EXECUTIVE INSIGHTS

Clinical Trial Challenges: Patient Recruitment and Diversity

The biopharmaceutical industry has experienced significant growth over the past decade, underpinned by the increasing volume of assets in development, their complexity and precision, and an increasingly competitive clinical trial landscape. A challenge that is only exacerbated by growth is the difficulty in identifying, enrolling and retaining patients required for clinical testing. However, the status quo for finding and retaining the right patients is insufficient and has not been optimized in trial processes.

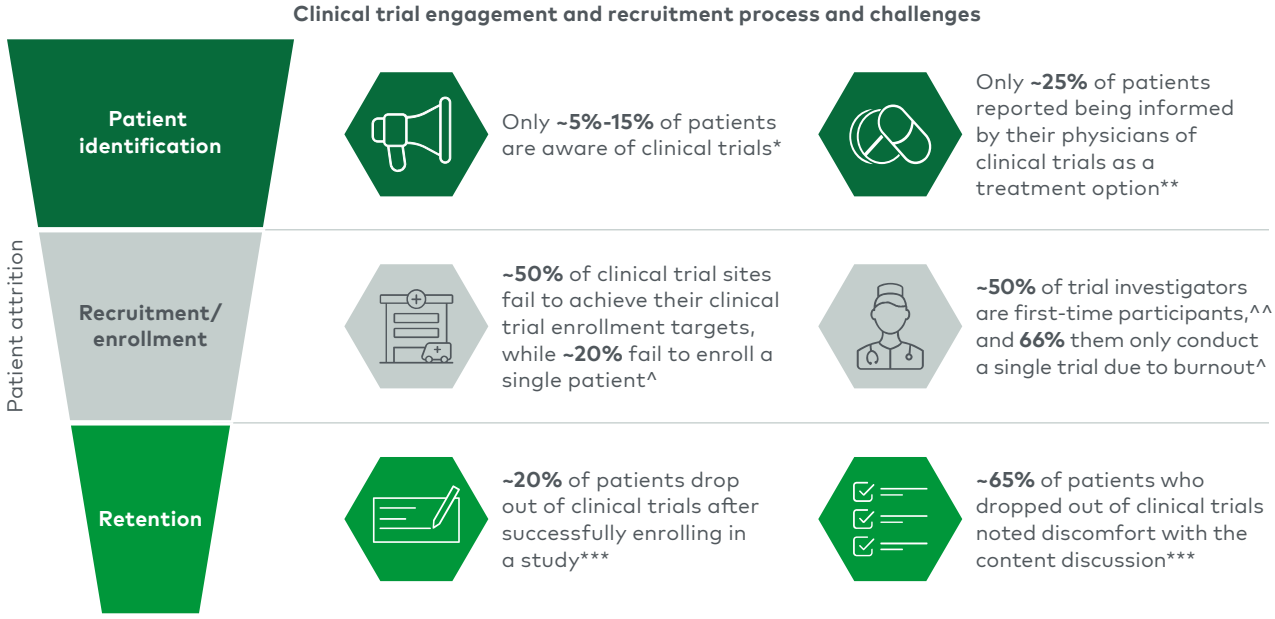
Current strategies primarily focus on enrolling enough patients to meet endpoints, and they lack proactive targeting to efficiently connect the right patients to the right trials. Only 27% of volunteers screened are eligible to participate in a clinical trial, driving up costs to screen a large number of patients to compensate for high attrition rates.[1]

In recent years, phase 1 and phase 2 recruitment budgets rose by 157% and 108%, respectively, in part to meet enrollment goals.[2] In addition, several macro industry trends are slated to amplify these preexisting challenges: More complex therapies enter clinical development each year, requiring novel trial designs to target and retain an increasingly precise subset of patients. Furthermore, U.S. regulations passed in January aim to improve diversity in clinical trial populations and will require proactive, thoughtful patient targeting and engagement to meet this critical requirement.

Clinical trial challenges of patient identification, recruitment/enrollment and retention

While challenges exist across the entire clinical trial execution process, particular challenges can be seen acutely when zooming in on patient identification, recruitment/enrollment and retention. The major pain points across each are distinct (see Figure 1).

