Is Your Protocol Leading to Success? The Importance of Early Engagement

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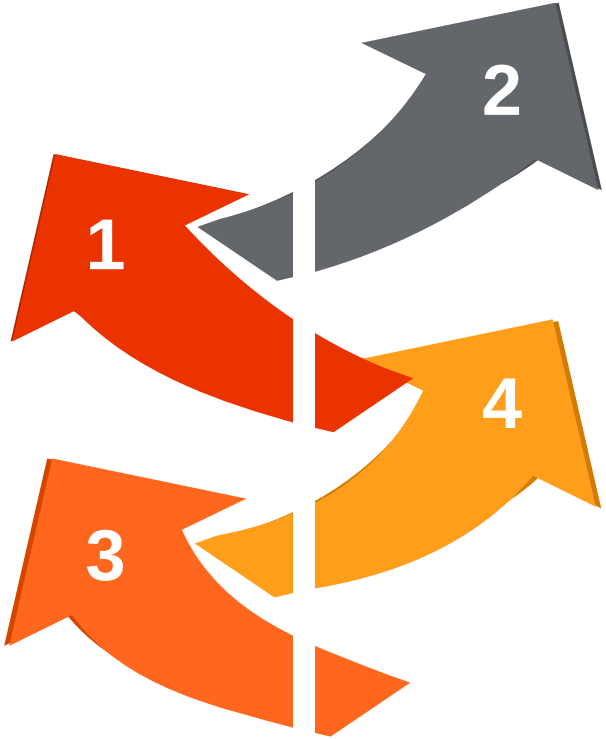
Trends in Clinical Trial Design Complexity

To meet the increasing demand for high-quality data, clinical trials have become more complex.

Competition for sites and patients is an increasing pressure for trial completion.



Site visits and the number of procedures conducted during a visit are increasing

Diversity and inclusion is now a critical success factor for many trials

Success rates for approvals are not keeping pace with R&D spend

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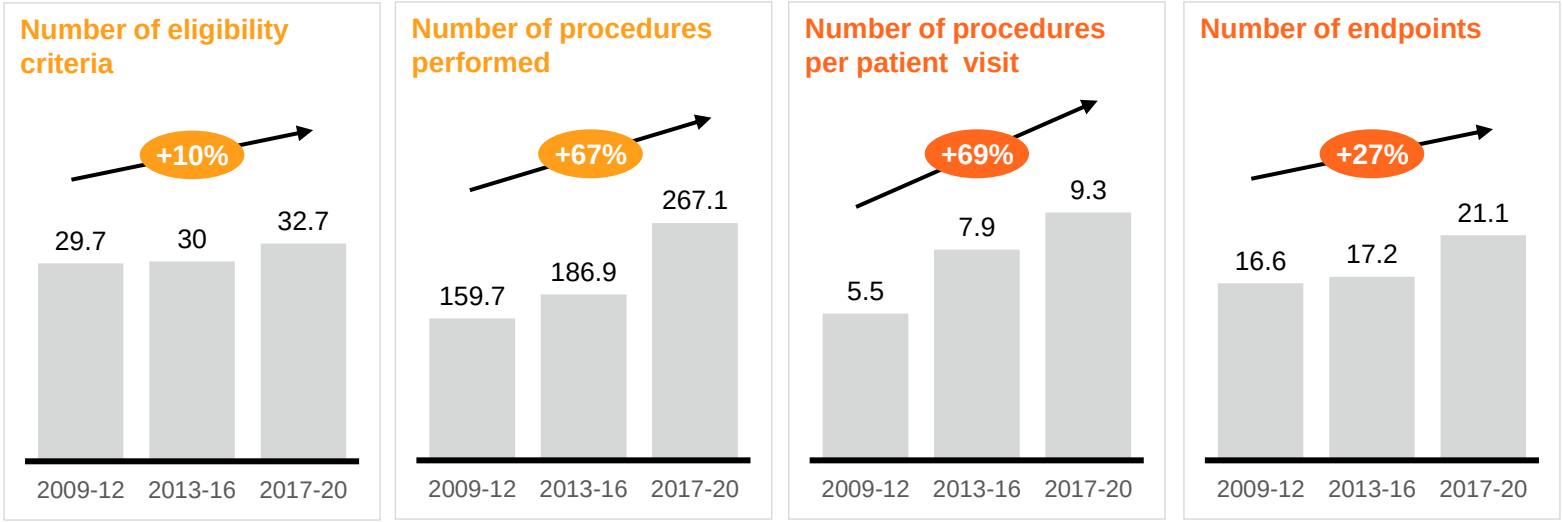
Increasing Data and Evidence Requirements

