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How Decentralized Approaches Mitigate Pandemic-Driven Enrollment Challanges

An Analysis Comparing Subject Enrollment and Discontinuation in Decentralized and Traditional Clinical Trials from January-September 2020

REPORT

IN PARTNERSHIP WITH

Lokavant

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Introduction

The COVID-19 pandemic has had a transformative impact on the delivery of clinical trials. The implementation of social distancing, quarantines, and stay-at-home orders has resulted in unprecedented delays and disruptions to operations across the globe, and thousands of trials have been suspended or stopped in 20201. The pandemic has also served as an accelerant for the adoption of technology-based innovations that have steadily been gaining traction for years. Perhaps the most significant evolution in clinical trial design and delivery throughout 2020 and into 2021 has been the wide-spread adoption of technologies to facilitate decentralization of clinical trials via solutions like digital recruitment, virtual visits and eCOA captured via telehealth.

According to the Society for Clinical Data Management (SCDM), one of the primary risk areas associated with clinical trials has been the dependency on research staff being continuously and physically on-site. Simple deviations to staff schedules, such as challenges to daily commute or personal leave, can cause delays to data entry, and to site initiations and enrollments2. In 2020, COVID-19 has transformed these constant background risks into pressing global issues. Several studies have sought to understand the broad impact of COVID-19 on clinical trials, but few have shown how this impact has differed between traditional site-based trials and those employing decentralized approaches for trial data collection. Now, more than a year after initial quarantines and stay-at-home orders took effect, we are able to start to understand whether the application of decentralized methods has allowed certain clinical trials to overcome these challenges.

The analysis described is not intended to be a comprehensive assessment of the impact of decentralized approaches on clinical trial success. The authors selected two (2) trial performance metrics pertinent to clinical trial success and conducted the analysis with the goal of providing relevant information for industry, as research sponsors look to integrate lessons from 2020 into future clinical trial designs. Additional analyses will be conducted in the future to supplement the analysis described below to more comprehensively and holistically address how decentralized trials fared in other performance focus areas against traditionally designed trials in 2020.

Scope of Analysis and Methodology

To better understand the impact of decentralized approaches on clinical trial success during pandemic-driven shutdowns, THREAD and Lokavant conducted an analysis to understand how clinical trials delivered on the THREAD DCT Platform, and traditional clinical trials with traditional site-based patient visits, adapted to the pandemic over the first three quarters of 2020. This time period allowed for observation of pre-COVID performance in January and February, immediate response to widespread quarantine and shelter-in-place orders in March and April, and subsequent peri-COVID performance through September.

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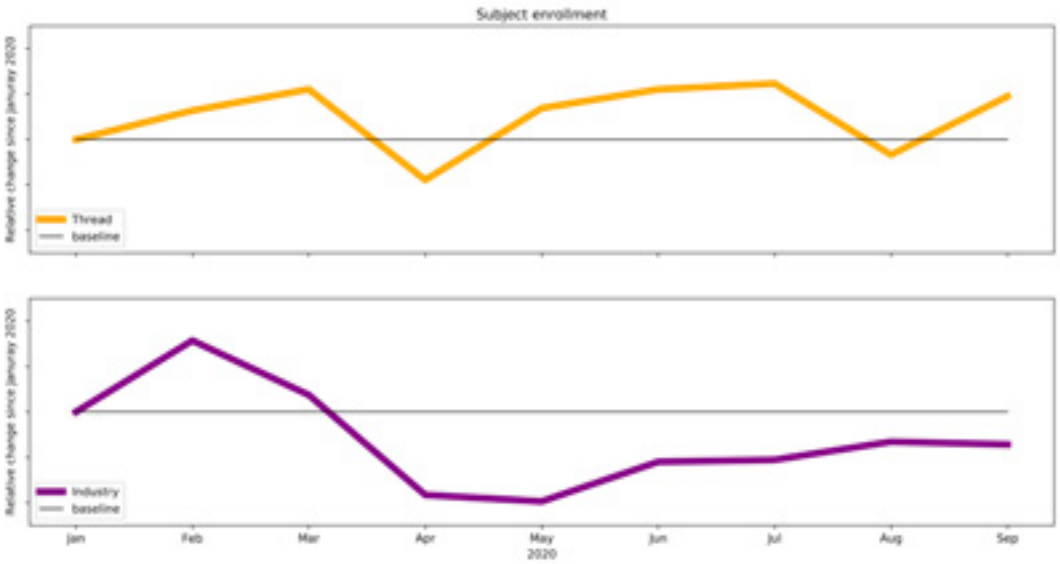
For the initial analysis, THREAD provided operational performance data from ongoing decentralized trials within the selected time window and two (2) metrics corresponding with available THREAD operational performance data were selected from Insight, Lokavant's clinical operations benchmarking solution: Subject Enrollment Rate and Subject Discontinuation Rate. The relevant Industry Benchmark, taking into account key parameters of the THREAD Data Set, was calculated utilizing Insight, which draws on comprehensive operational data on over 1,300 historical trials and near real-time data on on-going studies. To avoid any complications with direct comparison of absolute values across THREAD and Industry trial datasets, respective datasets were min/max normalized and results are shown relative to respective January reference points.

