parexel®

Are you using real-world evidence?

RWE strategies span the development lifecycle

With Heart™

Insights

The real world has a lot to teach us about developing medicines

Parexel's experts offer a roadmap and best practices for current RWE applications across three development arenas:

- Early asset planning
- Clinical development: Meeting regulatory expectations
- Medical marketplace: Demonstrating value in the real world

In each section of this e-book, we highlight examples of recent Parexel projects that illustrate the power of RWE to improve decision-making and to drive cost- and time-saving development strategies.

As you consider RWE applications—perhaps to identify relevant biomarkers, to simulate an external control arm or to support a health technology assessment(HTA) application—keep in mind that the full benefit of real-world evidence comes at the earliest stages of development. Through the lens of RWE, experts working at each step of the development process can look ahead to align functions, anticipate needs, and address challenges proactively across the product lifecycle.

RWE practice is strategic and its hallmark is connectivity. Applied in early development stages, RWE maps the development pathway. It informs clinical functions like designing innovative trials and enhances post-marketing functions like safety signal detection. RWE has the power to turn traditional, lock-step development phases into a continuum of aligned operations, from selecting an optimal development candidate to assessing a therapy's impact in real-world use. Along the way, RWE can boost efficiencies by improving patient enrollment and anticipating regulatory responses. On the horizon, RWE is enabling innovations like novel trial designs that use computer-modeling to build external control arms (ECAs).

Go straight to the source: RWD are varied and vast

A wide range of healthcare domains generate high-volume data that can be accessed to understand disease conditions, patient experience, and the impact of therapies in large populations. These data are the fountainhead of RWE practice. In addition to existing sources, real-world data can be generated to meet specific needs using prospective studies, original market and health economic research, quality-of-life assessments, and patient and caregiver interviews.

RWE is developed using real-world data—electronic health records, health claims, registries, published literature—and applies tools and statistical methodologies, such as artificial intelligence (AI) or Bayesian modeling, to deepen researchers' understanding of the therapeutic landscape. RWE can deliver profound insights at every stage of the drug development lifecycle, from elucidating the disease condition and patient experience, to fulfilling the information needs from regulators and payors.

Real-world data (RWD) sources

Primary sources

- Site-based clinical studies
- Clinical outcome assessments (COAs)
- Prospective disease registries
- Patient and caregiver interviews and surveys
- Wearables and sensor data (glucose monitoring, activity trackers)

Secondary sources

- Electronic health records (EHRs)
- Health insurance and medical claims
- Prescription and pharmacy data
- Hospital data networks
- Safety databases, FDA Sentinel System
- Genomics/proteomics databases, national and commercial
- Medical literature, historic clinical trials

RWD forms the basis for RWE and can be extracted from a broad range of sources

RWE in early asset planning: Charting the course

Traditional siloed development leaves you vulnerable to poor choices, missed opportunities, and sluggish operations enroute to regulatory approval and reimbursement. RWE can map the journey—alert you to potential roadblocks and pitfalls, avoid rework and offer new solutions. Insights from real-world data forge better development pathways and reduce risks for non-approval. Ultimately, a foundation built from RWE supports the delivery of therapies that more closely match patient needs.

The greatest benefits come from deploying RWE at the earliest stages of development. Begin with an in-depth view of the disease landscape to understand unmet medical needs and patient perceptions of treatment value. From this vantage point, RWE can inform identification of biomarkers, selection of endpoints and patient populations, guide trial design and prepare you for regulatory expectations. RWE strategies will be in place when the therapy reaches medical practice to support post-approval safety studies, reimbursement strategy, formulary acceptance, and label expansion.

What RWE can do

Map the disease landscape to:

- Assess disease mechanisms, co-morbidities, standard-of-care.
- Trace disease burden, patient journey, clinical practice patterns.
- Identify relevant patient and physician communities.

Exploit the growing utility of biomarkers to:

- Identify appropriate patient populations.
- Support study design through selection of appropriate testing and endpoints.
- Identify predictive biomarkers to tailor inclusion/exclusion criteria.

Model patient characteristics and current treatment to:

- Understand epidemiology: incidence and prevalence in patient populations.
- Assess safety event rates, risks/ benefits in patient subgroups.
- Understand health outcomes and unmet patient needs.

