



From Start-up to Sustainability: The New Reality of Research Site Operations

From Episodic Challenges to Structural Conditions in Clinical Research

Clinical research sites remain indispensable as the operational backbone of the clinical trial ecosystem. They are where scientific hypotheses are translated into patient/participant interactions, data collection and regulatory compliance. Yet, as identified in a recent survey of over 600 clinical research sites, sites are operating within a system under sustained and intensifying strain. Many of the pressures documented in 2025 continue in 2026, reshaping what it means for a research site to remain viable, competitive and prepared for the future.

Site readiness is no longer an episodic or transactional state. It is not something that can be switched on at study start-up and set aside at closeout. Instead, readiness has become a continuous operational condition, one that must be actively sustained amid volatility in funding, accelerating protocol complexity, proliferating technologies and persistent workforce fragility. Sites are being asked to do more, faster and with greater precision, often without proportional relief in administrative burden or structural support.

This shift has profound implications not only for sites themselves, but for sponsors and CROs who depend on their capacity. The sustainability of sites is no longer a downstream concern. It is a foundational prerequisite for the advancement of science and the timely delivery of therapies to patients.

Escalating Trial Complexity: From Challenge to Structural Feature

Among all pressures facing research sites, clinical trial complexity stands out as the most persistent and consequential. In 2025, 35% of sites identified trial complexity as their single greatest challenge, making it the most frequently cited barrier across all site types. The Tufts Centre for Drug Development (CSDD) documented increasing levels of trial complexity over the past decade, including scientific (e.g., eligibility criteria) and operational design elements (e.g., number of planned visits). While trial complexity may be considered a byproduct of innovation, it is a defining structural characteristic of modern clinical research.

Complexity manifests across multiple, interrelated dimensions. Protocols now routinely include more endpoints and procedures, resulting in more data requirements. Amendments have become more frequent, often released before a site has activated the trial. Some amendments are expected, such as those related to trial design (e.g., adaptive designs). Per the Tufts CSDD Report, on average, studies across all phases have 2.1 to 2.3 substantial amendments, with Phase II/III trials often having 2.7 to 3.5 amendments, with each requiring 6.9 changes. Operational requirements continue to expand, encompassing extensive training, layered compliance obligations and

increasingly intricate logistics. Technology demands have multiplied, with sites required to navigate multiple platforms and vendors within a single study. At the same time, data expectations have grown, with expanded requirements for collection, monitoring and reporting.

While all sites feel the effects of this escalation, the expression of complexity differs markedly by site size. Larger sites such as academic medical centres, integrated health systems and site networks often report higher absolute levels of complexity due to larger and more diverse trial portfolios, greater participation in oncology and advanced therapies and more layered internal governance structures. These sites manage scale, but at the cost of agility.

Smaller sites, including independent research centres and physician practices, experience complexity more acutely despite managing fewer studies. With fewer specialised staff, limited infrastructure redundancy and minimal capacity to absorb non-core procedures or frequent amendments, complexity translates directly into operational strain. The result across site types is a growing capacity squeeze, in which staffing, timelines and finances are stretched simultaneously, leaving little margin for error.

Study Start-up Delays: A Persistent Bottleneck in Site Readiness

Study start-up remains one of the most persistent structural bottlenecks in the clinical research lifecycle. In 2025, 31% of sites identified start-up as a top challenge, ranking it second only to trial complexity. Despite targeted process improvements over the past several years, start-up inefficiencies endure, particularly as studies become more administratively demanding.

Delays are driven by a familiar but unresolved constellation of factors: prolonged budget development and contract negotiation, increasingly complex coverage analyses and billing compliance requirements, and misalignment or slow responsiveness from sponsors and CROs. Each of these steps introduces friction; together, they create extended periods of 'white space,' during which sites carry cost and uncertainty without the ability to initiate patient/participant activity.

Notably, the burden of start-up delays falls unevenly across site types. Larger sites are disproportionately impacted, with 39% citing start-up as their top challenge compared with 18% of smaller sites. Decentralised research administration, multiple internal stakeholders and layered approval pathways contribute to longer timelines.

Smaller sites often move more quickly through initiation but are far more vulnerable when delays occur. Idle time can destabilise staffing models and cash flow, undermining sustainability even when eventual activation is achieved. Start-up efficiency is no longer an operational nice-to-have; it is a core component of site readiness, requiring tighter alignment across foundational elements such as

coverage analysis, budgets and clinical trial management system builds.

