

Modernizing Clinical Trials: Digital Technologies and the Cloud



Developing and bringing a new drug to market is costly, with estimates ranging from \$650 million to \$2.9 billion, a 145 percent increase over the last ten years.¹ Execution of clinical trials is historically the most expensive part of the process, accounting for around two-thirds of total R&D costs², and taking upwards of 10 to 15 years to complete. Factors contributing to these high costs include enrollment of patient cohorts that are not optimal for the trial, unproductive trial sites, low patient engagement and difficulty in sharing and analyzing resulting data.

The problems begin with the limitations of sponsors' ability to identify patients in the active disease state and determine the best sites to enroll them. By one calculation, around 30% of clinical trial sites never enroll a subject.³ These unproductive trial sites delay data generation and cause a large amount of wasted effort, which contributes to the high cost of drug development.

Similarly, once a trial is underway, sponsors need agile tools to incorporate the use of mobile technologies, such as wearables and mobile devices, which could generate a wealth of data while promoting better patient engagement. To compound matters, the difficulty associated with sharing, aggregating and analyzing trial data can limit the speed and efficiency of studies at each step in the process.

The efficient generation of high-quality clinical trial data is critical to success for new therapeutics. Yet,



companies continue to struggle with the challenges of enrollment, engagement and data sharing. Against this backdrop, pioneering companies are turning to the AWS Cloud to modernize their clinical trials with the analytic capability to optimize studies by predicting the right patients to enroll, securely coordinating and sharing data and incorporating regulated digital technologies.

HOW SCALABLE CAPACITY CAN STREAMLINE TRIAL DEVELOPMENT

Companies such as Bristol-Myers Squibb are performing *in silico* clinical trial simulations using cloud-based high-performance computing (HPC) to help them optimize the design of early-phase trials. Bristol-Myers was able to reduce total analysis time by 98% by running simulations in support of a pediatric phase 1 study on the AWS Cloud instead of their on-premises system.⁴ It can be challenging to scale the computational power necessary to run trial simulations on-site, as it ties up resources and causes bottlenecks for other researchers. However, virtually unlimited HPC resources can be accessed on-demand in the AWS Cloud.

“Because of the compute capacity that we’re able to derive from AWS, we can now hand out dedicated

¹ <https://www.policymed.com/2014/12/a-tough-road-cost-to-develop-one-new-drug-is-26-billion-approval-rate-for-drugs-entering-clinical-de.html>

² MEASURING THE GLOBAL BIOMEDICAL PULSE The Biopharmaceutical Investment & Competitiveness (BCI) Survey – 2015. Available at: <https://www.pugatch-consilium.com/reports/BCI%202015%20-%20Measuring%20the%20Biomedical%20Pulse.pdf>. (Accessed: 5th September 2018)

³ Non-Enrolling Sites Come at a Price | Geeks Talk Clinical. Available at: <https://blog.mdsol.com/non-enrolling-sites-come-at-a-price>. (Accessed: 5th September 2018)

⁴ AWS Case Study: Bristol-Myers Squibb. Amazon Web Services, Inc. Available at: <https://aws.amazon.com/solutions/case-studies/bristol-myers-squibb/>. (Accessed: 11th December 2018)

compute environments to our PK scientists. Instead of being able to run hundreds, they can now run thousands of clinical trials to prepare these optimized design runs,” Russell Towell, a Senior Solutions Specialist at Bristol-Myers Squibb, said.⁵ By using these cloud-based trial simulations, they were able to reduce the number of subjects by one-third, and reduce the length of the study by almost a year.

Utilization of highly scalable, on-demand cloud-based computation power for in silico clinical trial simulations can help in the upfront optimization of these trials, decreasing patient and trial site burden and potentially speeding time to completion.

OPTIMIZING PATIENT AND TRIAL SITE SELECTION WITH ADVANCED ANALYTICS

The average clinical development program takes 10 to 15 years to complete, in part due to protocol

complexity and patient recruitment and retention.⁶ The current process of protocol design involves a labor-intensive process by which researchers use benchmark studies and historical data to predict the protocol feasibility based on its projected rate of recruitment, which are often immediately outdated given an ever-evolving competitive landscape.

