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THE POWER OF DIGITAL TECHNOLOGIES IN TRANSFORMING CLINICAL TRIALS

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Shveta Bakshi, Director, Axtria Inc.
Nidhi Jolly, Senior Manager, Axtria Inc.

INTRODUCTION

Pharmaceutical companies are increasingly focusing their research and development (R&D) efforts on niche markets, particularly treatments for rare diseases and personalized medicine. They are targeting patient subsets with particular genetic biomarkers, thus segmenting broader disease categories into rarer disease genotypes. This focus indicates that drugs are becoming more complex, as can be seen with the gene and cell therapy products that are entering the market.[1] Additionally, regulators and payers are expecting clinical trials to demonstrate not only efficacy and safety but also improved patient outcomes. As a result of these market developments, clinical trial design and execution has become more complex.

While the pharmaceutical industry has progressed over the years to keep pace with shifts in healthcare, the clinical trial process still needs to evolve, particularly in terms of the drug development timeline, high R&D costs, and risk of failure. It takes an average of ten years for a new drug to come to market, and the average cost to research and develop each successful drug is high, estimated at $2.6 billion.[2] Furthermore, only about one in ten drugs that enter clinical trials receive Food and Drug Administration (FDA) approval. Inability to demonstrate efficacy or safety, flawed study design, participant drop-outs, and unsuccessful recruitment have contributed to the low success rate of clinical trials.[3]

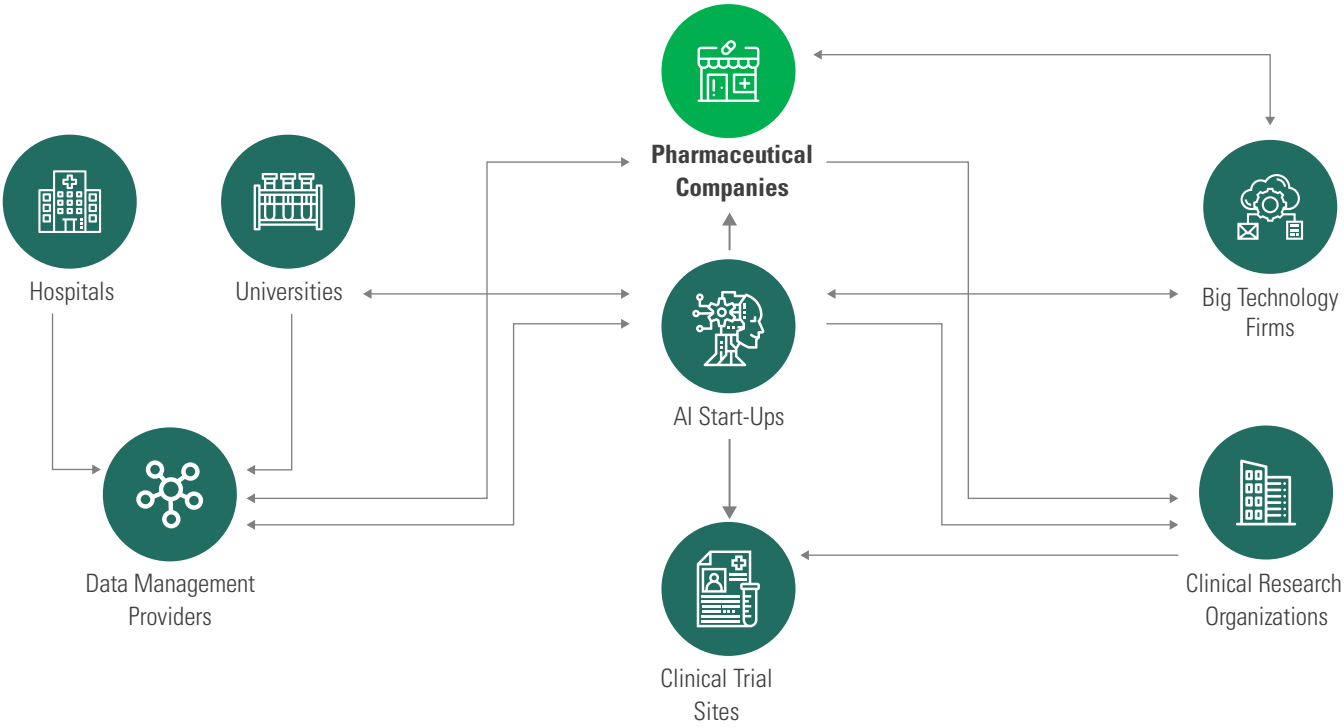
However, there are indications that practices are slowly evolving. As the world advances to a more digitalized era, clinical trials are transforming through the adoption of new technologies to drive superior outcomes, reduce costs and development cycles, and enhance stakeholders' (e.g., patients, investigators, sponsors, etc.) interactions. Digital technologies, such as artificial intelligence (AI), wearable and mobile technologies, and advanced analytics, offer significant opportunities to disrupt the pharmaceutical business operating models and improve the clinical trial process in several ways. This includes targeted recruitment of trial participants, identification of promising study sites, making efficient use of massive new data sets, and supporting early decision-making with increasingly powerful advanced analytics models. Furthermore, the pharmaceutical industry is laying greater focus on patient engagement and understanding the patient experience throughout the drug development process to improve clinical outcomes. However, unless the pharmaceutical industry adopts a holistic and patient-centric approach to transform clinical trials digitally, the coming times will continue the slow trend of moving from analog to digital processes.