Workforce Shortages and Staffing Instability: A Chronic Constraint

Staffing constraints continue to exert a profound influence on site performance and resilience. In 2025, 30% of sites identified staffing as a top challenge, ranking it third overall. While some degree of staffing stabilisation was seen since the 'Great Resignation,' of 2021-2022, this issue has both broadened and deepened, extending beyond traditional coordinator and regulatory roles to encompass the broader scientific and operational workforce.

Sites report persistent difficulty recruiting and retaining qualified personnel amid rising workloads, increasingly complex protocols, and widespread burnout. Competition for talent across healthcare systems and industry has intensified, further shrinking an already constrained labor pool.

Here again, impact varies by site size. Larger sites face challenges related to workforce specialisation, unpredictable trial pipelines, and funding volatility – particularly in relation to NIH and other government sources. Smaller sites confront a different but equally destabilising reality: limited backup capacity, heightened sensitivity to turnover, and significant operational disruption when even a single role remains unfilled.

The cumulative effect is a system operating with diminishing flexibility. Without structural intervention, workforce constraints may directly impede innovation and trial delivery, threatening not only site sustainability but the broader research enterprise.

Recruitment and Retention: Patient/Participant Experience as a Strategic Imperative

Recruitment and retention pressures remain a continual operational barrier, cited by 28% of sites as a top challenge in 2025. While this represents a slight improvement from surveys conducted in prior

years, enrolment challenges are directly linked to participant burden, protocol design and site capacity.

Smaller sites report recruitment and retention as a more prominent challenge, with 32% citing it as a top issue. Smaller patient databases and limited brand recognition may constrain their reach, particularly as inclusion and exclusion criteria grow more restrictive.

Larger sites often recruit from broader populations but continue to face their own enrolment headwinds. Increasingly complex eligibility criteria, higher participant burden and the demands of oncology and advanced therapy trials all contribute to slower accrual and the risk of greater attrition.

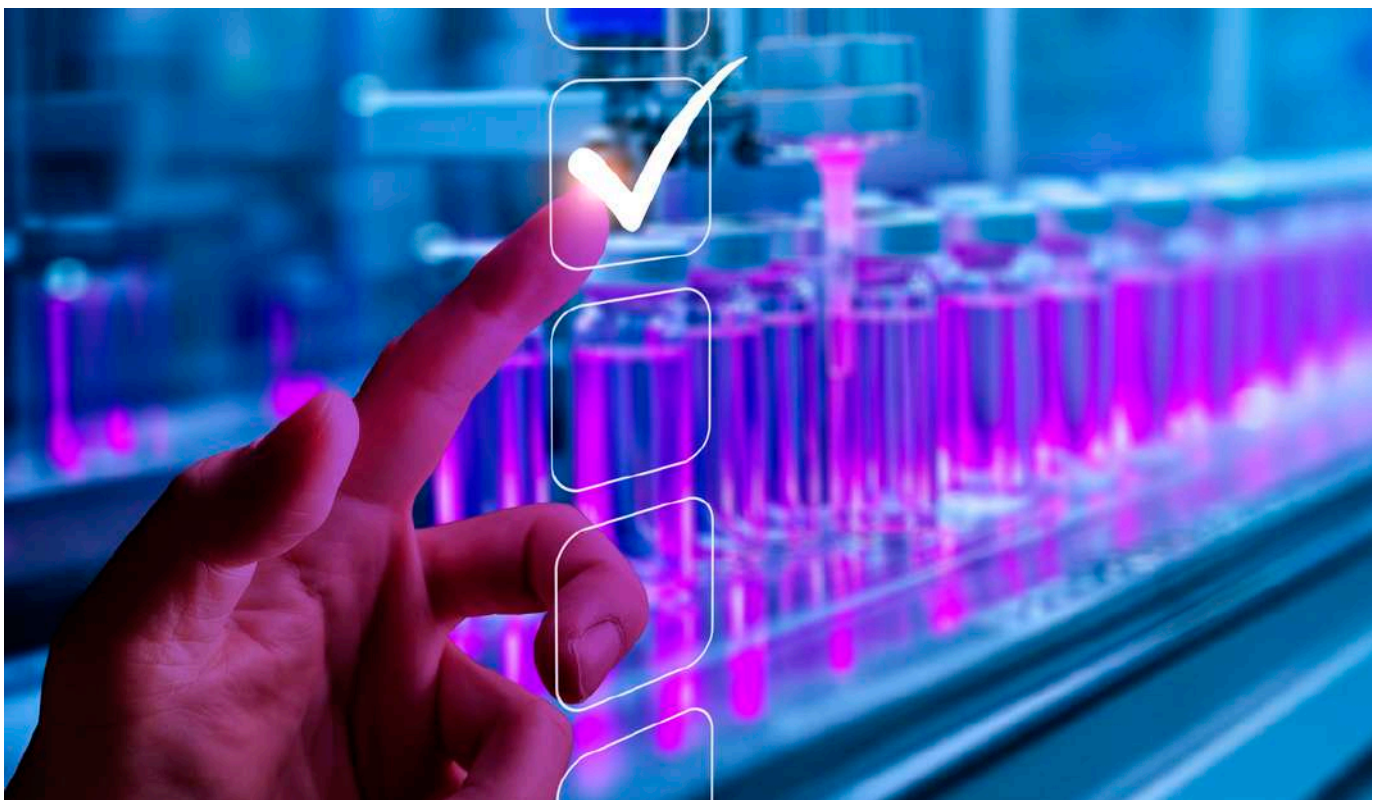
Of critical note, participant experience is no longer ancillary to operational success. It is a strategic determinant of enrolment speed, retention and data quality. Sites that lack the capacity to support participants through increasingly demanding protocols face compounding challenges, potentially impacting both timelines and outcomes.

