
GSK's Innovative Protocol Design Lab: Challenging the status quo during protocol design and study delivery planning

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The challenge

A key element of GSK's R&D strategy is to leverage data and analytics to deliver on our ambition of identifying and accelerating the next generation of transformational therapies to meet the needs of patients. In recent years, there has been an explosion in the availability of clinical study data and real-world data.¹ An increasing number of empirical findings are being derived from big health data, with such findings being relevant to drug development and clinical trial design.²⁻⁴ Platforms are now available that provide easy access to, and analysis of, such data.^{5,6} This is coupled with advances in the use of machine learning and artificial intelligence.⁷⁻¹¹ Trials may further benefit from focusing on patient-centric approaches to collecting participant insights and data in a more personalised manner.^{12,13}

Leveraging, analysing, and visualising data when designing clinical trials has the potential to optimise protocol designs and accelerate clinical trial delivery. These datapoints and insights are critical to understand the competitive landscape, disease prevalence, patient burden, and historical site performance. The importance of this is more evident as a result of the COVID-19 pandemic, during which additional challenges were faced for trial recruitment, communication with stakeholders and site staff, delivery of interventions, and data collection.¹⁴ Furthermore, when coupled with information such as referrals, claims data, patient registries, and biobanks, companies can start to transform delivery by using data to target and enrol eligible patients.

The December 2020 report on protocol complexity from the Tufts Center for the Study of Drug Development indicated that most protocols have at least three substantial amendments.¹⁵ Trial amendments are costly, with a substantial amendment to a phase III protocol often being in excess of \$500,000.¹⁶ Furthermore, the duration of clinical trials has increased over the past 10 years and protocols include more endpoints; a patient undergoes approximately 263 assessments in a typical phase II or III trial.^{15,17} Therefore, trial complexity, together with enrolment, remain significant challenges across industry. Moreover, with the advent of precision medicine and targeted therapies, and an increasing demand for novel treatments in oncology and rare diseases, the volume of clinical trials is expected to rise. This means the demand for simpler and less burdensome trials for our patients is greater than ever. In order to meet this challenge, we must make investments in the use of data and analytics and drive a culture shift that puts the patient at the centre of our clinical development; we must modernise clinical trials, optimise our protocols, and enhance recruitment.¹⁸⁻²²

Inception of the Protocol Design Lab

At the end of 2019, GSK launched the first iteration of the Protocol Design Lab (PDL). The intent was quite simple. We wanted to proactively leverage data informatics and patient insights to provide clinical study teams with rich information regarding the science (the appropriate endpoints, eligibility criteria, and procedures) and the operational delivery (is the study viable, can it be simplified, can we leverage decentralised solutions to decrease burden?). To bring this to life, GSK invested in real-world datasets that are effective in characterising diseases of interest.

GSK also ensured that multi-disciplinary teams had access to the data, which could be used to challenge early concept designs. The ambition was to optimise the protocol designs, developing more patient-centric protocols that translated into improved enrolment cycle times and a reduction in overall protocol amendments. By creating operationally viable protocols with clearly differentiated study delivery plans for each separate study, GSK could unlock more value to patients. Gaining actionable patient insights, modelling patient recruitment scenarios, generating geospatial maps, and developing accelerated enrolment strategies were all fundamental drivers for success.