To take an in-depth look at technology intervention in increasing speed, scale, efficiency, and effectiveness of clinical trials, the objective of this report is to:

- Provide an overview of the evolving clinical trials ecosystem
- Explore how digital technologies can create value across the various stages of the clinical trial process (from trial design to execution to closeout)
- Identify the role of data analytics to support early decision-making and improve R&D productivity

THE CHANGING CLINICAL TRIAL ECOSYSTEM

FIGURE 1: THE NEW CLINICAL TRIAL ECOSYSTEM



Source: HIT Consultant[4]

The clinical trial ecosystem is evolving with the emergence of digital technologies. Several players, such as AI start-ups, big technology firms, and data management providers, are now a part of the ecosystem that was previously exclusive to pharmaceutical companies and clinical research organizations (CROs).

Pharmaceutical companies are increasingly partnering with CROs that have invested in data science skills as they provide access not only to specialized advanced analytics expertise but also to a wide range of potential trial participants. Several niche AI start-ups with these skills have also entered the field by partnering or contracting with pharmaceutical companies to develop new methods of obtaining, tracking relevant clinical and socioeconomic data, and using deep learning and advanced analytics models to create simulations for patient interface improvement.

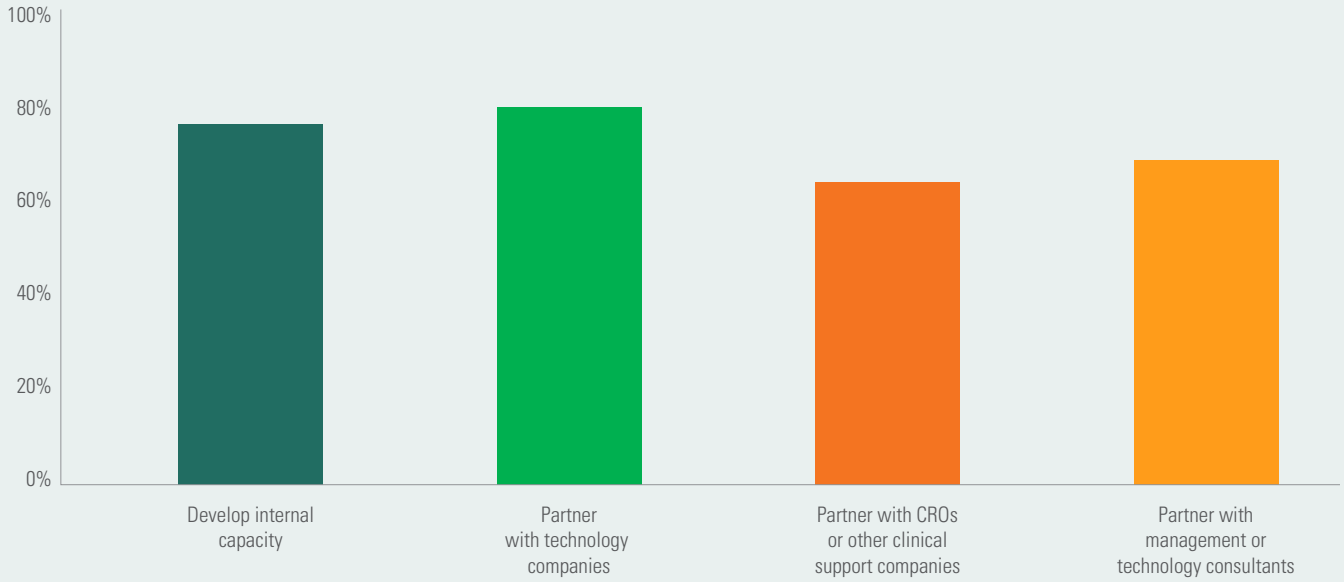
In most cases, the AI start-ups work directly with the pharmaceutical company sponsoring the trial and optimize it using their own de-identified data (gathered directly from hospitals and universities), and in several cases additional clinical trial data from the pharmaceutical company. Subsequently, they partner with the assigned CRO to implement the trial. In addition, data management providers focusing on extracting and de-identifying data are entering the ecosystem as a link between AI start-ups and data providers (such as hospitals, universities, and pharmaceutical companies).

Big technology firms are an integral part of the clinical trial ecosystem, and pharmaceutical companies are partnering with these players for initiatives converging advanced data science, medical knowledge, and technology. For example, Amazon has launched Comprehend Medical, a natural language processing (NLP) service that uses machine learning (ML) to extract relevant medical information (such as medical condition and medication regimen) from unstructured text (such as doctors' notes, clinical trial reports, and patient health records). Insights gained from this data can help pharmaceutical companies recruit patients for the appropriate clinical trial in a timely and cost-effective way.[5]

