futureproofing
CLINICAL TRIALS

Chapter 1:

The Rise of Integrated Intelligence

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Eroom's Law illustrates a concerning trend in drug discovery: despite technological advances, the number of new drugs approved per billion dollars spent on R&D halved every nine years from 1952 to 2012,[1] exacerbating financial strains on healthcare systems and limiting patient access to new treatments. Today, developing a single medication can exceed $2 billion and span a decade, with nearly half of this investment allocated to clinical trials where only one in 10 therapies entering Phase 1 trials are approved.[2-4]

In this series, we will discuss the challenges that are currently facing our clinical trial framework and implementation, as well as a few key methods with which we may overcome these challenges and improve the planning, execution and achievement of clinical trials and their associated findings.

While randomized clinical trials (RCTs) are essential for assessing the safety and efficacy of medical interventions and fundamental to evidence-based healthcare decision-making,[5-7] the current U.S. clinical trial model faces significant limitations hindering the progress of crucial treatments for submission and approval. These limitations include:

Diversity & Representation: inequitable representation in trials leads to incomplete data and biased findings.[8]

Recruitment & Enrollment: Approximately 80% of clinical trials fail to meet enrollment deadlines, risking delayed benefits for patients and costing sponsors $600,000 to $8 million per day of lost time in market.[9,10]

Implementation & Management: Challenges in trial location, participant understanding, and discontinuations can compromise outcomes.

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It is time to evolve beyond the current model and embrace a more adaptive[11,12] and technology-driven approach. By adopting innovations in trial design, enrollment, and execution, we can enhance trial outcomes and increase the chances of successful drug commercialization, bringing new treatments to those who need them most.[13]

Approximately

80% of clinical trials fail to meet enrollment deadlines

Three key areas in the current U.S. clinical trial framework require timely remediation.

Exclusion: Challenges in Diversity, Equity, and Inclusion Efforts

Increased diversity in clinical trials is necessary for developing safer and more effective treatments. However, persistent failures to recruit representative populations remain a significant issue, limiting the impact and generalizability of trial outcomes. Up to 20% of clinical trials either terminate early due to recruitment failures or complete with less than 85% of the planned enrollment,[14] highlighting systemic challenges in inclusivity.

Evidence-based medicine relies on inclusive trials to produce robust results. Yet, women, Black, Indigenous, and other People of Color, older adults, and those with comorbidities are consistently underrepresented. In 2020, only 8% of trial participants were Black, 6% Asian, 11% Hispanic, and 30% were aged 65 and older,[15] revealing significant underrepresentation among these groups. These disparities affect the validity of findings and pose ethical and practical challenges for health systems.

Section 907 of the Food and Drug Administration Safety and Innovation Act (FDASIA) underscores the need for trial diversity. It mandates the FDA to outline recommendations for enhancing the completeness and quality of demographic subgroup analyses in safety and effectiveness data and labeling, aiming to improve data accessibility to stakeholders.[16] Additionally, the FDA Reauthorization Act of 2017 (FDARA) advocates for broader eligibility criteria and representative enrollment, prioritizing inclusivity without compromising safety or efficacy.[17,18] Despite these efforts, achieving comprehensive diversity remains voluntary among trial sponsors and stakeholders.

Addressing these disparities is essential for equitable access to effective treatments and ensuring the reliability of medical research across diverse populations.[14]

Patient Barriers in Awareness & Understanding of Clinical Research

Despite the critical role of clinical trials in advancing medical treatments, many barriers hinder participation. Reasons often cited for participants' declining involvement include cost, time constraints, transportation issues, and distrust of researchers.[19,20] Additionally, complex trial designs, strict eligibility criteria, and inconsistent implementation further complicate enrollment efforts.[20]

Many patients lack awareness and understanding of clinical trials, including their potential benefits and risks, the consent process, and core methods such as randomization and placebos, which can seem unfair or unethical.[21] Historical, cultural, socioeconomic, and prejudicial factors may also contribute to lower participation rates among women and minority groups, who may also fear stigma, adverse health effects, and loss of control in trials.[20]

Misconceptions about clinical trials, such as the belief that they are only suitable for terminally ill patients or concerns about the ethics of randomization, can perpetuate fears and misunderstandings.[22,23] These factors underscore the urgent need for patient-centric approaches to clinical trial design and communication to enhance diversity, enrollment rates, and overall trial outcomes.