To satisfy the growing need for data and evidence, clinical studies are employing more restrictive eligibility criteria and requiring patients participate in more frequent and longer visits.



Growing protocol and trial complexity

Source: Ther Innov Regul Sci. 2023; 57(1): 49–56 (Tufts CSDD)

Impact of Protocol Complexity on Trial Delivery

Clinical Trial Sites

- Fewer sites willing to participate
- Research staff spends more time on training than patient care
- Study fatigue

Patients

- Number of patients who enroll in clinical studies continues to decline
- Slow patient enrollment rate and low retention
- High dropout rate

Trial Execution

- High rate of protocol non-compliance, deviations and violations
- Lower data quality
- Costly execution of the protocol

Onerous Clinical Trial Protocols Contribute to Longer, Costlier Trials and High Failure Rates

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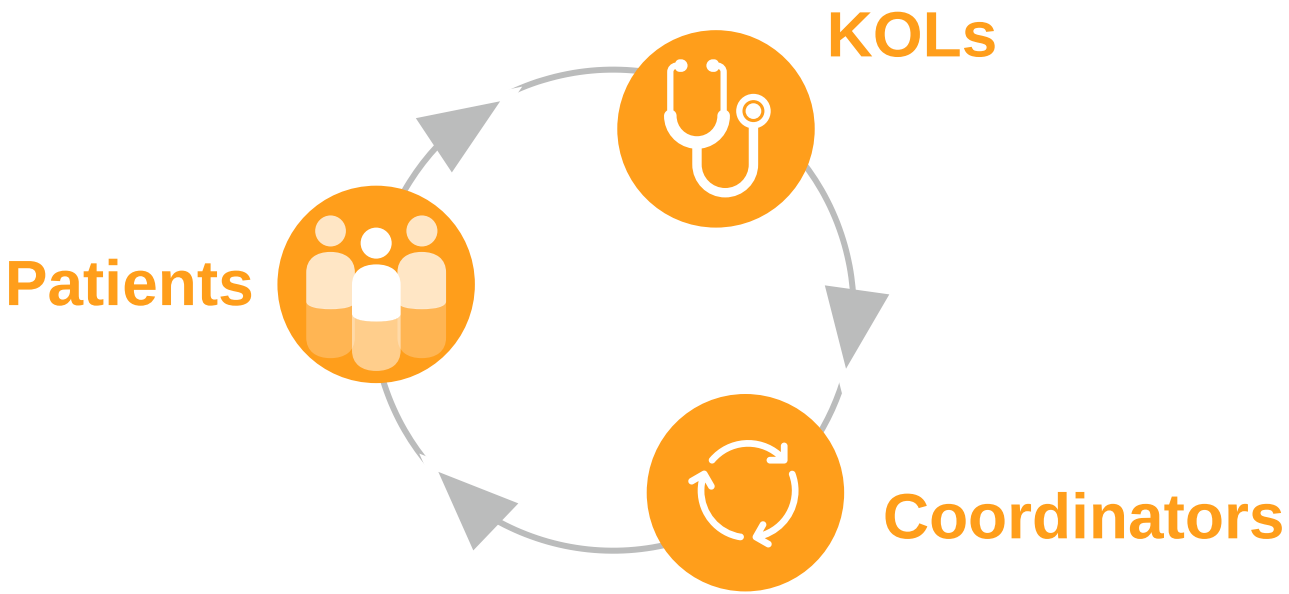
Pain Points Observed