According to a 2019 survey (conducted among executives, managers, and professionals in biopharma and medical device development companies) by ICON, a global CRO, more than 55% of survey respondents claimed they were partnering with technology companies, making it the number-one partner choice.[5]

FIGURE 2: WHAT STRATEGIES ARE YOU PURSUING TO IMPLEMENT DIGITAL TECHNOLOGIES?

317 Number of Qualified Responses
Breakdown of responses:



THE DIGITAL REVOLUTION OF CLINICAL TRIALS

Pharmaceutical industry stakeholders (such as universities, CROs, and pharmaceutical companies) are increasingly recognizing the potential of digital technologies to transform the clinical trial process. Furthermore, regulatory agencies are showing greater interest in the development of digital technologies to ensure that the data acquired in clinical trials is collected systematically and rigorously, and with a focus on providing real benefits to patients (while not compromising privacy or leading to other ethical problems). With these developments, adjustments to traditional clinical trial practices have become necessary, compelling pharmaceutical companies and their trusted partners to adapt to the changing needs.

Below is a description of innovative solutions that have the potential to make the various stages of the clinical trial process more streamlined and patient-centric:

IMPROVING CLINICAL STUDY DESIGN

Adaptive Clinical Trials: The pharmaceutical industry has started recognizing that a classically structured clinical trial does not provide enough flexibility to utilize the continuously emerging data that is produced as the trial progresses. Adaptive designs are increasingly being considered in planning clinical trials as they can facilitate flexibility and efficient use of resources such as time and money. By constantly calibrating mid-course assessment of a clinical trial's performance, adaptive designs permit course corrections that can lead to improved results.[6] A study conducted by the CRO, ICON, indicates that the use of adaptive trials across portfolios, as encouraged by regulatory agencies in both Europe and the US, could reduce trial costs by up to 25%.[7] In 2019, about 80% of Amgen Inc.'s (a US-based biopharmaceutical company) clinical trial designs were adaptive.[6]

