Powering Smarter Trial Design:

How Comprehensive Protocol and Site Performance Data Can Enable Better Trial Execution

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Clinical trials are becoming increasingly complex.

Many sponsors are now targeting smaller, more diverse patient populations, while facing heightened competition for the best sites. In this environment, trial design plays a fundamental role in shaping recruitment and retention, operational efficiency, cost, and overall study performance.

To help facilitate trial optimization — and mitigate the risk of costly delays later — sponsors are turning to data to inform trial design. But comprehensive, high-quality datasets can be difficult to come by. Public resources, like ClinicalTrials.gov, may contain only a fraction of the potentially available protocol and performance data. And while data obtained from full-service vendors often contains helpful insights, it may be limited to protocol and performance data collected within that organization.

The delayed timing and significant data gaps can make it difficult, or nearly impossible, to model how changes in protocol design affect the trial's operational success: "Adding endpoints and associated procedures to a protocol is relatively easy, but connecting those elements to the burden on sites and participants can be extremely difficult to predict without sufficient comparable data," says Melissa Hutchens, vice president of Research & Benchmarking at WCG. "You need to be able to model how each aspect of the protocol might impact results to meaningfully de-risk your program."

Between 2015 and 2025, there has been a:

30% increase in protocol endpoints

60% increase in study procedures

During that time, protocol deviations have nearly tripled, and there has been more than a:

50% surge in substantial amendments[1]

[1] https://www.appliedclinicaltrialsonline.com/view/shining-a-light-on-the-inefficiencies-in-amendment-implementation

Greater complexity increases the risk of trial failure — and the chance of missing recruitment targets.

Any addition to the protocol has the potential to up the burden on participants and site staff, extending timelines and costs. And sponsors who devise protocols based on their previous work — and include endpoints or study requirements from previous trials — risk creating a "snowball effect" that can exponentially increase complexity.

"Sponsors naturally draw on their track record within a given therapeutic area. Experience running non–small cell lung cancer trials, for instance, means you understand which endpoints have been prioritized," says Hutchens. "But what happens when the team wants to add just one more for the needs of this specific trial? These seemingly small additions, layered on top of existing endpoints and procedures, increase operational and participant burden while offering limited incremental insight. And in some cases, they undermine the trial's likelihood of success."

Eventually, small protocol additions make patients reluctant to participate in trials if they involve procedures that are more burdensome than the current standard of care and also have the potential to increase attrition. Top sites feel the burden too and may choose not to participate in operationally burdensome trials in favor of more streamlined and operationally efficient ones.

Without historical benchmarking data that allows organizations to accurately compare trial designs to outcomes, it can be near-impossible to identify the tipping point between sufficiently robust and overly burdensome on sites and participants.

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Without these comprehensive insights, sponsors may not have the ability to accurately forecast site performance — and anticipate how this impacts trial costs and timelines.

Designing a protocol without comprehensive historical benchmarking and performance data poses a significant challenge: Sponsors lack the needed data to track historical site performance to predict whether sites can deliver the results they expect. As a result, they may miss opportunities to identify when sites are likely to underperform for their specific trial — and act accordingly to support the trial timeline.

"Sponsors often rely on existing relationships to help guide site selection because, without comprehensive performance data, that can be an effective way to manage risk," says Mette Andersen, general manager, Data, Analytics & Insights at WCG. Relying on existing relationships may also mean sponsors miss opportunities to find the ideal sites with capabilities suited to a specific protocol and lose out on chances to build relationships with new sites that could support the trial.

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Pairing comprehensive protocol with site performance data powers smarter trial design from the ground up.

The solution to this uncertainty? Leveraging comprehensive protocol data, alongside historical site performance data, across the lifespan of the study.

Access to a broad spectrum of protocol data helps sponsors understand what has worked and what hasn't across similar past trials.

The real transformation comes from modeling prospective protocol designs against historical benchmarks, enabling sponsors to set realistic expectations for real-world performance.