Figure 1
Clinical trial patient journey pain points

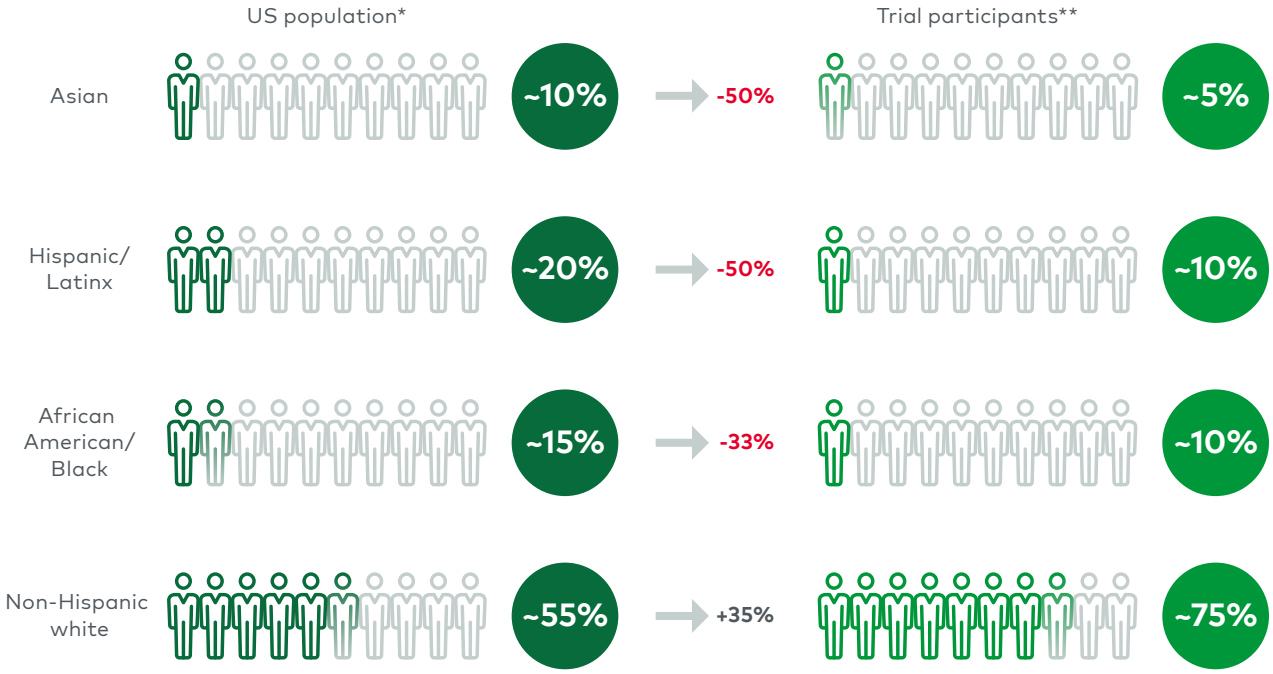


*2019 Covance Presentation on overall patient awareness, Coalition of Clinical Trials Awareness
**Anderson et al., 2018
***Advarra
^Tufts Center for the Study of Drug Development
^^Fordyce et al., 2019

Alongside these challenges, clinical trials do not adequately represent diverse participants beyond white males, creating gaps in understanding how diseases, preventive factors and treatment effectiveness differ across populations.[3] Women of "childbearing potential" were banned by the U.S. Food and Drug Administration (FDA) from participating in clinical research studies until 1993 and still face underrepresentation today,[4] and only approximately 25% of global trial participants are people of color (see Figure 2).[5]

Recent legislation seeks to remedy this inequitable participation in clinical research. Congress will now require clinical trial sponsors to submit a diversity action plan when submitting a study protocol to the Department of Health and Human Services for all phase 3 or pivotal trials, as well as most device studies, including goals for enrollment, a rationale and a plan for achieving those goals.[6] Over the next 12 months, the FDA will finalize the guidance on the format and content of the plan, but sponsors should take action now as they will need to proactively integrate this plan with their clinical research processes. For smaller biotechs that are looking for capital, having a well-planned-out approach to achieving targeted and diverse patients for clinical trials may better position them for investment, partnership and acquisition opportunities.