Roadblocks to Digital Transformation

While digital health technologies (DHTs) have the potential to enhance clinical trials, they also present challenges in uptake. Industry and regulatory bodies have been slow to embrace the digital transformation needed to evolve the clinical trial framework. This hesitation is compounded by the sluggish adaptation of regulatory guidelines essential for clarifying and simplifying the market entry of DHTs in validating trials.[12]

Despite advances in technology and AI, misconceptions about digital transformation persist. Many fear it could remove the human element from clinical trials, affecting result authenticity.[12] Telemedicine often faces criticism for eroding the empathetic doctor-patient relationship, leading to impersonal care. Concerns about its safety and effectiveness compared to traditional care, along with regulatory and compliance challenges, further complicate matters.[24]

The return of stricter regulations following COVID-19 has also hindered digital trial adoption.[25] To promote digital uptake, especially for rare diseases and underserved populations, addressing health disparities and concerns about data reliability and privacy is essential.[24]

Despite these challenges, there are opportunities to reform the U.S. clinical trial framework, improving trial equity, increasing enrollment, and enhancing overall impact. This series of papers explores each of these opportunities in the hopes that they will provide inspiration, motivation and insights that will support sponsors and other clinical trial stakeholders as they look to futureproof the clinical trial model.

The Rise of Integrated Intelligence

The plethora of new technologies that have evolved over recent years offers us opportunities for an evolved clinical trial framework that will both improve and optimize the enrollment and impact of trials. Opportunities in this space include the addition of artificial intelligence (AI) capabilities to optimize trial design and management, recruitment, and trial site location.

1. Plain Language Utilization

One effective strategy for enhancing participation and reducing disparities in clinical trials involves clear and straightforward communication. Higher levels of health literacy increase individuals' interest and likelihood to engage in research,[26] whereas lower health literacy can complicate understanding of trial details and lead to participant anxiety.[27] In the United States, only 12% of adults possess proficient health literacy, with Hispanic individuals experiencing more pronounced disparities,[28] potentially influenced by factors such as language and educational barriers, limited healthcare access, and other cultural considerations.

Here, technological advancements like AI and large language models can help adapt trial information to accommodate varying literacy levels. AI-powered chatbots, for example, can be valuable tools for clarifying trial specifics and ensuring participant comprehension.[29] Additionally, AI can enhance efficiency across critical trial processes, including patient screening, matching, and monitoring. In fields like pediatric oncology, AI has notably reduced the administrative burden associated with patient recruitment.[30]

However, while exploring this potential, it is equally important to address the biases inherent in AI models to uphold fairness and equity in presenting information and making decisions during clinical trials.

2. Geospatial Modelling

Geospatial modeling is a powerful method for analyzing complex factors by visualizing specific data layers. It assists in pinpointing particular locations or regions that could be beneficial for focusing research efforts. These areas might include places where groups of people, such as those with certain health conditions or demographic characteristics, are concentrated (hotspots). It also refers to identifying regions where vulnerable populations reside, such as areas with limited access to healthcare or higher rates of certain health issues. By conducting detailed disparity analyses and selecting trial locations that minimize patient travel burdens, geospatial modeling can help ease and expedite clinical trial enrollment.

Advanced geospatial modeling tools go a step further, providing more granular visualizations using de-identified patient data and additional datasets, including information from advocacy groups, healthcare providers, and social media metrics. These tools enable the development of prioritized trial location scores based on factors like accessibility, competition analysis, and historical enrollment rates, aiming to maximize patient engagement.

Additionally, geospatial modeling can enhance trial inclusivity by integrating digital health technologies and remote services, leveraging healthcare provider networks to increase clinical trial participation.

3. Digital Twins & Synthetic Humans

Digital twins and synthetic humans are virtual models created using data from electronic health records and other sources. They're not meant to replace people but to help by predicting outcomes based on large datasets.

In clinical trials, digital twins can be used to analyze participant eligibility, motivation, and suitability, which are often significant challenges in efficient recruitment. They can also assist in pre-qualifying trial participants and optimizing management strategies, providing a foundational understanding of patient populations before trials begin.

By reducing the number of patients required for control groups, digital twins can expedite trials and increase the chances that participants receive experimental treatments instead of placebos, thus addressing retention issues. As digital twin models improve and make more accurate predictions, the size of control groups could potentially be reduced by 75% or more, significantly shortening the time needed to enroll patients and enhancing the overall efficiency and reliability of clinical trials.

While the challenges to our clinical trial framework may seem great, the growth opportunities are even greater. Cross-industry collaboration and advanced technologies promise to streamline trial processes, enhance data accuracy, and reduce costs.

These efforts, along with others we will explore through this series, could accelerate the delivery of innovative treatments to patients, offering faster access to potentially life-saving therapies and yielding better outcomes worldwide. This transformation isn't just about improving clinical trials but fundamentally reshaping how healthcare is delivered.

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To learn more about the ways in which JPA Health is applying innovative data science and integrated intelligence to improving clinical trial planning and execution efforts, please reach out to **Colleen Carter at ccarter@jpa.com**.

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