"It's crucial to break down the siloes between protocol and outcome data. That's the only way to truly model whether a protocol with X, Y, and Z attributes is likely to succeed with the time and budget you've allotted to it," says Andersen. "It also lets you know how changes to the protocol design will impact its success. If your medical monitor wants to add an additional endpoint, you can use historical data to help inform the discussion on whether it's truly necessary — and, if you decide to add it, model how it will impact the cost and timeline of the trial."

Reduce unnecessary complexity and relieve participant burden to enhance the participant and site experience.

These modeling exercises can serve as a jumping-off point to identify unnecessary complexity within your proposed trial design and anticipate how it may impact both sites and participants.

"Measuring additional endpoints is one source of potentially unnecessary complexity, but it's far from the only one," says Andersen. "There's also the procedures to consider. If your endpoint initially calls for four biopsies to meet it, you can model whether you can sufficiently answer the scientific question in three biopsies or two biopsies," she explains. "It gives you a chance to map out the participant journey and find ways to streamline that experience to minimize attrition and design more patient-centric trials."

Similarly, sponsors can identify aspects of their protocol that may appear simple on paper but prove operationally complex in practice. Rather than calling for blood draws at 16-hour intervals, for example, which would bring site staff and participants to the site after hours, sponsors can model whether they would achieve an equivalent result by collecting samples the next morning, at a time that's more convenient for participants and sites.

"Access to protocol and performance data allows you to find this kind of 'low-hanging fruit' that you can potentially remove or adjust to enhance the participant and site experience, without threatening the scientific rigor of the trial," Andersen says. "Designing the trial from the ground up allows you to streamline the experience for everyone involved to facilitate site selection and recruitment, while still ensuring you're meeting historical benchmarks for success."

Build stronger site relationships to support ongoing clinical development.

Streamlining trial design doesn't just help reduce site and participant burden for a single trial. It can also help bolster your brand as a site-friendly sponsor.

As a sponsor, your reputation precedes you at sites. Top sites know if you're easy to work with, or if they're likely to struggle with organizational complexity. Designing your trial with the site experience in mind helps your trial stand out among the competition — and it lets sites know you're a strong partner who will help them succeed.

Predict and measure site performance based on historical benchmarks.

Pairing the protocol with historical performance data also helps sponsors make data-driven decisions about site selection. This can help sponsors confirm whether their "tried and true" sites will meet the needs of a specific protocol and identify top-performing sites to start building relationships with.

"Site selection is both an art and a science. You need the right mix of key opinion leaders (KOLs), super-enrollers, and quick start-ups to help set the trial up for success, and existing relationships count for a lot," says Andersen. "But bringing historical performance data and protocol modeling into the mix allows you to add more science to the process."

Pairing protocol and performance data allows sponsors to track how sites have historically performed with protocols similar to theirs, so leaders can make decisions based on demonstrated track records rather than sites' self-reported performance predictions. As sponsors increasingly face competition to attract top-performing sites, data can also help leaders model the potential benefits of expanding the study into new global markets where they may face less competition.

Identifying opportunities to improve site performance during and after the trial.

The same scenario-planning tools that can inform trial design also help sponsors measure performance and adjust forecasts throughout the trial. Sponsors can compare site performance to historical benchmarks once the trial is underway, identifying early if they may need to onboard additional sites to reach their targets and act swiftly to mitigate the impact on the trial's overall success.

Identifying underperforming sites creates opportunities for sponsors to investigate the key challenges impacting performance, and the steps sponsors may be able to take to help. "You may be able to transform less competitive sites into top performers for your trial by investing in communications and training, for example, or supplying sites with more resources," says Andersen. "That can help you unlock better performance from even research-naive sites."

The End Result: More opportunities to manage risk across clinical development.

Leveraging protocol and performance data throughout clinical development helps sponsors mitigate potential enrollment, retention, and timeline risks and optimize clinical trials from the very beginning.