Figure 2
Disparities in US clinical trial enrollments across races



*2020 U.S. Census
**2020 FDA Drug Trials Snapshots Report

The need for equitable representation within clinical trial research populations will exacerbate the already difficult patient identification, recruitment/enrollment and retention processes that sponsors face, though solutions can be implemented to streamline these processes and ensure trials are representative of the populations and diseases being studied.

"Going forward, achieving greater diversity will be a key focus throughout the FDA to facilitate the development of better treatments and better ways to fight diseases that often disproportionately impact diverse communities," says FDA Commissioner Dr. Robert M. Maliff.[7]

A recent example of a failure to achieve equitable representation within clinical trials occurred during the development of COVID-19 vaccines. White individuals comprised a disproportionate majority of trial participants, while virtually all minority groups were underrepresented.[8]

In this critical moment of vaccine development, failure to create a diverse and racially representative clinical trial population risks harm to underrepresented groups. A 2020 study hypothesized that SARS-CoV-2 subunit peptides utilized in formulating COVID-19 vaccines may not be as robustly displayed by the major histocompatibility complex in diverse participants who are underrepresented within clinical trials, thereby reducing efficacy.[9]

This raises the concern that racially homogeneous clinical trials may inadvertently produce treatments that are effective for groups that are overrepresented in clinical trials and potentially less effective for those that are underrepresented. In this instance, further studies supported by real-world clinical data showed similar vaccine efficacy in diverse populations, though this example serves as a sentinel event to highlight the importance of creating diverse trial populations in order to ensure treatments are effective for everybody.[10]

The need for a proactive, integrated approach to clinical trial strategy

Contrary to the status quo for trial execution — which focuses on getting patients into investigational therapies at a sufficient rate to meet endpoints — solving for these challenges, including fostering diversity within clinical trial populations, will require an integrated and proactive approach (see Figure 3). As no one component is sufficient, an integrated approach that focuses on four interwoven components will shape trial strategy to have longitudinal and meaningful impact (described in greater detail in a prior L.E.K. Consulting *Executive Insights*).[11]

Figure 3
Four-component framework to develop an integrated clinical strategy

Source: Lek.com, "Building Clinical Trial Leadership in Biopharma," https://www.lek.com/insights/ei/building-clinical-trial-leadership-biopharma; L.E.K. research and analysis

1. **Put patients first —** Sponsors need to own and prioritize ensuring potential, current and past patients are supported and engaged as the critical participants they are as trials evolve. Especially important to diversity efforts, sponsors should consider the unique needs and perspectives of underrepresented patient populations.

2. **Intentionally cultivate your site ecosystem —** Sponsors need to identify the correct sites to target, onboard and cultivate longitudinal relationships at both traditional and emerging site types in order to meet portfolio needs while also developing relationships with new sites and investigators.
3. **Align incentives —** Sponsors need to work to ensure that sites receive the proper operational, reimbursement and logistical support to serve as the face of the trial to patients and to conduct trials in a sustainable, positive way that meets the needs of their business.
4. **Choose wisely —** Sponsors need to proactively position themselves as the leader on trials and avoid information disintermediation by sites and/or third parties.

Additionally, achieving diversity action plan goals will require intentionality across these four components to address operational, technical and logistical challenges (e.g., transportation, translation services, administrative support for hospitals with limited resources), as minority patient populations are typically served by underfunded, research-naive hospitals.[12]

As each trial's and sponsor's circumstances are unique, focusing on the four key components in an integrated approach can take several forms, for example:

- Developing long-term relationships with patient populations through sites, patient support networks and physician outreach to drive identification of and engagement with relevant patient populations
- Integrating patient recruitment solutions with site selection solutions and combining on-site and technical solutions to tailor recruitment to individual patient needs
- Using tailored communication (e.g., email, mobile app and/or text) and milestone tracking to flag adherence issues before dropout to increase patient retention
- Conducting decentralized clinical trials to provide patient-centered care in order to promote recruitment and retention

Clinical trial ecosystem players have begun to develop solutions across the four components

Various pharmaceutical services vendors and technology companies have begun to develop solutions to help mitigate the pain points noted above. Regarding the first key component of developing long-term relationships with patient populations by meeting them where they are, players including Javara are developing solutions to enable both experienced and trial-naive clinicians to participate in clinical trials by embedding the necessary clinical research staff and infrastructure into their practices.