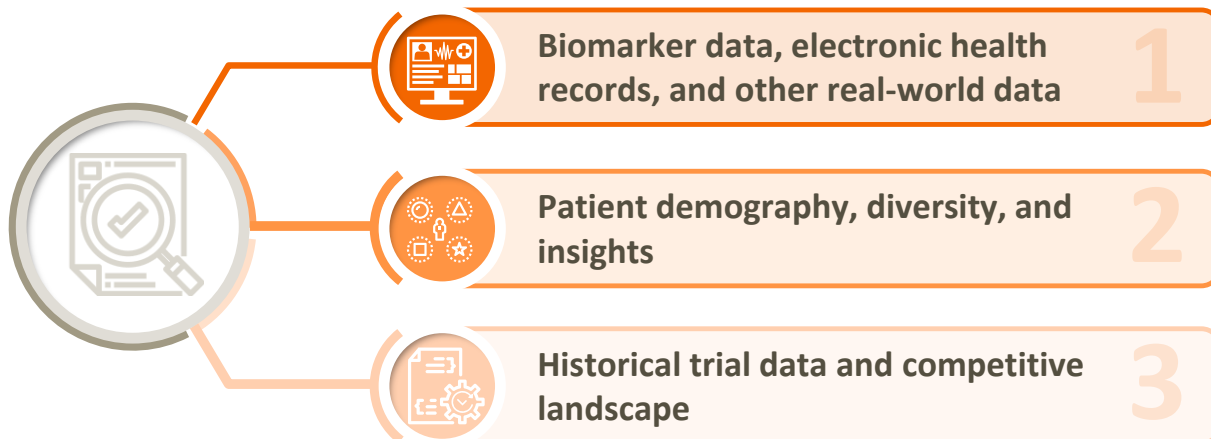
Methodology

The PDL was introduced as a framework to ensure leverage of the latest digital platforms, data, and analytics to drive study planning and decision-making at a point early enough in the study development process to be impactful. The PDL is a facilitated review of key areas that have the potential to impact the timeline, budget estimates, and the operational viability of the study. The review is held early in the planning stage, to allow enough time for actions to be impactful or for additional data to be gathered. The process includes a kick-off meeting to give clarity to the data that need to be generated for the PDL and to assign accountabilities for the associated actions. The data and information are added to an initial Study Delivery Plan. The kick-off meeting is followed by the PDL meeting where the clinical study proposal and sections of the Study Delivery Plan are reviewed and constructively challenged.

The success of the PDL is a result of several key factors:

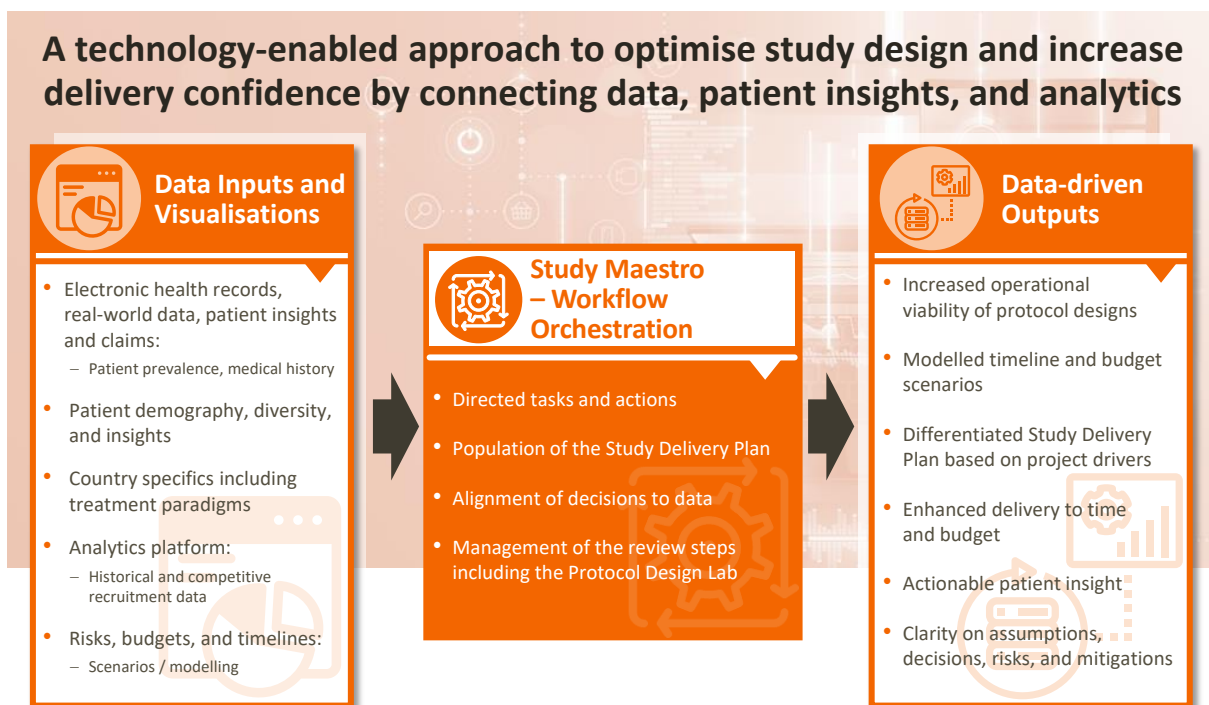
- Driving the cultural change
 - The importance of the early operational focus was set as a senior leader expectation; and it was included in personal objectives
 - The PDL was linked to the existing study planning process, with outputs being a key input for downstream activities.
- Leveraging data
 - There is an expectation that all studies should have data gathered to support early planning from three key areas (**Figure 1**): 1. real-world data to help to optimise the inclusion/exclusion criteria; 2. patient demography and insights to enable targeting of key demographic groups and to support optimisation of the study design from a patient perspective; and 3. historical trial data and competitive landscape analyses to support country selection and realistic enrolment plans.
 - The PDL committee actively reviews the data gathered and checks that the study team is utilising the information to drive decisions and study design.
 - The PDL committee ensures that the study teams engage with the appropriate subject matter experts for the key data sources to drive consistent and optimal use of the tools.
- Respectful challenge
 - The PDL is positioned as a peer review with the express purpose of supporting the study team to develop the optimal operational approach and being prepared for challenges from governance review.
 - The study teams know that the review meeting is a “safe place” to have a robust conversation.