Instead of:	Sponsors can:	Outcome:
Adding operational complexity with potentially unnecessary endpoints or procedures.	Create optimized designs for answering scientific questions and meeting regulatory standards.	**Sponsors create a better experience for sites and participants, without sacrificing scientific soundness.**

Instead of:	Sponsors can:	Outcome:
Identifying sites based on previous relationships (with your organization or via your CRO).	Leverage high-quality site performance data to identify sites likely to excel at your specific trial design.	**Sponsors can feel confident building relationships with new sites — including those in new markets — to help meet recruitment goals and timelines.**

Instead of:	Sponsors can:	Outcome:
Relying on sites' own often-inflated enrollment estimates to forecast costs and timelines.	Look to high-quality site performance data to more accurately assess site feasibility.	**Sponsors can create more accurate forecasts, and identify opportunities to improve site performance from the outset, before lagging performance impacts the trial.**

Turning Insight Into Action: Three strategies to leverage data effectively for trial design within your organization.

1. Start with self-reflection on your current processes.

The first step to optimizing trial design involves diving into the data to examine what your organization is already doing well and where you may have opportunities to improve.

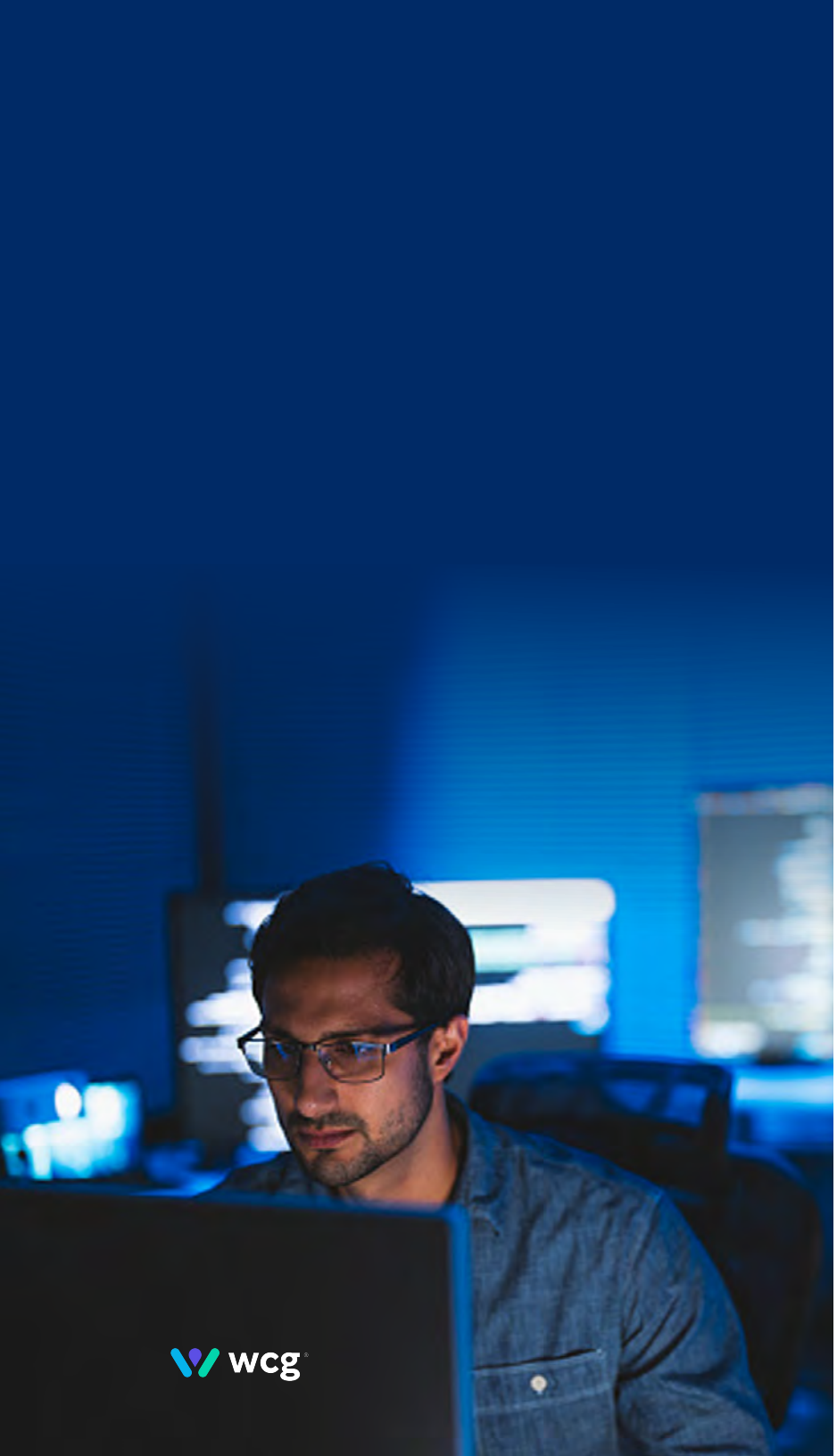
Sometimes, you've done everything right on paper. You've selected high-performing sites with a trial protocol that seems streamlined to you, but the performance just doesn't match the expectations. The data allows you to identify when that's happening, so you can reach out to discuss how you can help.