Improving Protocol Designs: Several technology start-ups are working towards making it easier for pharmaceutical companies to improve protocol design and study execution. For example, Protocols.io is an open access repository for scientific methods and protocols that allows clinical trial investigators to easily access proven methods for use in their studies. Another start-up, Trials.ai, is leveraging AI to analyze large sets of genomic data, journal articles, past clinical studies, and other forms of research to determine appropriate study designs for pharmaceutical companies.[8]

ADVANCING PATIENT RECRUITMENT

Patient Recruitment via Social Media: For a more targeted approach to finding patients, many pharmaceutical companies are recruiting patients for clinical trials through social media, rather than relying on trial sites to drive recruitment. For example, for its first entirely virtual trial on migraine, Amgen leveraged social media to recruit and enroll 70 patients with the support of Amgen Tweets and a migraine blog on Facebook.[9]

Genetic Screening to Identify Target Population: Genetic screening is being used in some trials to identify and select population subsets with specific biomarkers known to influence drug outcomes. As the availability of biomarkers increases, the screening will improve, and a larger number of patients will be screened faster. Developments in genetic screening will also establish genetic differences between both cultures and individuals to determine the type of patients that will most benefit from the drug in question. In November 2018, The US FDA granted accelerated approval to Vitrakvi (larotrectinib). Developed by Loxo Oncology and Bayer, Vitrakvi is indicated for the treatment of adult and pediatric patients with solid tumors that have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion. This initial indication was approved based on clinical trials that included only 55 patients. Due to the small patient cohort, the FDA declared that continued approval might be contingent upon verification of clinical outcomes in further confirmatory trials. The approval of this therapy reflects advances in the use of biomarkers to guide drug development and the more targeted delivery of medicine.[10]

Synthetic Control Arm (SCA) to Improve Trial Efficiency and Reduce Costs: The large number of participants needed for trials and participants' fears of being assigned a placebo (an inactive drug or treatment used in a clinical trial), can be reduced by using an innovative approach called synthetic control arms. A synthetic control arm collects real-world data (RWD) from previous clinical trials, electronic health records (EHRs), administrative claims data, disease registries, patient-generated data from fitness trackers or home medical

The US-based pharmaceutical company, BristolMeyers Squibb, created an innovative digital patient engagement platform, Study Connect, for patients, caregivers, and healthcare providers to find and connect with new studies, by facilitating trial awareness, engagement, and participation. Study Connect has several features, including a referral program, condition screener, educational material, and a call center. The technology platform lets patients create an account, search for studies, save studies, answer pre-screener questionnaires, and be a part of a social media community. [9]

equipment, and others. The data is then used to model or simulate the expected results comparing them with those on the clinical trial. A synthetic control arm can increase efficiency, reduce delays, reduce trial costs, and speed life-saving therapies to market by reducing or eliminating the need to enroll control participants. While there has been limited use of synthetic control arms, they have already been successfully used in regulatory decision-making.

Improving the Clinical Trial Enrollment Process: Some technology start-ups are assisting pharmaceutical companies with patient enrollment by determining if patients meet inclusion criteria. Other start-ups such as PatientWing, an online recruitment platform, allow researchers and pharmaceutical companies to easily create mobile-friendly, SEO optimized landing pages and embeddable forms that makes the application process simpler for patients.[8]

E-consent to Seek and Document Patient Consent: In its infancy, e-consent is used to seek and document patient consent using electronic methods (such as images, video, audio, and other resources to empower patients to make informed decisions). The objective of using this technology is to make the informed consent process simpler and less technical for patients. Janssen Pharmaceutical is working towards implementing eConsent globally, as well as across all its clinical studies, following the completion of its pilot studies in 2018.[11]