Figure 1: Three key areas of data collection for the PDL.



- Workflow orchestration
 - The generating of the Study Delivery Plan and the PDL meetings as well as subsequent process steps are managed by a workflow orchestration tool, Study Maestro, built within the Appian low-code environment (**Figure 2**).
 - The tool drives tasks and meetings and gives visibility to the information and to progress.
 - A planned iteration will enable the data generated from a variety of sources to be automatically made visible within the relevant areas in Study Maestro.

Figure 2: Overview of PDL methodology.



Case studies

In thinking about the impact of the PDL we can refer to the three key areas highlighted earlier. In the area of patient demography and insights we partner with our Patient-Focused Development and Clinical Trial Diversity teams early in the protocol development process and specifically to identify areas of study design and burden. The PDL also leverages tools that provide an early indication of the patient burden from the study schedule of activities. This has enabled focused engagement in a timely manner to ensure that insights from patients are received in time to guide the study design or other elements of the study, such as informed consent language. Examples of this include a reduction in the number of endoscopic procedures over the duration of one study and the use of home nursing services to reduce the number of visits for another. Furthermore, we are exploring and investing in novel approaches linked to virtual reality and behavioural science approaches to uncover the motivators and challenges associated with patient enrolment in clinical trials.

For real-world data, we have leveraged electronic health records, claims data, and other sources to enable rapid and iterative review of study inclusion/exclusion criteria. The ability to focus on key eligibility criteria to understand the potential impact on recruitment of clinical trial participants has resulted in a dynamic and cross-functional review. Examples of the optimisation of inclusion/exclusion criteria have been as simple as an adjustment in age criteria for a study, yielding >15% more eligible participants, through to the removal of an exclusion criterion associated with prior treatment with a biologic, which yielded a 10% increase in eligible participants. Leveraging platform capabilities within these solutions has also enabled the identification of potential new sites for recruiting that were not previously considered in early feasibility assessments.