Insights from RWD forge better development pathways and reduce risks for non-approval.

CASE STUDY

Begin at the beginning: One developer's RWE roadmap

Research teams that focus on late-stage marketing and outcomes evaluation are well versed in the use of real-world data. But preclinical and clinical researchers are more likely to be focused on pre-approval clinical trials rather than the applications and benefits of RWE. In early asset planning, RWE brings together multifunctional groups to create a streamlined clinical development plan. This RWE roadmap helps make the best use of limited financial resources and accelerates decision-making while building consensus among team members otherwise focused on siloed operations.

Parexel recently helped a pharmaceutical customer use RWE to optimize a development plan for a rare disease therapy with a cardiology indication, currently in the pre-investigational new drug (IND) phase. The first step was to assemble the multidisciplinary team to delineate a vision for the product, from pre-approval to medical use in broad populations. The group comprised more than a dozen experts from medical, clinical operations, regulatory affairs, marketing, and pharmacovigilance. At each step of development, they planned tactics using RWE—starting with an in-depth profile of the product class: disease and patient characteristics; treatment and market environments; and regulatory and payor expectations. Next, they would focus on problems and data-driven solutions.

Given the scarcity of participants for rare disease trials, the team anticipated the need for an external control arm. Data from secondary data sources (EHRs, health claims data) would be used to identify target patient populations; to consult patient and disease advocacy groups to communicate goals and support enrollment; and to design an innovative trial including an ECA. They knew they would need publications to communicate therapeutic use and benefits; RWE literature searches provided information to develop publications for prescribers and patient groups. Anticipating regulatory safety mandates, they used RWE to support the design of a prospective observational study. The cost of rare disease therapies would pose marketing and reimbursement challenges; real-world data would be collected from sources including economic studies, marketing research and patient interviews to support pricing and demonstrate product value to payors.

This RWE roadmap helps make the best use of limited financial resources and accelerates decision-making while building consensus among team members otherwise focused on siloed operations.

RWE in clinical development: Meeting regulatory expectations

RWE insights not only speed clinical processes but also allow researchers to look deeper into patient needs and see farther to predicted outcomes. In the process, real-world data applications increase speed and efficiency in operations aimed at regulatory approval.

Overcome bottlenecks. Real-world data can be used to overcome chronic delays in trial enrollment and startup. RWE leverages health claims and prescription data to identify high-performing clinical sites and potential trial participants. RWE identifies social media-based patient advocacy groups to build targeted recruitment campaigns. More rapid enrollment in more efficient sites means less time and cost to market.

Build external control arms. Applying artificial intelligence and modeling methodologies, RWE leverages data to build external control arms that minimize the number of patients enrolled in a trial and reduce time necessary for evaluation. ECAs provide usable data for both regulatory and HTA applications.

Enrich patient-centric practice. RWE is the foundation of patient-centric research. Data from patient interviews, PROs, or other COAs are used to design trials that engage participants and to conduct studies that include meaningful endpoints. Real-world data identify unmet medical needs and help evolve more patient-centric standards of care.

Bridge pre- and post-approval: Technology-driven advances like risk-based quality management require more and more integrated operations. RWE accelerates this trend, blurring functions across pre-clinical, clinical and marketing silos. Strategically, an RWE roadmap developed in early-stage development charts this holistic approach. Tactically, RWE-driven preparations during phase II/III can reduce time and cost for required or voluntary post-approval safety studies (PASS). Regulators now accept PASS submissions based on models generated from health claims, EHRs, registries and other RWE sources. Using prospective observational studies, RWE can collect safety information for use in HTAs and health related quality of life (HRQOL) assessments.

At the cutting edge of RWE are applications in innovative trial design and pharmacovigilance.

What RWE can do

Empower innovative trials:

- Combine site-based data with EHR and registry data to conduct hybrid studies for phase II/III trials.
- Enhance data from single-arm trials using external/historic controls.
- Replicate the comparator arm in single-arm trials using external/historic data sets.
- Create external control arms to validate more rigorous comparison to patients in active treatment arms.

Advance safety evaluation:

- Use AI to capture and discover rare events in large datasets: literature reviews; FDA Sentinel Initiative.
- Use biomarker analysis to predict and monitor rare events; improve risk assessment in clinical trials.
- Identify patients who may be at increased risk for AEs and patients likely to have improved outcomes.