Technology Burden and Fragmentation: When Enablement Becomes Overhead

Technology adoption continues to accelerate across clinical research, yet integration and interoperability lag. In 2025, 22% of sites identified the number of technologies and vendors required for trials as the greatest driver of complexity.

The burden is particularly pronounced for smaller sites. Twenty-five percent cited difficulties with sponsor-provided technologies, compared with 17% of larger sites. Without dedicated IT support, smaller teams must rely on already stretched staff to manage training, troubleshooting and data reconciliation across multiple platforms.

The primary principle to emphasise technology should alleviate, rather than increase, the burden on sites. When evaluating new tools, ask whether they streamline existing processes or introduce





unnecessary complexity for site teams. Without better alignment, standardisation and integration, the promise of digital enablement risks being undermined by the operational overhead it introduces.

Funding Volatility and Financial Uncertainty: A Structural Risk

Financial volatility has become a defining feature of the site operating environment. The 2025 report details broad effects from NIH funding cuts and paused or cancelled industry trials, with ongoing uncertainty expected in 2026.

Larger sites are more likely to be affected by NIH cuts, with 24% reporting impact from both NIH funding reductions and industry pauses, compared with 9% of smaller sites. Smaller sites are more likely to report no immediate impact but express concern about future disruptions.

In 2025, sites responded to these uncertainties by reducing discretionary spending, freezing positions or reducing the number of staff, and increasing their reliance on industry-sponsored trials – strategies that may provide short-term relief but introduce longer term vulnerabilities.

Capacity Constraints and the Redefinition of Readiness

One of the clearest indicators of systemic strain is declining site capacity to take on new studies. In 2025, 45% of sites reported that operational challenges were limiting their ability to participate in new trials. This constraint extends into 2026, reinforcing the reframing of readiness as a continuous operational asset rather than a pre-study checklist.

Nearly half of larger sites (49%) report restricted capacity, compared with 39% of smaller sites. Larger portfolios, greater administrative burden and higher exposure to funding volatility compound over time, constraining growth even in well-resourced environments.

Advanced Therapies: The Next Wave of Complexity

In addition to prevailing challenges, the swift development of cell, gene and other advanced therapies is introducing further complexity. As of late 2025, there are over 3,200 active or planned cell and gene therapy clinical trials worldwide, with over 1,300 gene therapy candidates alone in development for cancer. Beyond these, innovative therapies in oncology, neurology/central nervous system disorders, cardiovascular and musculoskeletal diseases continue to introduce unprecedented logistical, infrastructural and safety requirements.

For sites without prior experience in these modalities, advanced therapies represent a step change in readiness requirements. Rather than replacing existing challenges, they compound them – raising the

stakes for workforce expertise, infrastructure investment and long-term follow up obligations.

Conclusion: From Managing Challenges to Building Resilience

Research site challenges are no longer episodic disruptions they are structural conditions. Clinical trial complexity, staffing shortages, funding volatility, technology burden, and rising participant expectations interact in ways that amplify risk and constrain capacity.

The defining shift entering 2026 is the move from reactive problem solving toward proactive, continuous operational optimisation. Sites that endure will not simply be those that work harder, but those supported by proportional protocol design, streamlined start-up processes, integrated technologies, stable and supported workforces and true partnership with sponsors, CROs and research service providers.

The future of clinical research depends on the sustainability of its sites. Addressing these challenges is not optional. It is foundational to scientific progress, to equity in research participation and to the delivery of therapies that improve and save lives.

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