In the area of historical trial data and the competitive landscape, the PDL utilises a number of resources to inform our recruitment planning and modelling. We are moving towards the integration of these data sources to develop models that better predict and optimise our recruitment planning strategies and provide scenarios that are responsive to changes when the study is ongoing. Examples include supporting a team in GSK who developed a model to consider the impact of the COVID-19 pandemic and leading an effort to understand the impact of COVID-19 restrictions on other infectious diseases; we are now looking to develop these approaches further for other, non-COVID related factors.

In addition to specific areas of focus, some of which are outlined above, the PDL also provides value as a central resource that drives consistency in the way that data and analytics are leveraged during protocol design and study delivery planning. This ensures relevant and timely support from subject matter experts and has enabled sharing of best practices regarding the utility of specific service providers related to, for example, decentralised clinical trials approaches, electronic consent, and patient recruitment.

Conclusion and future areas of focus

Our mandated PDL, technology-enabled process workflow, and clear expectations and lines of accountability, have provided the framework for change. Moving forward, we see the importance of starting our conversations even earlier. Early planning underpins everything, and this starts with our medicine vision, our integrated evidence and clinical development plans, which shape our study concepts. We will continue to evolve our PDL process, technology, and analytics using agile methodology. As the framework is now established, we will be able to swap in or out different datasets and enhance our analytics. As new biomarkers emerge, and additional data sources become available, cutting-edge data analytics and technology advances will exponentially increase our predictive capability and ultimately match potential eligible patients to our clinical trials.

Whilst the TransCelerate Patient Protocol Engagement Toolkit is now routinely used during protocol development to embed patient perspectives in clinical trials,²⁰ there is untapped potential to co-create protocols with patients via interactive dialogue at scale. We have experimented with small-scale patient crowdsourcing to gain insights on our trial designs; explored various patient burden coefficient ratings and tools that evaluate the impact of procedures and assessments; and held simulations of study visits with patients.

Our focus is now also shifting towards the use of behavioural science.^{22,23} In a spirit of treating patients as clinical trial consumers, investigations are underway to gain deeper and comprehensive insights at scale (>300 patients rather than a handful). We are exploring novel technologies and patient sub-populations to understand better how the needs of different patient cohorts link to their engagement and motivation to be involved in a clinical trial; e.g. demography, media preferences, affluence, education, etc. Creating different patient profiles will inform our methods of engagement and interaction. Our ultimate desire is to co-create protocols with patients via novel approaches such as gamification to uncover the motivators and challenges associated with patient enrolment in clinical trials.

Another important factor is understanding how we create optionality for patients and sites. This links with our decentralised clinical trials strategy and how we assess which potential solution or technology will provide the greatest benefits. We will also continue to pay attention to cultural and change management support. Ensuring respectful challenge and data-derived conversations will be crucial for developing simple and innovative study designs, which will maximise potentially eligible patient populations and minimise the burden to patients. Our hope is that this will ultimately increase operational certainty and transform trial delivery.

References

1. Veeva. Where to in 2020? PharmaTimes magazine. 2020. Available at: http://www.pharmatimes.com/magazine/2020/march_2020/where_to_in_2020.
2. Singh G, Schulthess D, Hughes N, Vannieuwenhuysse B, Kalra D. Real world big data for clinical research and drug development. *Drug Discov Today*. 2018;23(3):652-660.
3. Spannheimer A. The growing value of RWE. IQVIA. 2020. Available at: <https://www.iqvia.com/library/white-papers/the-growing-value-of-rwe>
4. Liu R, Rizzo S, Whipple S, et al. Evaluating eligibility criteria of oncology trials using real-world data and AI. *Nature*. 2021;592(7855):629-633.
5. Fierce. Fierce innovation awards: Life sciences edition 2020. 2020. Available at: https://pages.questexnetwork.com/Life-Sciences-Innovation-Report-2020_Landing-Page.html?_ga=2.78925650.73433822.1620997659-1434647424.1620997659.
6. Fassbender, M. Sanofi partners with TriNetX to speed drug development timelines. 2018. Available at: <https://www.outsourcing-pharma.com/Article/2018/01/16/Sanofi-partners-with-TriNetX-to-speed-drug-development-timelines#:~:text=Sanofi%20has%20announced%20a%20partnership,accessible%20federated%20health%20research%20platform>.
7. Deloitte Centre for Health Solutions. Intelligent Clinical Trials. 2020. Available at: https://www2.deloitte.com/content/dam/insights/us/articles/22934_intelligent-clinical-trials/DI_Intelligent-clinical-trials.pdf.
8. Woo M. An AI boost for clinical trials. *Nature*. 2019. Available at: <https://www.nature.com/articles/d41586-019-02871-3>.
9. Woo M. Trial by artificial intelligence. *Nature*. 2019. Available at: <https://media.nature.com/original/magazine-assets/d41586-019-02871-3/d41586-019-02871-3.pdf>.
10. Mietsa E. AbbVie goes all-in on wearables and digital technologies. 2019. Available at: <https://www.clinicalleader.com/doc/abbvie-goes-all-in-on-wearables-and-digital-technologies-0003>.
11. Harvard Business Review. Competing in 2020: Winners and losers in the digital economy. 2017. Available at: <https://hbr.org/resources/pdfs/comm/microsoft/Competingin2020.pdf>.