2. Stay curious about the gaps in your data and seek out opportunities to close them.

Of course, the quality and breadth of data are critical to making sound, data-driven decisions. And MacDonald recommends looking into the potential gaps in the data available to you — gaps that you may unknowingly fill with assumptions.

Ask yourself if you're truly making decisions based on the most comprehensive data available. Are you limited to publicly available data? Are you limited to data collected from a single CRO?

Supplementing your data strategy with a holistic, CRO-agnostic data source helps ensure you can make decisions based on trials that most closely resemble your own. Most importantly, datasets that combine protocol with performance data allow you to turn that data into actionable insights that set your trial up for success.



3. Make data-driven optimization the “new normal.”

While each clinical trial is unique and requires a bespoke approach to optimization, sponsors can set their clinical development programs up for success by embedding data-informed optimization into their processes.

You don’t necessarily need to reinvent the wheel each time. It’s human nature to resist starting from scratch. But we encourage customers to take a deep dive into the data as their optimal first step, rather than defaulting to their own prior protocols as a starting point. Site capabilities, competition within treatment areas, and advances in technology all evolve; so what was optimal for your trial five years ago may not be optimal for a similar trial today.

Approaching data-focused optimization as a necessary first step allows sponsors to adapt in dynamic environments, she says. “It means you can feel confident that each trial is optimized for success from the ground up.

Design Smarter Trials With The Right Data

As trials continue to grow more complex, and sponsors vie for site and participant availability, streamlining trial design is critical to set programs up for success. By analyzing protocol information alongside site performance data, sponsors can more accurately anticipate challenges that may arise during clinical development and take action to manage those risks within the trial design, helping avoid costly delays later.

See your trial before it starts with ClinSphere Trial IntelX™.

Every protocol choice, from visit schedules to eligibility criteria, impacts how a trial performs. WCG's new technology platform, ClinSphere Trial IntelX™, empowers clinical trial sponsors and CROs with unified intelligence, combining predictive analytics, protocol insights, and operational data into one powerful decision engine.

The result: The ability to predict trial outcomes before the first participant is enrolled.

Trial IntelX is:

- Industry-wide
- Built on:
  - 80,000+ complete protocols, and
  - 40,000+ operational performance-benchmarked trials

Sponsors can use AI and real-world performance and operational data to forecast:

- Timelines
- Enrollment
- Site and participant burden with greater precision

Learn how Trial IntelX can help you design smarter, site- and patient-centric trials.

Learn more →

WCG is the decision backbone behind clinical research, combining trusted oversight with intelligence that scales judgment and reduces risk across the trial lifecycle. With decades of experience and the industry's deepest dataset powering responsible AI, we help teams make confident decisions that keep trials moving forward for the therapies at every stage of development.

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