized controlled trials (RCTs) to evaluate what is happening in normal clinical practice. This includes clinical and economic data reported from six main sources:

- Supplements to traditional registration RCTs
- > Large simple programs
- > Disease or patient registries
- > Administrative/claims data
- Health surveys, such as the Medical Expenditure Panel Survey
- Electronic health records and medical chart reviews, for example CPRD¹

USING PATIENT GENERATED REAL-WORLD DATA TO DRIVE BETTER INFORMED HEALTHCARE DECISIONS	5
---	---

The question of how RWD supports RWE and how they are distinguished has been grappled with in recent years, but is now relatively well-established. Perhaps the best way of visualizing it is by using an analogy: different RWD sources can be thought of as distinct 'streams' that feed into RWE 'rivers'. Each RWD stream represents different raw, simple facts, as a single component of the larger research plan. The RWE rivers bring all the RWD streams together, enabling the organization of RWD so that a conclusion or final decision can be made.

Drawn from robust, anonymous and patient level RWD, RWE is driving forward targeted analyses that reveal valuable facts about patient outcomes. While still at an early stage, RWD and RWE are becoming increasingly used to complement traditional RCT data to inform important healthcare decisions. This suggests that RWD are having a significant impact on the healthcare industry that will only grow in the years to come.

REAL-WORLD EVIDENCE

While the definition of RWE is still evolving, most proponents associate RWE with the insights derived from multiple sources of RWD for the purpose of informing healthcare decision-making.

RWE has the potential to support all three phases of the product lifecycle:

- > Clinical research
- > Pre-regulatory approval (launch)
- > Post-approval (in-market)

REAL-WORLD DATA SOURCES

Different RWD sources can be thought of as distinct 'streams' that feed into RWE 'rivers'

SUPPORTING DATA Supplemental data to support further submissions LARGE SIMPLE TRIALS **MEDICAL RECORDS** Observed programs with large Data from paper or electronic **Real-World populations** health records REGISTRIES **INSURANCE CLAIMS** Observed cohorts of patients with Record of treatments and disease/treatment of interest procedures billed to payers SURVEYS Research surveys completed by patients in hospital or at home **REAL-WORLD EVIDENCE (RWE)**

THE BENEFITS OF RWE IN INFORMED HEALTHCARE DECISION MAKING

RWE-informed healthcare benefits range from demonstrating product safety and value to informing future program designs. As such, RWE is impacting decisions such as product reimbursement and market access now more than ever.

For example, a recent survey by the European Commission found that an increasing number of countries use RWE to supplement RCT results for their decision-making processes for reimbursement and pricing, and in supporting Safe and Timely Access to Medicines for Patients (STAMP).² The US Food and Drug Agency (FDA) has also recently released draft guidance on using RWE to support regulatory decision-making for medical devices, further indicating its growing importance to the industry.³

In addition, pharmaceutical companies and medical device manufacturers are also starting to realize the great commercial potential of RWE and the added value it can provide. Hughes et al. estimate that RWE can potentially generate \$1 billion for a top-10 pharmaco product when it is applied collectively in six major areas.⁴

While some of these areas have been generally well-accepted by the industry, other areas have only recently been identified as having potential value. This possibly reflects a shift from opportunistic applications to a more systematic strategy.⁴ Below we outline the six areas where RWE provides advantages across the product lifecycle, starting with the initial development phase, moving on to those during launch, and ending with the in-market stage.



Clinical development

RWE can improve how a product is developed, such as through enabling translational research and improving program recruitment and simulation. Consequently, a top-10 pharmaco could deliver approximately \$100-\$200 million from applying RWE to its clinical development alone. This is mainly due to the long-term benefits of RWE application, such as by tapping electronic health records to increase patient enrollment rates.⁴

Safety and value demonstration



Using data gathered from RWE platforms to demonstrate the safety and value of a new product is now increasingly being adopted by companies that are faced with brand challenges and the potential to lose revenue. Some of these companies have subsequently received rapid responses from regulators and third party journal publications to support continued market access and reimbursement.⁴

Initial product pricing and market access

Some companies have reported that RWE can support and contextualize results from RCTs that decision-makers would otherwise find difficult to interpret, helping them to negotiate initial pricing and better articulate the value of a new drug or device.⁴ In turn, payers can see tangible evidence supporting these arguments.⁵ As such, RWE can speed up the initial submission to market and duration of national reimbursement decision-making so that products can enter the market faster.





Productivity and cost savings

RWE-enabled productivity and cost savings are starting to be accomplished across all stages of the product lifecycle. For example, a company used its RWE platform to run an observational program at only 2% of the original budget.⁴ RWE can thus save costs as well as reduce duplicate primary market research. As such, it is estimated that RWE is worth about \$100 million in terms of cost savings for a top-10 pharmaco product.⁴

Improving launch planning and tracking



RWE can be used to help with launch planning and tracking. For example, a company created patient journeys based on RWE, shared these insights with physicians to gain treatment and outcome forecasts, and consequently improved launch commercial forecasts by 20%. As such, a top-10 pharmaco product could expect RWE-informed launch planning and tracking to improve its revenue by \$150 million.⁴



Commercial spend effectiveness

Marketing and sales effectiveness can be enhanced by RWE through deepening understanding of the patient journey and physicians' decision-making processes. Using this data can help companies perform patient centered analytics and physician-patient segmentation to inform their commercial spend, increasing the promotional effectiveness of a product by up to 50%.⁴



Clearly, RWD programs and their data contributions to the wider RWE base are becoming increasingly important both for informing regulatory and reimbursement decisions, and for adding significant value to a company's product across all stages of its lifecycle. As more companies, regulators and other decision-makers start to strategically use RWE across a wider number of applications, its numerous benefits as a real-life complementary data source to RCTs, the additional value it can generate, and its advantages to patient care, will very likely continue to grow.