12. Neuer A. Sharpening the focus on patient-centricity as pandemic continues. *Applied Clinical Trials*. 2021. Available at: <https://www.appliedclinicaltrialsonline.com/view/sharpening-the-focus-on-patient-centricity-as-pandemic-continues>
13. Singhal S, Kayyali B, Levin R, Greenberg Z. The next wave of healthcare innovation: The evolution of ecosystems. McKinsey & Company. 2020. Available at: <https://www.mckinsey.com/industries/healthcare-systems-and-services/our-insights/the-next-wave-of-healthcare-innovation-the-evolution-of-ecosystems>.
14. Mitchell EJ, Ahmed K, Breeman S, et al. It is unprecedented: trial management during the COVID-19 pandemic and beyond. *Trials*. 2020;21(1):784.
15. Tufts Center for the Study of Drug Development. Protocol complexity working group study. Final results report. December 23, 2020.
16. Getz KA, Stergiopoulos S, Short M, et al. The impact of protocol amendments on clinical trial performance and cost. *Ther Innov Regul Sci*. 2016;50(4):436-441.
17. Globe News Wire. Rising protocol design complexity is driving rapid growth in clinical trial data volume, according to Tufts Center for the Study of Drug Development. 2021. Available at: <http://www.globenewswire.com/en/news-release/2021/01/12/2157143/0/en/Rising-Protocol-Design-Complexity-Is-Driving-Rapid-Growth-in-Clinical-Trial-Data-Volume-According-to-Tufts-Center-for-the-Study-of-Drug-Development.html>.
18. TransCelerate. Modernizing clinical trial conduct. 2021. Available at: <https://www.transceleratebiopharmainc.com/initiatives/modernizing-clinical-trial-conduct/>.
19. Huang GD, Bull J, Johnston McKee K, et al. Clinical trials recruitment planning: A proposed framework from the Clinical Trials Transformation Initiative. *Contemp Clin Trials*. 2018;66:74-79.
20. TransCelerate. Planning for patient engagement. 2019. Available at: <https://www.transceleratebiopharmainc.com/ppet/planning-for-patient-engagement/>.
21. Jain NM, Culley A, Micheel CM, Osterman TJ, Levy MA. Learnings from precision clinical trial matching for oncology patients who received NGS testing. *JCO Clin Cancer Inform*. 2021;5:231-238.
22. VanEpps EM, Volpp KG, Halpern SD. A nudge toward participation: Improving clinical trial enrollment with behavioral economics. *Sci Transl Med*. 2016;8(348):348fs313.
23. Gruba M. Applying behavior change strategies to patient engagement in clinical research. *Clinical Researcher*. 2020: Available at: <https://acrpnnet.org/2020/04/14/applying-behavior-change-strategies-to-patient-engagement-in-clinical-research/>.