Both Data Sets comprise a mix of study phases, therapeutic areas, and geographies. The THREAD Data Set includes hybrid and fully decentralized trails, and one registry study.

Results

Subject Enrollment

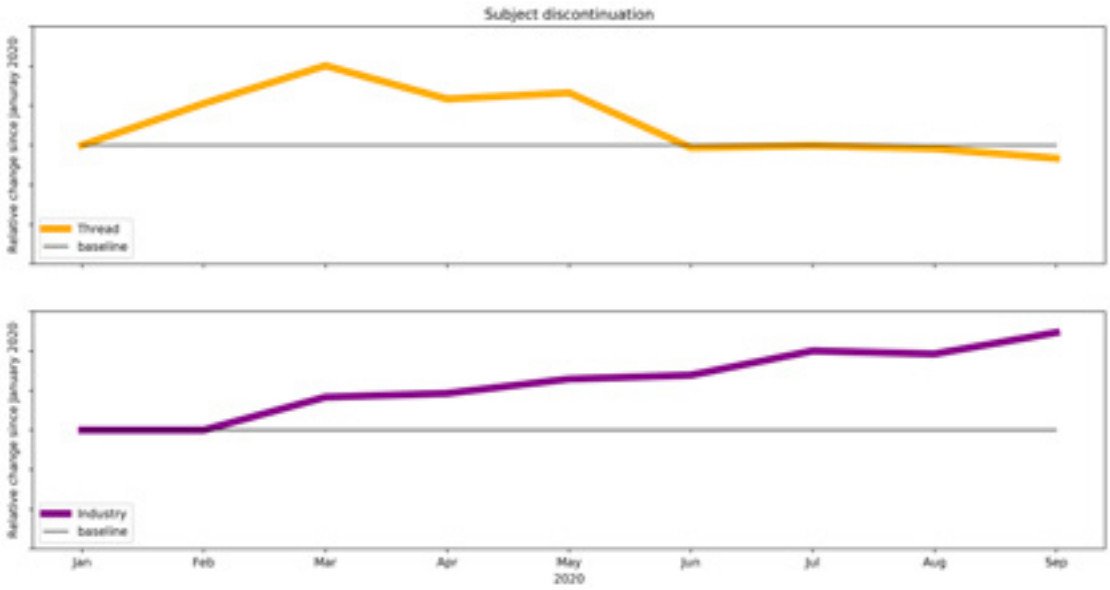


The analysis of subject recruitment demonstrates that, while trials in the THREAD Data Set observed a decline in enrollment relative to a January baseline in March, at the onset of widespread quarantine and shelter-in-place orders. Enrollment then rebounded between April and May. Additionally, recruitment for these trials continued to exceed the pre-COVID baseline value in five out of the six months from May to September. The Lokavant Industry Benchmark observed an earlier and steeper decline in subject recruitment from February to April. Enrollment improved from April to June but stabilized below its corresponding pre-COVID baseline value.