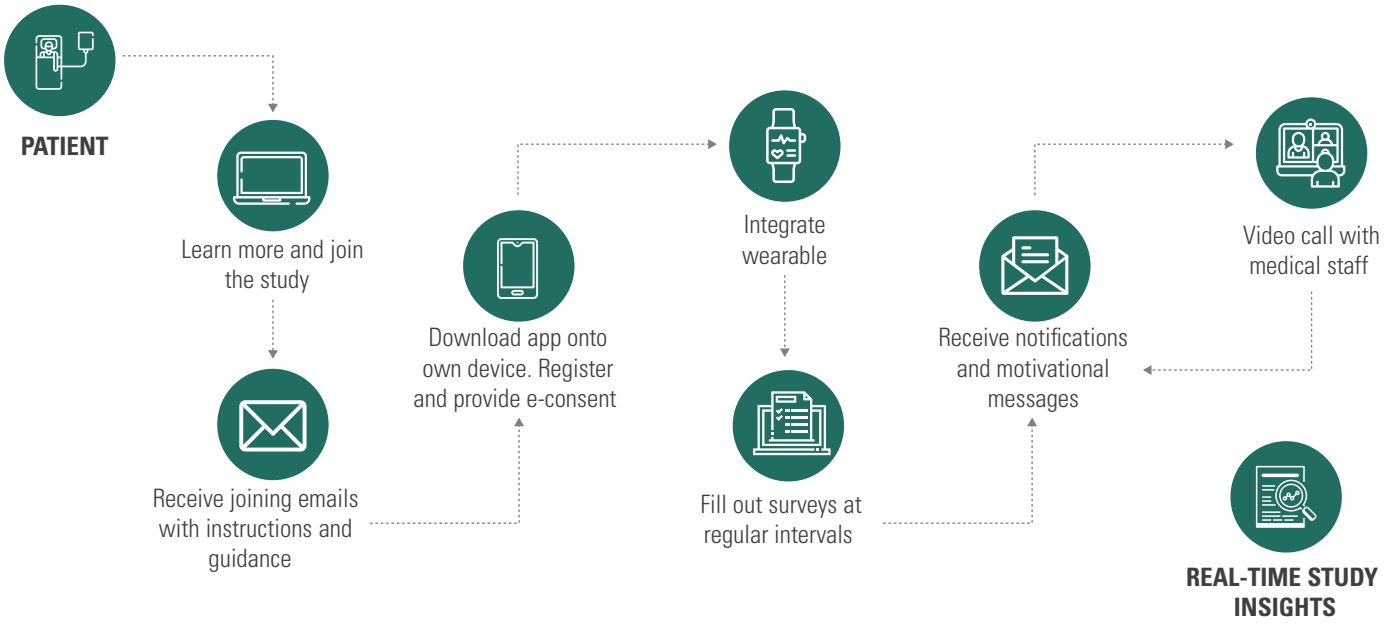
Expanding Access to Clinical Trials through Remote Monitoring: With advances in technology such as remote monitoring or remote delivery of service (includes wearable devices, bring your own device, and chatbots), trials are increasingly shifting from large centers and closer to patients. This makes patient participation easier and more convenient, while sponsors benefit from an increased pool of patients who are more likely to stay in a trial. The technology for remote monitoring of blood glucose, blood pressure, and mobility tracking already exists and has been put on a firmer footing with the launch of digital therapeutics. Remote monitoring (via phone or video calls) of ongoing or upcoming clinical trials is currently being encouraged by regulatory agencies in Europe, UK, and the US to ensure patient safety during the coronavirus pandemic.[12]

IMPROVING CLINICAL TRIAL RETENTION

Increasing Patient Adherence: Several start-ups are focusing on improving medication adherence with smart pillboxes or pill bottles, virtual pillboxes, and behavioral economics-based incentives. AiCure, an advanced data analytics company, is also working towards improving medication adherence with digital forms of directly observed therapy (DOT), which involves a person or an AI application observing patients take their medication.[8]