Company Type: Small, Mid to Large Biopharma – Preclinical to Clinical

	Company entering a new therapeutic area	Standardized trials with defined I/E and routine endpoints	KOLs are not aligned with the trial design	Underperforming clinical trial
Pain Points	▪ Diffuse strategy for trial conduct and endpoints due to trial complexity ▪ Trial overburdened with endpoints, assessments and patient visits to sites	▪ Superficially the trial appears straightforward to complete but the challenge to recruit sites and patients has markedly increased	▪ The sponsor needs to be made aware of the potential risks to medical and operational success ▪ Risk of underestimating the challenges and risks to trial completion	▪ An ongoing clinical trial is failing to meet key performance milestones

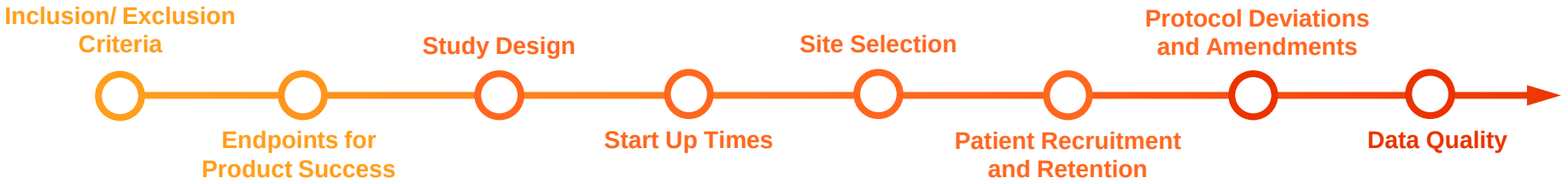
Key Stakeholders

Clinical trial benchmarking needs to be complemented by active early stakeholder engagement.



Impact on Protocol and Study Execution

Early interaction with key stakeholders positively influences clinical trials along a variety of dimensions.



Syneos Health Protocol Optimizer

Syneos Health's Protocol Optimizer

The risk of trials is reduced for sponsors when we actively engage with key stakeholders.

Conduct in-depth interviews with key stakeholders to:

- Reduce potential burden on patient and site
- Identify pain points along the clinical trial journey to deploy additional resources
- Actively engage with the community during product/drug development

Sample Discussion Topics

Patients

- Diagnosis and treatment journey
- Bothersome symptoms
- Barriers to clinical trial participation
- Reaction to the schedule of visits/burden of study design
- Perspectives on inclusion/exclusion criteria and study design

KOLs

- Characteristics of their patient population/ referral patterns
- Potential challenges and best practices recruiting and enrolling patients
- Perspectives on the clinical study and minimum clinically important difference required

Coordinators

- Best practices on enrolling and recruiting patients
- Burden on study design
- Potential challenges operationalizing the protocol design

Protocol Optimizer Solution

Proactively de-risk a protocol and ensure the trial design is patient friendly through engagement with PIs, site coordinators, and patients.

BUSINESS QUESTIONS ADDRESSED

- How enthusiastic are principal investigators and patients with the therapy and the trial design?
- Are there protocol changes that will enhance the level of enthusiasm for the trial?
- What are potential operational challenges to the study as per PIs and site coordinators?
- Are there concerns from patients regarding the frequency of the schedule of events?