To aid in these efforts, companies are looking to artificial intelligence and machine learning (AI/ML) to help expedite and optimize patient recruitment. For example, Knowledgent has built an Intelligent Trial Planning (ITP) application on the AWS Cloud that uses AI/ML to predict the feasibility of clinical trials and forecast recruitment timelines. The ITP platform enables study design teams at pharma organizations to run prediction analysis in minutes, not weeks,

5 *Bristol-Myers Squibb on AWS - Customer Success Story*. (2013). <https://www.youtube.com/watch?v=Vi96WrxASgo>

6 *How long a new drug takes to go through clinical trials*. *Cancer Research UK* (2014). Available at: <https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/how-clinical-trials-are-planned-and-organised/how-long-it-takes-for-a-new-drug-to-go-through-clinical-trials>. (Accessed: 11th December 2018)





allowing them to iterate faster and more frequently. Powered by machine learning, real-time scenario planning helps to facilitate smarter trial planning by enabling researchers to determine the most optimal sites, countries and/or protocol combinations.

“Just by eliminating poor performing sites, trial teams have the potential to reduce their trial cost by 20%. And by making data-driven decisions that are significantly more accurate, we can plan and execute clinical trials faster, leading to hundreds of thousands in cost savings for every month saved in a trial,” Ari Yacobi, Chief Data Scientist at Knowledgent, said.

To accomplish this type of predictive power large amounts of data needs to be securely stored and quickly shared, a benefit of utilizing a cloud-based platform. The ITP application leverages the secure storage capacity of AWS, as well as other AWS services, to clean, aggregate and integrate the data and ensure that data scientists have the ability to query it. The use of the highly scalable cloud-based computational power and advanced machine learning algorithms on AWS Cloud can help pharma companies to efficiently and effectively predict and plan clinical trial design and recruitment, decreasing overall clinical trial timelines.

UTILIZING HISTORICAL CLINICAL TRIAL PATIENT DATA TO INFORM CLINICAL DEVELOPMENT

Computational power and AI/ML is only one part of the puzzle, though. These resources can only yield meaningful insights when turned on extensive, timely and accurate data, and when informed by a thorough understanding of the natural history of a disease. Pharma companies have looked to their prior experience, medical literature and emerging real-world data (RWD) to meet this need.

However, none of these resources are perfect. Published literature is static and covers just a few data elements about one trial at a time. RWD is far more voluminous but can be undermined by differences between patient populations, unsystematic data collection and a limited geographic coverage. Finally, the sponsor’s own historical clinical trial data is inherently limited to the scope of its earlier studies and is laborious to standardize for meta-analysis. All of these shortcomings hinder researchers’ ability to make data-driven decisions.

Recognizing the need for fit-for-purpose data address these challenges, Medidata has made available a pool



of standardized clinical data covering thousands of trials from multiple sponsors that enrolled millions of patients in all parts of the world. Medidata has stored the data on the AWS Cloud and through their Synthetic Control Database™ is providing a unique patient data source that is available, actionable and consumable to improve decision making in trials from design through submission.

Because Medidata's database is built on the AWS Cloud, researchers can interact with the Synthetic Control Database via a highly customizable and flexible visualization tool built entirely with AWS services. Among the many benefits of using the Synthetic Control Database, drug sponsors can more precisely calculate sample sizes, improve statistical accuracy, and understand the natural history of disease and background rates of serious adverse events. Companies that use the resource to improve decision-making stand to increase accuracy, reduce costs and shorten timelines in clinical trials.

UNLOCKING THE POTENTIAL OF MOBILE TECHNOLOGIES

Clinical trial sponsors have traditionally generated most of their data when patients visited trial sites, but have lacked the ability to continually assess the effect of their therapies on people as they went about their everyday lives. The emergence of smartphones, wearables, ingestibles and other devices has given sponsors new capabilities, enabling them to see a fuller picture of the safety and efficacy of their

products. Subsequently, these mobile technologies rely on the cloud for secure and reliable transfer of data to trial sponsors.