Reducing Patient Drop-out: Efforts are also being made for clinical trial drop-out prevention and participant engagement. For example, Brite Health, a company that provides an AI platform for clinical trials, is working to reduce clinical trial drop-out. The company's product analyzes structured and unstructured patient data and sends personalized messages and notifications to patients to continue participating in the trial. The product also predicts the patients that are most likely to drop out and notifies staff members, so they can intervene.[8]

FIGURE 3: DIGITALLY ENABLING THE PATIENT JOURNEY DURING THE CLINICAL TRIAL PROCESS



Source: Pharmaphorum[13]

Sponsors involved in digital trials cite the following key benefits of digitalization[14]

- Cost-reduction by 50% per participant in comparison to current onsite clinical trials
- Increased recruitment and diversification by making trial participation convenient
- Increased data collection on participants, since they can be monitored over longer periods (up to 75 times more)
- Improved data quality based on a participant's natural environment rather than data collected onsite

CLINICAL TRIAL DATA ANALYTICS

Several of the innovative approaches that are being adopted by pharmaceutical companies to efficiently design and conduct clinical trials rely on vast volumes of data collected from a variety of disparate sources. These data sources include current and past clinical trials, real-world evidence (RWE) from registries, EHRs, labs, pharmacies, and insurance claims, patient-reported outcome apps, imaging, genomics and molecular studies, etc. Below is a list of some major data sources with a brief description of how data is deployed, to meet various objectives[5]:

1. **Structured clinical data** includes data from current and past clinical trials, RWE from registries, and peer-reviewed studies. Clinical trials are viewed as the most reliable source of data, and this data is therefore used for a wide variety of purposes that can improve clinical study efficiency. Clinical data from previous trials can be valuable for streamlining current trial protocols by predicting potentially high-performing study sites. Data captured from active trials can help make go/no-go, adaptive study changes earlier, and help close out studies faster. Registry data is being increasingly required by regulators to evaluate real-world use of therapies as a condition of approval. While analyzing registry data alone might not prove reliable enough to support approval, the data assists in identifying possible label extensions and in supporting reimbursement decisions - particularly when combined with other RWD from EHRs, pharmacies, and insurers.
2. **Traditional clinical data** consists of data from clinical EHRs as well as from labs, pharmacies, and insurance claims. EHR data is beneficial for guiding study design and exclusion criteria, as well as identifying promising study sites. This data is also proving to be extremely valuable for identifying patients at high risk of developing chronic diseases, specifically when merged with genetic data. Other uses include producing RWE for value-based payment models.
3. **Emerging RWD sources** comprise mobile clinical monitors, patient-reported outcome apps, internet of medical things such as motion detectors, as well as imaging, genomic, and molecular studies. Mobile monitoring and apps provide a detailed picture of everyday life that is extremely valuable in guiding development decisions and supporting value-based payment. Genomic, proteomic, and imaging studies provide data that can be used for diagnosis, monitoring, and therapy development.
4. **Emerging supplemental, environmental, economic, and social data** includes data on weather, insurance status, education, and income markers, which may

influence therapy response and study success. This type of data can be crucial for accurately interpreting mobile monitoring data. For example, high pollen count or pollution can affect asthma or COPD, possibly generating a blip in response that might otherwise be attributed to a trial medication. Supplemental information helps filter out this kind of noise in datasets, possibly reducing the time and size of trials.

Since big data is diverse in its sources and quality, and massive in its volume, it takes a considerable amount of effort to evaluate, normalize, and structure it so that it can be reliably used for analysis. AI-enabled technologies have the potential to organize and analyze the increasing amounts of data gathered as part of pharmaceutical R&D. The application of AI, combined with an effective digital infrastructure, can also enable the constant stream of RWD to be cleaned, aggregated, coded, stored, and managed. In addition, electronic data capture (is a system of capturing and managing clinical trial data on a digital platform to replace traditional paper-based data capture) can reduce the impact of human error in data collection and enable seamless integration with other databases. If the blockchain system is further added, this data can be securely captured and retrieved. Blockchain technology provides a web-based framework that permits patients and researchers access to their data. It also allows for user confidentiality, protecting patient privacy during the exchange of data between parties.