> DATA FROM RWD PROGRAMS ARE INCREASINGLY IMPORTANT FOR INFORMING REGULATORY DECISIONS

THE IMPORTANCE OF THE PATIENT VOICE TO RWE

Traditional RCTs do not tend to include assessment of the patient experience, which many now argue is one of the most important factors to consider when developing a new medicine and making decisions about its value. Therefore, RWD programs are increasingly focusing on the patient voice to gain additional real-life insights that RCTs cannot provide, such as practical input into future study design and patients' personal experiences of illness and care.

Patients undergoing RWD programs allow program sponsors, stakeholders and other healthcare decision-makers to gain valuable insights, including:

- > Outcomes that are important to patients
- Why patients make certain decisions, such as treatment preference, adherence to treatments, and treatment satisfaction in the real world
- > Patients' experiences of illness and care that clinicians and investigators would not otherwise have access to
- Practical input into future study design, and successful study execution

RWD PROGRAMS FOCUS ON THE PATIENT VOICE TO GAIN REAL-LIFE INSIGHTS Ultimately, this information, when analyzed and interpreted, contributes to a rich source of RWE that can inform a wide range of important healthcare decisions throughout all stages of the product lifecycle. These RWE-informed healthcare benefits range from demonstrating product safety and value to informing future program designs. As such, RWE is impacting decisions such as product reimbursement and market access now more than ever, resulting in pharmaceutical companies beginning to realize the true potential of patient collected RWD and the value it can provide.

RWD PROGRAMS INCLUDE:

- Registries: product, disease, and pregnancy registries
- Quality of life and patient outcomes:
 RWE to support benefits/claims in product labeling
- Safety outcomes/REMs: safety and risk monitoring over long periods of time; also monitoring off-label use
- Pragmatic trials: trials designed to test the effectiveness of interventions in a real-world setting
- Comparative effectiveness: studies to provide evidence of effectiveness in different populations
- Health outcomes/health economics: critical support for formulary approval or reimbursement efforts

CONCLUSION

Patient generated RWD programs assess the effectiveness of new treatments in a real-world setting by making use of the patient voice and tracking patient journeys as they go about their normal daily lives. These RWD programs contribute to a rich source of RWE that can inform a wide range of important healthcare decisions throughout all stages of the product lifecycle - development, launch and in-market. This means that RWE can be used by decisionmakers to assess the added value offered by a new treatment that cannot be provided by traditional RCTs. Clearly, RWD and RWE have important implications for national reimbursement and regulatory decisions, as well as improving holistic assessments of new treatments and ultimately patient care, both now and in the future.

In the second ebook of this series, we look at how technology can be used to reduce the burden of the collection of patient generated RWD, while improving data quality, ultimately providing better, cleaner analysis of RWE to create better informed healthcare decisions. **RWD PROGRAMS INFORM ON A WIDE RANGE OF IMPORTANT HEALTHCARE** DECISIONS

REFERENCES

- Garrison, L.P., Neumann, P.J., Erickson, P., Marshall, D., and Mullins, D. (2007). Using Real-World Data for Coverage and Payment Decisions: The ISPOR Real-World Data Task Force Report. ISPOR, 10: 326-335.
- European Medicines Agency (2016). Paper for STAMP Meeting 10 March 2016: Update on Real World Evidence Data Collection. Accessed 08/02/2017: http://ec.europa.eu/health//sites/health/files/files/committee/ stamp/2016-03_stamp4/4_real_world_evidence_background_paper.pdf
- Food and Drug Agency (2016). Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices. Accessed on 08/08/2017: http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/ guidancedocuments/ucm513027.pdf.
- 4. Hughes, B., Kessler, M., and McDonell, A. (2014). Breaking New Ground with RWE: How Some Pharmacos are Poised to Realize a \$1 Billion Opportunity. A White Paper from IMS Health, pp. 1-24. Accessed 08/02/2017: http:// www.imshealth.com:90/files/web/Global/Services/Services%20TL/rwes_breaking_new_ground_d10.pdf.
- 5. Hughes B, Kessler M. RWE market impact on medicines: A lens for pharma. IMS Health Access Point 2013; 3(6): 12-17.

ABOUT ERT

ERT is a global data and technology company that minimizes uncertainty and risk in clinical trials so that our customers can move ahead with confidence. With more than 45 years of clinical and therapeutic experience, ERT balances knowledge of what works with a vision for what's next, so it can adapt without compromising standards.

Powered by the company's EXPERT[®] technology platform, ERT's solutions enhance trial oversight, enable site optimization, increase patient engagement, and measure the efficacy of new clinical treatments while ensuring patient safety. Over the past four years, more than half of all FDA drug approvals came from ERT-supported studies. Pharma companies, Biotechs, and CROs have relied on ERT solutions in 9,500+ studies spanning three million patients to date. By identifying trial risks before they become problems, ERT enables customers to bring clinical treatments to patients quickly – and with confidence.



