



# Observational Research: The Need for a Customised Operational Approach

Aligning Strategy, Design, and Execution for Real-World Evidence

## Abstract

Observational research has become a cornerstone of real-world evidence (RWE), offering insights into treatment effectiveness, patient experience, and healthcare delivery in actual medical practice settings. Yet many studies are operationalised — generally inadvertently — using frameworks designed for randomised controlled trials (RCTs), resulting in inefficiencies and misaligned methodologies.

This paper explores the strategic and operational distinctions between RCTs and observational studies, advocating for a purpose-built approach that reflects the unique landscape of real-world research. By aligning infrastructure with scientific and strategic intent, sponsors can ensure their studies are not only methodologically sound but also fit for the terrain they seek to navigate.

## Strategic Context and Methodological Contrast

RCTs are engineered for precision and control. Their design emphasises reproducibility, standardisation, and internal validity — requiring strict protocol adherence, intensive site monitoring, and centralised data verification. This structure is essential for regulatory submission, where every variable — in particular, subject inclusion/exclusion criteria — must be tightly managed.

Observational studies, by contrast, are built to operate in and to reflect environments as dynamic as is the real world. Their purpose is to capture outcomes as they unfold in routine clinical practice, where variability is not a flaw but a feature. These studies must be responsive to context, flexible in design — typically including quite liberal inclusion criteria — and calibrated to observe rather than intervene. When observational research is forced into rigid frameworks, it risks losing the very qualities that make it valuable.

In short, each study type is designed for a different kind of journey. RCTs follow a fixed route and carry heavy loads; observational studies require sportscar-like agility, adaptability, and a lighter operational footprint.

## Designing for Purpose: From Strategy to Execution

Effective observational research begins with a clear articulation of strategic goals. Whether the focus is clinical effectiveness, economic impact, patient-reported outcomes, or long-term safety, the operational design must be reverse-engineered from these objectives.

This alignment influences every aspect of study execution:

- Protocols should reflect real-world care pathways, not idealised or experimental treatment scenarios.
- Data collection methods must minimise disruption to standard practice.
- Site and patient engagement strategies should reduce burden while enhancing participation.
- Analytical plans must accommodate bias and variability without compromising interpretability.

When infrastructure is tailored to the study's purpose, execution becomes smoother, more efficient, and better suited to the landscape. The goal is not to retrofit a high-performance design onto a rigid frame, but to build something purpose-fit from the ground up.

# Operational Domains in Observational Research

## Study Design and Strategic Intelligence

Observational protocols require thoughtful calibration. They must be flexible enough to capture diverse clinical realities, yet structured enough to support meaningful analysis. This often involves a “fly on the wall” approach — observing without obstructing, and designing operational support with minimal disruption in mind.

Fundamentally, the strategic rationale underlying the observational study frames the overall research intent. Typically, the desire to establish real-world evidence is discretionary — not a regulatory requirement; that said, establishing real-world overall research intent. Typically, the desire to establish real-world evidence is discretionary — not a regulatory requirement: that said, establishing real-world value has become a de facto requirement for market access and accelerated acceptance by physicians, patients, and payers. As such, the study and its findings become a strategic asset for its sponsor, and that reality cannot be compromised by an inappropriate operational platform.

Strategic intelligence also includes understanding the disease landscape, treatment heterogeneity, and patient experience. These factors inform outcome selection, inclusion criteria, and data sources, shaping the study’s ability to generate meaningful and actionable insights.

The best operational approaches are those that embrace real-world complexity with finesse — like a well-tuned system that responds to the road rather than resisting it.

## Program and Project Management

Observational studies benefit from adaptive planning and agile execution. Project management must accommodate evolving site realities, shifting timelines, and variable data flows. Transparent communication and milestone tracking are essential but must be balanced with the flexibility required to preserve observational authenticity.

Coordination across stakeholders — sponsors, sites, data teams, and vendors — requires a shared understanding of the study’s purpose and constraints. This alignment helps avoid unnecessary escalation and ensures that operational decisions consistently support strategic goals.

In this context, project managers act less as traffic controllers and more as navigators — guiding the study through changing conditions while keeping sight of the destination.

## Site Engagement and Support

Sites play a pivotal role in observational research, but their workflows differ significantly from those employed in interventional trials. Effective site support includes:

- Leveraging electronic medical records (EMRs) to pre-populate case report forms
- Minimising medical monitoring requirements (since monitoring for protocol adherence is, essentially, unnecessary when there are no procedural mandates)
- Providing targeted training on observational protocols (which, again, typically mandate only the collection of data)
- Emphasising collaboration and soft skills in sponsor-site interactions

The aim is to integrate seamlessly into existing clinical routines, not to overhaul them. Sites should feel supported, not burdened — able to contribute data that reflects their standard practice without unnecessary detours.

## Data Management and Analytics

Real-world data presents unique analytical challenges. Missingness, confounding, and selection bias are inherent features, not flaws. Analytical strategies must be designed to adjust for these factors (when possible) while preserving the contextual richness of the data.

Epidemiological and statistical expertise is essential, as is a reporting framework that reflects the observational nature of the study. Participant updates, stakeholder summaries, and peer-reviewed publications should all be tailored to the study's design and audience — avoiding the temptation to over-interpret or sanitise findings.

In this domain, the goal is not to engineer a perfect ride, but to understand how the system performs under real-world conditions.

## Partnering for Observational Excellence

Choosing the right research partner is critical. Observational studies require teams who understand their philosophical and operational distinctions — not just from a technical standpoint, but from a strategic one.

### Experienced partners bring:

- Familiarity with pragmatic and non-interventional designs
- A standardised approach and infrastructure, yet optimised for flexibility and contextual relevance
- Staff trained to navigate the subtleties of real-world research
- A fundamental understanding and respect for the underlying strategic rationale (while, at the same time, without compromising science)

They know when to intervene and when to observe. They recognise that the goal is not to eliminate every variable, but to understand it in context. And they build platforms that reflect the study's mission — not ones inherited from unrelated models.

The best partners don't just follow the map — they understand the terrain. And can navigate the road with the appropriate vehicle.

## Conclusion

Observational research is not a simplified version of an RCT — it merits a distinct methodological approach with its own strategic imperatives and operational demands. Success depends on aligning infrastructure with intent, designing protocols that reflect reality, and partnering with teams who understand the terrain.

When the design fits the purpose, and the execution reflects the environment, observational studies can deliver insights that are timely, relevant, and transformative. The road may be less controlled, but with the right vehicle and the right team, it leads exactly where it needs to go.



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