Furthermore, applying advanced statistical models to the wide range and granularity of available data can significantly improve clinical R&D productivity. These include modeling and simulations, and cumulative analysis using sequential, Bayesian, and meta-analytic techniques. These models are specifically valuable for conducting smaller studies that are gaining significance as therapies increasingly target limited populations.[5]

Pharmaceutical companies frequently require a comprehensive view of their clinical trials covering multiple global sites to make informed decisions. Therefore, consolidating all data on a 'shared analytics platform' not only leads to better collaboration and integration but also provides insights across measures ranging from enrollment rate and screening failure rates to protocol deviations. An effective analytics platform integrates advanced analytics, including predictive analytics, at every stage of the process to provide actionable insights to users. It incorporates a self-learning system, designed to improve predictions as well as data visualization tools to identify trends and patterns to initiate appropriate action.

In the future, the huge increase in clinical data generation, along with analysis technologies, could play a crucial role in transforming care from mitigation to anticipation (predict and prevent) to improve patients' quality of life.

In 2018, Novartis set up the Sense tower, a digitally-enabled nerve centre in Switzerland, to monitor its worldwide clinical trials in real-time.[15] The company also created a proprietary ML predictive-analytics platform, Nerve Live, that allows analysis of clinical operations data to generate insights about ongoing activities. For example, in some of its pilot clinical studies, Novartis found that the platform can assist the global drug development teams to plan and simulate country-allocation scenarios for clinical studies, such as choosing the best sites, tracking trial enrollment, and predicting patient enrollment curves.[16]

CONCLUSION

Clinical trials are becoming more complex as pharmaceutical companies focus their R&D efforts on treatments for rare diseases and personalized medicine, and on demonstrating improved patient health outcomes. However, pharmaceutical companies have started deploying digital technologies to simplify and streamline the clinical trial process in a variety of ways. This includes targeted recruitment of patients, identification of promising study sites, making efficient use of massive new data sets, and supporting early decision-making with increasingly powerful advanced analytics models.