As the Clinical Trials Transformation Initiative (CTTI) noted in recent recommendations,⁷ systems that ensure the authenticity, integrity and confidentiality of data over its entire lifecycle are essential to the effective adoption of mobile technologies. These systems must pull in data from multiple sources and make it available to authorized users, without compromising security.

AWS IoT services like AWS IoT Analytics and AWS IoT Device Management excel at connecting such physical devices to the cloud for secure data collection, management and analysis. Teams across pharma and healthcare companies want to incorporate wearables or other devices into their trials and in some cases are already pulling IoT and mobile device data into secure cloud environments for analysis. For example, with the support of uMotif software on the AWS Cloud, Manchester University in the United Kingdom ran a research program looking at the effect weather had on people suffering from rheumatoid arthritis and chronic pain. According to uMotif CEO Bruce Hellman, 13,500 patient participants used the app on their tablets or smartphones, provided 38 million data points and

⁷ CTTI Recommendations: Advancing the Use of Mobile Technologies for Data Capture & Improved Clinical Trials. Available at: <https://www.ctti-clinicaltrials.org/sites/www.ctti-clinicaltrials.org/files/mobile-devices-recommendations.pdf#Pg2Ln13>. (Accessed: 7th September 2018)

“demonstrated that we could successfully support large-scale medical studies with our AWS solution.”⁸

Adoption of mobile devices and accompanying cloud-based systems will improve the management and monitoring of trials. Devices can securely stream data to cloud environments, equipping sponsors to rapidly glean new insights into the safety and efficacy of their drugs. Mobile devices can also enable remote communication, reducing the need for patients to visit study sites and decreasing both the cost of clinical trials and the burdens they place on participants.

THE FOUNDATION OF A NEW ERA FOR CLINICAL TRIALS

Cloud-powered initiatives at Bristol-Myers Squibb, uMotif, Medidata and other companies are modernizing clinical trials, resulting in studies that are faster, cheaper and less burdensome for patients. Their utilization of the cloud will upend the traditional clinical trial model and streamline patient enrollment, patient engagement and data collation.

⁸ Hellman, B. uMotif Case Study – Amazon Web Services (AWS). Amazon Web Services, Inc. Available at: <https://aws.amazon.com/solutions/case-studies/uMotif/>. (Accessed: 11th December 2018)

“My prediction is that clinical trials in 10 years’ time will be hard for us to recognize. Increasingly they will occur at patient homes or at their private doctors. Patients may potentially wear their sensor devices, flash pictures of their lesions from their cell phones, submit patient reported outcomes on their tablet computers, perhaps even receive their study drugs by drone,” Leonard Sacks, M.D., of the FDA’s Office of Medical Policy, said in a presentation on electronic technology in clinical trials.⁹

The coming era of virtual and otherwise technology-enabled clinical trials will require highly-scalable, secure and compliant services to fulfil its potential. Every time a patient submits data from home or a healthcare professional provides remote reassurance to a participant, the cloud will be working in the background. The cloud offers the ability to utilize powerful computation, as well as ever-evolving machine learning intelligence, to continue to drive innovations that will enable higher-quality data from clinical trials and accelerated delivery of drugs to market. ●

⁹ Electronic Technology in Clinical Trials. Available at: <https://www.fda.gov/downloads/drugs/newsevents/ucm441299.pdf>. (Accessed: 11th December 2018)

For over 12 years, Amazon Web Services has been the world’s most comprehensive and broadly adopted cloud platform. AWS offers over 125 fully featured services for compute, storage, databases, networking, analytics, robotics, machine learning and artificial intelligence (AI), Internet of Things (IoT), mobile, security, hybrid, virtual and augmented reality (VR and AR), media, and application development, deployment, and management from 60 Availability Zones (AZs) within 20 geographic regions, spanning the U.S., Australia, Brazil, Canada, China, France, Germany, India, Ireland, Japan, Korea, Singapore, Sweden, and the UK. AWS services are trusted by millions of active customers around the world—including the fastest-growing startups, largest enterprises, and leading government agencies—to power their infrastructure, make them more agile, and lower costs.

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