VALUE FOR DRUG DEVELOPER

- Understanding of clinical trial feasibility from the investigator, site coordinator and patient perspective
- Operationally optimized clinical protocol with considerations as how to increase enrollment and decrease dropouts
- An aggressively de-risked and optimized, clinical protocol design

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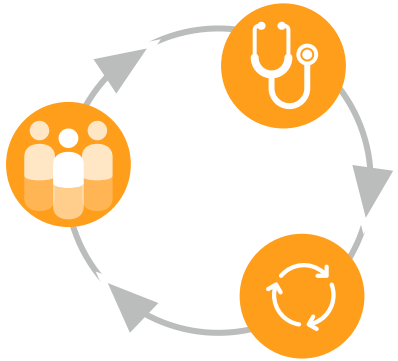
Protocol Optimizer Approach

Protocol Optimizer combines key inputs with insights from patients, coordinators, and investigators to de-risk the achievement of key metrics as well as impact optimal protocol design and trial operations.

Inputs for Interviews

- Indication Strategy
- Target Product Profile
- Clinical Development Plan

Stakeholder Interviews

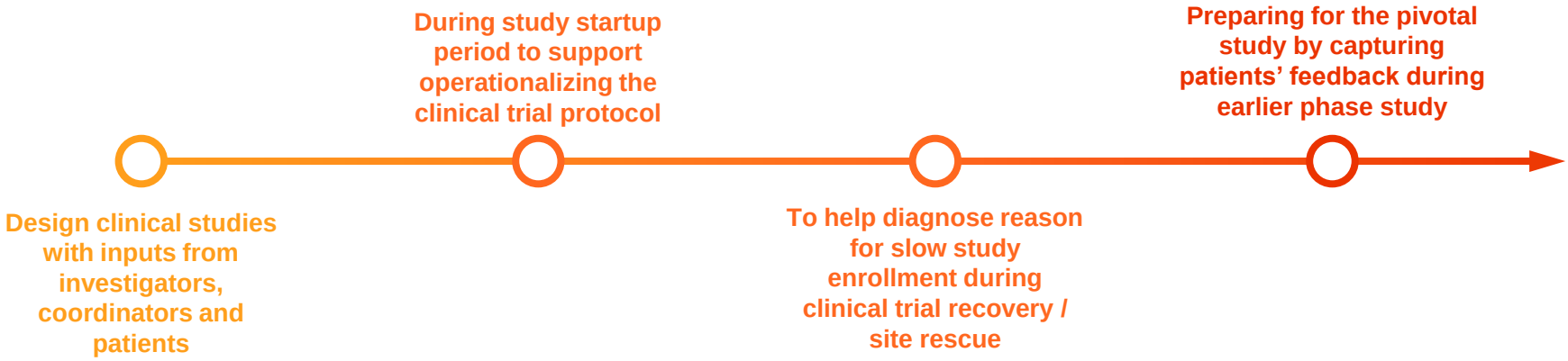


Impact on Protocol and Implications for Execution

- Site Selection and Recruitment
- Site Start-up Time
- Patient Enrolment and Recruitment
- Patient Retention
- Comparator for Product Success
- Endpoints for Product Success
- Protocol Deviations and Amendments
- Data Quality
- Inclusion / Exclusion Criteria
- Study Design

When Do You Need Protocol Optimizer

In addition to during protocol development, Protocol Optimizer can be deployed at later time-points to support study rescue or to capture patient experience during exit interviews.



Protocol Optimizer – Service Offering Process

Blinded, in-depth interviews will be conducted with investigators, site coordinators and patients to proactively de-risk and optimize trial conduct to create a protocol as patient and site friendly as possible.

	Market Research Plan	In-depth Interviews	Workshop
Activities	▪ Protocol synopsis review with the Sponsor and align on key questions and objectives of study ▪ Create a market research plan, including: ➢ Sample size ➢ Screening criteria ➢ Discussion topics ▪ Develop discussion guides and market research instruments	▪ Conduct interviews (double-blinded manner is optional) with agreed upon stakeholders on topics, including: ➢ Clinical trial feasibility ➢ Inclusion/exclusion criteria ➢ Site and patient burden ➢ Patient perspectives on trial participation ➢ Patient diversity considerations	▪ A workshop to communicate insights from interviews to internal stakeholders about the protocol and what should be implemented to optimize trial conduct, informing: ▪ Finalizing and operationalizing the protocol, ▪ Study branding ▪ Patient recruitment
Value	▪ Customized discussion guides for each stakeholder group to best assess how to optimize your protocol and de-risk your study	▪ Insights from interviews across stakeholder groups	▪ Final Deliverable for integration into the final protocol (powerpoint)
	~2-3 weeks	**~ 4-6 weeks**	**~ 2-3 weeks**