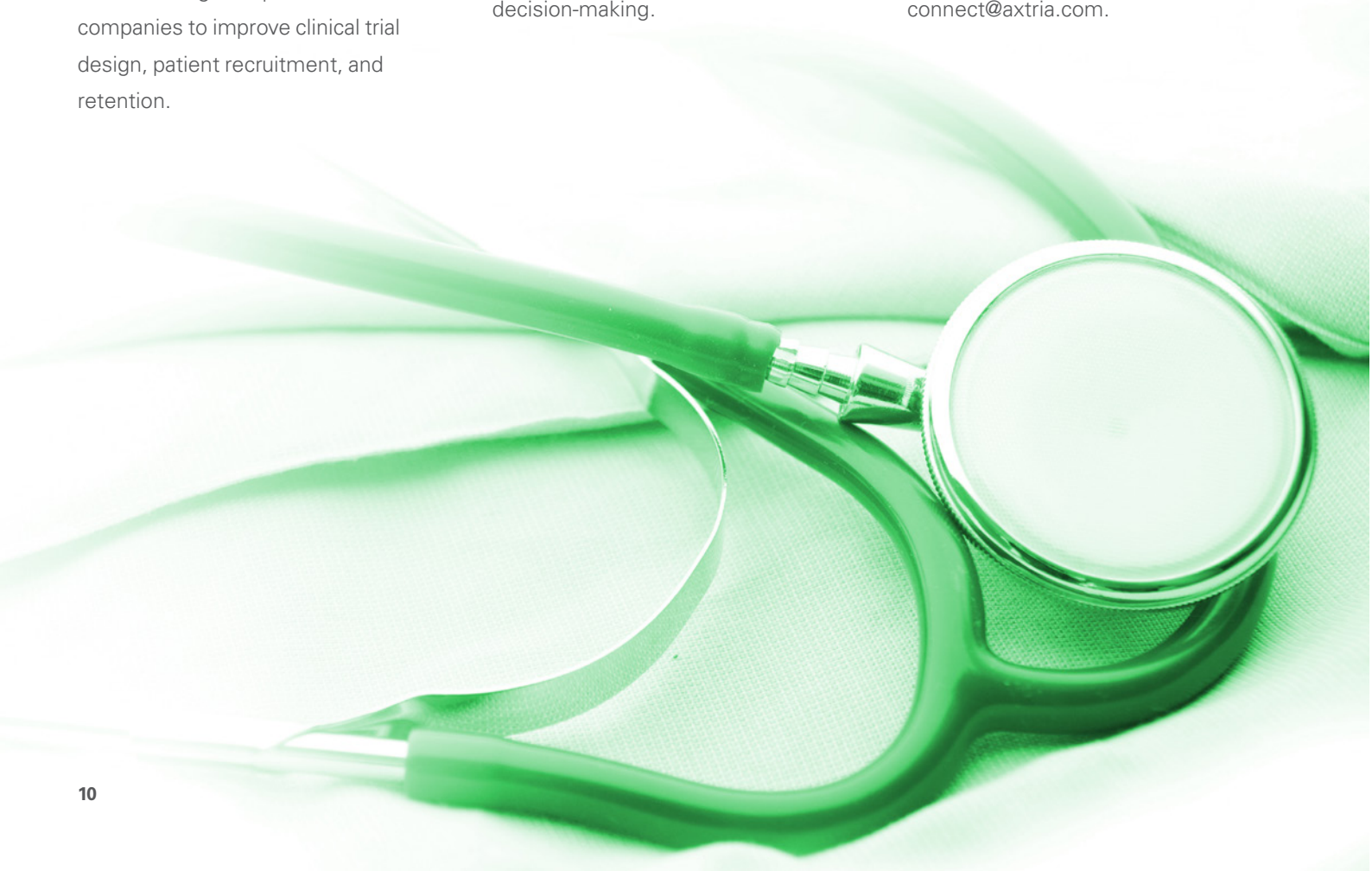
Furthermore, besides pharmaceutical companies and CROs, several other players such as AI start-ups, big technology firms, and data management providers, are now a part of the clinical trial ecosystem. They are partnering or contracting with pharmaceutical companies to improve clinical trial design, patient recruitment, and retention.

The industry is also laying greater emphasis on patient engagement throughout the clinical trial process. Pharmaceutical companies are deploying several innovative strategies that have the potential to make the clinical trial process more efficient and patient-centric. These include patient recruitment via social media, genetic screening, synthetic control arm, e-consent, remote monitoring, and virtual pillboxes to improve medication adherence. Many of these strategies rely on vast volumes of data that come from a variety of disparate sources such as current and past clinical trials, RWE from registries, EHRs, labs, pharmacies, and insurance claims, patient-reported outcome apps, etc. When advanced analytics techniques are applied to the wide range and granularity of data, it can potentially improve the drug development process and overall decision-making.

With this backdrop, it has become imperative for pharmaceutical companies to keep pace with the changing clinical trial environment, if they are to take advantage of the evolving landscape. This will require the development or acquisition of a range of digital capabilities, as mentioned earlier in the report. Focusing on greater patient engagement, developing a digitally savvy workforce, and data-driven decision-making is the way forward.

Axtria has expertise in data and analytics that encompasses all the different phases of the clinical trial process (from trial design and site selection to patient enrollment and retention). We assist our clients in creating and leveraging robust clinical trial data assets for a wide range of medical and commercial applications.

For more information, please email us at connect@axtria.com.



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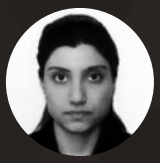
Shveta Bakshi
Director, Axtria Inc.
Tower B, Building 14, DLF Cyber City,
Gurugram, Haryana 122002
E: shveta.bakshi@axtria.com



Nidhi Jolly
Senior Manager, Axtria Inc.
Tower B, Building 14, DLF Cyber City,
Gurugram, Haryana 122002
E: nidhi.jolly@axtria.com

Contact Us

+1-877-9AXTRIA
info@axtria.com

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