RWE insights not only speed clinical processes but also allow researchers to look deeper into patient needs and see farther to predicted outcomes.

CASE STUDY

Supporting a rare disease drug approval: A RWE-based comparator cohort study

In this ground-breaking 2020 study, Parexel helped a biopharmaceutical customer build an external control arm to support a successful FDA submission for a novel therapy. The therapy was being developed for patients with no second-line treatment options—a population so small it qualifies as a rare disease.

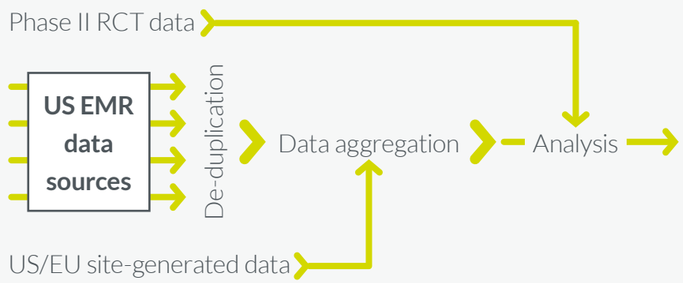
A phase II, single-arm study evaluated drug effects in more than 80 patients. The sponsor needed a comparator cohort to present sufficient data to regulators and healthcare decision-makers, but enrolling the necessary number of patients with the target condition was unfeasible. Facing ambitious timelines as well as recruitment challenges, the sponsor asked Parexel to develop a unique RWE-enabled study design.

With little precedence to guide them, a multidisciplinary team of clinical, regulatory, and RWE experts designed a study that combined data from EHRs, registries, health claims and other existing datasets in the U.S., with data from retrospective chart reviews from across Europe. Data were harmonized, aggregated and de-duplicated to match the trial patients with patients who had been treated with standard-of-care therapies. The project was complete in 15 months vs. the planned 24 months.

The expedited timeline allowed the sponsor to file with the regulatory authorities nine months ahead of schedule. The external control arm gave both FDA and EMA decision-makers the necessary information to grant market approval.

Current RWE practice focuses on using external and historic controls to enhance data from single arm trials and to replicate comparator arms for more robust comparison. On the horizon is the potential for RWE to generate substitute control arms—of special value for rare disease studies.

Novel Study Design



RWE in the medical marketplace: Demonstrating value in the real world

RWE is *the* critical tool for therapeutic evaluation in the medical marketplace. RWE observations of product performance in real-world medical use are essential to demonstrate your therapy's value to patients, care providers, payors and regulators.

RWD can be used to hone brand planning and marketing strategies, support reimbursement and formulary adoption, and provide the evidence needed for label expansion. Blurring silos once again, RWE observations of drug impact in large populations can reveal unmet medical needs and identify subpopulations that may benefit from a therapy that feed back to further clinical development.

What RWE can do

Build in-depth market profiles:

- Define the market based on potential patient populations and estimated revenue per patient.
- Understand time-to-event comparisons, survival extrapolations, and use of healthcare resources.
- Conduct burden-of-illness studies: identify potential market issues and patient perspectives.

Collect real-world use data in large populations:

- Understand effects in subpopulations and support label expansions.
- Use AI and predictive modeling to inform HTAs, treatment and economic decision-makers.
- Support publications and medical/patient communications.

Optimize reimbursement, support formulary adoption:

- Define product positioning; understand existing pricing models; strategize launch sequence.
- Develop health economic models to support formulary acceptance.
- Develop cost-effectiveness models to support reimbursement strategies and payor messaging.

RWE observations of product performance in real-world medical use are essential to demonstrate your therapy's value to patients, care providers, payors and regulators.

CASE STUDY

Using RWE to advance modeling: Better survival prediction for cancer therapies

Clinical trials necessarily rely on endpoints that can demonstrate drug effects in the short term. Demonstrating longer term survival—at one year, five years, and beyond—is essential to understand therapeutic value and economic impact. Methodologies used to identify prognostic factors and to predict survival rates—risk prediction modeling and advanced parametric modeling, respectively—are beginning to incorporate real-world data to increase their predictive power and reliability.