Recruitment for these trials continued to exceed the pre-COVID baseline value in five out of the six months May to September.

Subject Enrollment

The analysis of subject discontinuation similarly indicates that dropout rates for both decentralized trials and traditional site-based trials were significantly impacted at the onset of global quarantine and shelter-in-place orders. However, trials in the THREAD Data Set demonstrated a return to pre-lockdown subject discontinuation by June of 2020 while the Industry Benchmark presents a continuing rise in discontinuation through the end of September 2020.



The analyses presented indicate that decentralized clinical trials (DCTs) were able to return to their pre-COVID enrollment rates and discontinuation rates within 2-4 months of widespread global lockdowns in February and March of 2020. The analyses also indicate that traditionally designed clinical trials were both unable to return to pre-COVID enrollment rates and were continuing to see increasing discontinuation rates more than 6 months after lockdown measures came into effect. The THREAD Data Set contained studies using a range of decentralized approaches (from hybrid to fully decentralized), so how can we begin to explain how a decentralized design had such a profound impact on patient recruitment and retention?

Decentralized clinical trials were able to return to their pre-COVID enrollment and discontinuation rates within 2-4 months of widespread global lockdowns.

The Value of Decentralized Approaches

Virtual visits cannot replace in-person site visits for every study, but they can be used in place of some in-person visits (a hybriddecentralized study) and create a more flexible and patient-centric model to drive improved patient engagement. Some tangible ways virtual visits and remote patient monitoring technologies can help and have helped sponsors, CROs and clinical trial suppliers keep clinical trials moving forward both during and beyond the pandemic are:

Recruit candidates without needing to visit a site. Qualifying participants is an activity that can take place with home health assessments and a telehealth call to capture relevant information.

Minimize or eliminate travel for participants. Getting to and from frequent research site visits can be challenging, even under normal circumstances. Offering virtual visits and risk-based quality management is even more essential in a pandemic environment as it allows the study to continue even under strict quarantine requirements.

Maintain enthusiasm and trial momentum even amidst strict lockdowns. Telehealth virtual visits enable those conducting the study to easily communicate and share information with participants, stay in contact with patients and provide an opportunity to collect study data during a virtual visit from eCOA, CRFs, sensors, eDiaries and other assessments.

Strengthen relationships between researchers and patients. Trust-based relationships can take a long time to build, especially if contact is limited because of lockdown requirements. Telehealth enables those patient visits to continue with multiple short encounters, helping create a stronger personal relationship that drives retention. Ultimately, additional analyses need to be performed to understand how each of these value drivers impacted recruitment and retention outcomes for the decentralized trials in the THREAD Data Set, but perhaps the most important factor is that each of the trials had been designed with some form of decentralized technology embedded in the study. As global lockdowns started to come into effect in the early part of 2020, researchers running decentralized trials were able to increase the amount of decentralization in their study, allowing these studies to continue to experience the benefits described above. For researchers overseeing traditionally designed trials, implementing decentralized technologies was much more challenging because the protocol had not been designed with these technologies in mind; as a result, they were not in a position to effectively pivot.

Conclusions & Recommendations for Industry

The maturation of decentralized clinical trial features like telehealth, eConsent and eCOA means that going forward, technologybased solutions can and should be deployed in clinical trials routinely to allow for maximum operational flexibility. Even if the scope of these technology-enabled features is initially limited, inclusion at the outset ensures the ability to fluidly change data capture strategy mid-study if needed. This will be particularly important for trials initiated well into 2021 if COVID-19 diagnoses continue to rise globally and some countries re-apply certain lockdown measures. But, decentralization is not just a pandemic mitigation strategy. The technologies used to enable decentralized approaches have broad value for clinical research outside of a pandemic context.

DCT features should be deployed in clinical trials routinely to allow for maximized operational flexibility. Even if theinitial features scope is limited, inclusion at the outset ensures the ability to fluidly change data capture strategy mid-study if needed.