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Select Customer Feedback

Protocol Optimizer is well received by our customers

- "Overall, this **clearly contributes** to a much more refined version of the protocol that will be easier to implement and **will make this a successful trial**… and will **make this trial easier for patients and sites** while still generating all the data that we need"
- "I do think it [protocol optimizer] is **best practice**, it should be **deployed for later phase trials for sure**"
- “Very helpful… all the feedback… it has **clearly led to an improved version of the protocol**"
- "Your research was the **deciding factor** in changing the schedule of events"
- "There are things we can do regarding implementation here that can have **a big impact**"

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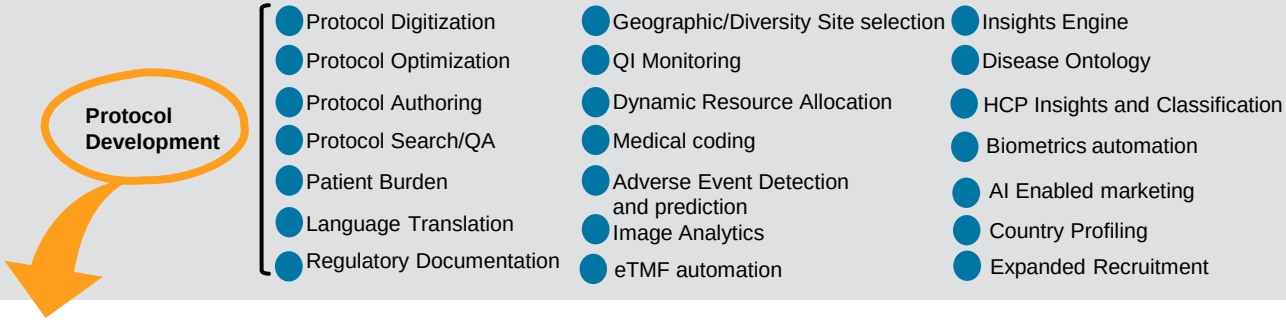
Exploring GenAI for optimizing end-to-end study design and execution

We expect customer programs to benefit from our investments in AI-enabled solutions for enabling better study design and introducing operational efficiencies across the growing portfolio.

Syneos Health Generative AI/ LLM Toolkit



In the past year, more sponsors are realizing the benefits of AI on protocol development…

* Draft new protocols faster -- reduce protocol creation from months to weeks
* Find ideal participants globally, including under-represented areas.
* Analyze countries for feasibility & commercial potential, optimizing recruitment.
* Manage cost and duration of trials (subject to trial complexity – e.g., manage patient burden, duration and enrollments)
* Minimize trial “rescue” through improved enrollment management and site issue monitoring
* Optimize protocols for approval and better success
* Help overall design failure vs trial failure

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Clinical Trial Benchmarking

GenAI can help isolate key influencing factors across a multitude of trial domains while at the same time offering solutioning support based on immediately relevant, data-driven intelligence

GenAI-generated comparative insights can help...

speed up trial design process

by quickly comparing and analyzing a trial's positioning relative to the historical and current trial landscape

accentuate market advantage

by identifying distinct features that may present market dis/advantages within the context of the current trial landscape

derisk trial design & operations

by detecting risk factors that might hinder trial success within a given therapeutic area and recommend risk mitigation tactics

understand patient & site burden

relative to similar trials and suggest strategies to lower overall burden to increase site engagement, patient enrollment, and retention

optimize protocols & trial design

by uncovering potential recruitment barriers and proposing areas for protocol optimization

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Recap

What to Remember