Testing a better model in an immuno-oncology therapy. Immuno-oncology (I-O) offers major advances. I-O activates the immune response and is especially effective in metastatic disease, with fewer side effects compared to chemotherapies. I-O also poses challenges, including immune-related adverse events in patient subpopulations.

Individualized risk prediction models could help to improve outcomes by elucidating the relationship between patient characteristics and responses to alternative treatments. But due to their complexity, these models are difficult to interpret and have limited generalizability without large numbers of cases available for simulation. Real-world data offer a solution: larger sample sizes and more diverse populations can help to validate predictive models and increase their generalizability.

Parexel experts recently developed a Bayesian Network (a probabilistic graphic model) to analyze relationships between patient profiles, adverse events, and survival outcomes for an open-label phase III trial that compared a novel I-O therapy for advanced renal cell carcinoma to an existing I-O treatment. To amplify the number of cases for the simulation, they used AI to identify patient profiles, matching characteristics and treatment, in two populations of 1 million patients, then modeled outcomes for the two treatment groups. The empowered model was able to identify characteristics associated with favorable outcomes.

Parexel experts have also recently developed a Bayesian advanced parametric model (APM) to improve the accuracy of long-term survival predictions for I-O therapies. The model uses real-world data to incorporate representation of realistic effects, such as heterogeneous response, treatment waning, and age-related mortality. In this case, the real-world data came from registry data and general population mortality data. The model was applied to predict overall survival in a phase III trial of an I-O therapy in non-small cell lung cancer. The model was found to provide reliable survival predictions over a lifetime scale even with limited follow-up data available, potentially allowing for support of HTA submissions at early database locks.

CASE STUDY

Supporting label expansion: RWE helps bring an orphan to market

In this case, the sponsor was preparing to launch a gene therapy as a one-time treatment for patients who have to routinely administer infusions to manage a rare disorder.

There were limited data from the single-arm clinical program. The sponsor had little precedent to inform reimbursement, and there was no existing knowledge of how managed entry agreements would be handled. Parexel designed an RWE strategy to develop the necessary data.

We advised this biopharmaceutical client to develop an analysis of costs and outcomes related to managing this disease to outline to the HTA bodies that long-term follow-up in this area is a viable option. RWE included outcomes from patient registries, prescription data and combined individualized ICD-10 data. This study is the basis of negotiations to support managed entry agreements across the Nordic markets.

The RWE-driven future of drug innovation is taking shape now, as patients move to the center of research processes and become curators of their own health-related data. The future promises greater RWE-enabled efficiencies and an innovation process that is closer to patients and more fully responsive to real-world healthcare needs.

Connect with Parexel to discuss how your team can move therapeutic evaluation beyond the clinic and into the real world by incorporating RWE into your development program. Let's start your journey toward more insightful and efficient drug development program together.

Expert spotlight

Matthew Gordon
Vice President, Real-World Evidence Strategy
Parexel International

Matthew leads Parexel's efforts to integrate innovative real-world evidence solutions throughout the product lifecycle. Matthew's experience covers a wide range of therapeutic areas, as well as strategic objectives from natural history programs, external control arm studies for regulatory approval, and global safety-surveillance mandate. His technical expertise includes program strategy and operational structure in disease and product registries, prospective pharmacoeconomic studies, and systematic reviews of scientific literature.

Sangeeta Budhia
Vice President, Head of Global Pricing and Market Access
Parexel International

Sangeeta develops global strategies, including pivotal clinical trials, long-term data collection studies, real-world evidence generation plans, and HEOR strategies prepared for the reimbursement challenges that each product will face. She has nearly 20 years of experience working within market access and health economics and outcomes research (HEOR), helping companies position their products for maximum uptake at an optimal price in the shortest possible time.

Jackie Vanderpuye-Orgle, PhD
Vice President, Global Head of Advanced Analytics
Parexel International

Jackie leads Parexel's efforts in conducting empirical research to underscore the differentiated value of assets across a range of therapeutic areas. She provides technical expertise and oversight on network meta-analysis, parametric modelling, predictive analytics, AI, and general statistical analysis workstreams. Her team focuses on identifying fit-for-purpose analytic solutions to leverage both clinical trial and real-world data to bring the right treatment to the right patient at the right time.

With Heart™

We're always available for a conversation

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