The pandemic has been a forcing mechanism for the adoption of decentralized trial technologies across the spectrum of trial stakeholders. Patients have become accustomed to interacting with their physician through telehealth, and physicians have adapted to engaging with data reported by patients, in-home healthcare providers (HCPs) and wearables. This forced adoption affords industry the opportunity to capitalize on this rapid learning in the healthcare ecosystem and design clinical trials that leverage these newly learned skills, resulting in greater patient centricity, while limiting site burden. Furthermore, by benchmarking the performance of hybrid decentralized trials in real time, practitioners can employ much needed technology with a full transparency into its impact on trial performance overall.

To learn more about protecting trial enrollment with DCT approaches, visit: THREADresearch.com

The Value of Advanced Benchmarking in DCT

Understanding the impact of decentralized approaches in clinical trials is a significant challenge as longitudinal data for clinical trial operations is just starting to become accessible in sufficient quantity for analysis. When the operational data is available, it is of limited use unless the appropriate benchmarks can be established to quantify impact. THREAD and Lokavant partnered together for this analysis to address this challenge.

As showcased in the above analysis, advanced benchmarking leverages comprehensive and up- to-date (near real-time) operational data from similar trials. As clinical trials evolve by by including more decentralized methods, the data available for this analysis is set to follow. As we continue to gather analytics data for decentralized models, additional analysis will become available. On the ground, practitioners can utilize advanced benchmarks not only to gain a snapshot of relative performance, but also to plan for studies effectively, manage trials proactively, and predict issues before they occur.

Below are some ways advanced benchmarking can support trial planning and execution:

Trial Planning

Enrollment forecasting: Forecast enrollment at all levels of granularity to gain unique foresight into subject recruitment at the site, country, region, and study level. Compare forecasting across sites and use real time data to adjust scenarios instantaneously.

Performance goal / risk threshold setting: Determine the right risk indicators and thresholds based on historical performance of the most relevant studies. Set thresholds across a comprehensive set of KRIs and/or focus on the metrics that matter most based on historical evidence.

Trial Execution

Predictive analytics: Use historical data on similar, or “benchmark” trials to deliver predictive analytics from First Patient First Visit, instead of waiting for your individual study to generate sufficient data to provide insight. Leverage the benchmark data and predictive models to predict issues before they happen.

Real-time performance benchmarking: Leverage benchmarks to understand exactly how your study is performing relative to an appropriate peer set in real time. Consider current issues impacting your study and similar studies, such as the rapidly changing COVID-19 environment, and measure the impact of mitigation strategies, such as the adoption of new data collection approaches.

Advanced risk-based monitoring: Put historical and real-time benchmarks to work to deliver advanced risk-based oversight to your studies. Focus not only on the KRIs that define quality issues, but the key risks that drive time and cost explicitly too.

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About THREAD

THREAD is a leading provider of a proprietary, decentralized research platform and suite of supporting services used by biopharma, CROs and life science organizations to remotely capture data from participants and sites during, in-between and in lieu of in-clinic visits. THREAD's platform and supporting services are helping customers to reduce study launch timelines, reduce study budgets with virtual visits and bring studies from the clinic to patients' homes. THREAD provides key platform features such as eConsent, eCOA/ePRO, sensors, reminders and telehealth virtual visits to support remote data capture, hybrid virtual studies and fully decentralized studies in key therapeutic areas. In 2019, THREAD was acquired by strategic health care investors Water Street Healthcare Partners and JLL Partners.

About Lokavant

Lokavant enables next-generation clinical trials through data-driven products, including Lokavant Insight, a clinical operations benchmarking tool, and its flagship product, Lokavant Oversight, a tech-enabled risk-based monitoring solution. Backed by over 1,300 de-identified clincal trials, Lokavant Oversight aggregates and delivers real-time data from disparate trial data sources, predicts issues during clinical development to mitigate trial risks, and empowers monitoring teams by visualizing critical study data. Lokavant Insight empowers clinical teams to benchmark clinical trial performance and analyze vital indicators of trial success and failure. For more information, please visit www.lokavant.com.

Citations

[1]The Lancet; https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31787-6/fulltext#coronavirus-linkback-header

[2]https://scdm.org/covid19-and-clinical-data/#1585038586556-746e3e2d-c717