Javara's partnerships with broad community-level healthcare organizations enable it to reach a more diverse patient population, and its innovative communication modalities allow Javara to bring awareness to potential trial enrollees and engender trust. Other companies are forming long-term relationships with diverse patient populations for narrower indications; for example, the OneOncology Research Network uses its operational expertise to facilitate clinical trials in a network of community oncology practices that have diverse patient populations and may lack the necessary trial infrastructure.

The second key component, cultivating the site ecosystem through integrating patient recruitment with site selection and tailored recruitment solutions, is being addressed by players such as SubjectWell and 83bar, which deploy educational campaigns and the creation of high-intent, qualified patient recruitment platforms to accelerate trial recruitment and minimize dropout rates. Lack of awareness of the benefits of clinical trials and how to enroll prevents most patients from enrolling in trials, and the lack of effective patient screening can result in high dropout and screen fail rates. Solutions are evolving to address these pain points and improve trial cost and time efficiency. Adoption of new strategic trial solutions is not limited to the U.S healthcare market. Our November 2022 report discussed China's adoption of smarter clinical trial tools, in addition to other strategic trends driving high-quality clinical development growth throughout the country.[13]

Aligning sponsor and site incentives, the third key component, has the goal of driving outcomes such as higher patient retention. Clincierge, a pharmaceutical services vendor, helps biopharma sponsors coordinate patient travel logistics for clinical trial participation, which is a service that can improve patient retention as well as trial population diversity due to the alleviation of transportation barriers.

Players such as Greenphire have developed other solutions to minimize financial barriers to clinical trial participation. Greenphire developed the ClinCard solution that automates study participant compensation with debit cards, virtual cards and direct deposit. The solution also includes a tax toolkit for sponsors and integrates with ConneX, a platform for travel services for clinical trial participants. Travel and financial barriers are a major reason for patient dropout, but emerging solutions are beginning to address these concerns to maximize sponsor and site incentives.

The last key component, strategically choosing where to sponsor clinical trials, extends beyond a sponsor determining at which sites it can establish itself as a leader and is rapidly beginning to encompass elements of decentralized clinical trials. Science 37 provides technology-enabled solutions to allow certain elements of clinical trials to occur remotely. The platform facilitates

virtual recruitment and enrollment, electronic informed consent, electronic sources, electronic clinical outcome assessments, and telemedicine, among other solutions, to reduce geographic constraints in clinical trials. Similar to previous solutions, technologies and services allowing distributed functions enable greater diversity within clinical trials due to the removal of transportation barriers.

Beyond pharmaceutical services vendors, companies in adjacent fields (e.g., biopharma, technology) are entering this space to develop solutions that address these same pain points through different pathways. For example, Roche has developed a clinical trial match application that can be utilized by oncologists to set up a new trial, which could help alleviate the pain point of the trial initiation process being a time-consuming one. Apple has developed ResearchKit and CareKit, which enable researchers to develop apps that facilitate the collection and aggregation of data on various medical conditions, making clinical trial operations more patient-centric and alleviating inequity with respect to clinical trial site accessibility.

While industry players have developed interesting solutions, sponsors that consider all four key components in an integrated clinical trial approach will have the greatest success in facilitating cost- and time-efficient trials with diverse patient populations.

Conclusion

While a number of point solutions to address patient identification, recruitment/enrollment and retention challenges exist in the market today, maximizing them will require a tailored strategy that is proactive and intentional toward and integrated with each of the four key components. Putting patients first, intentionally cultivating the site ecosystem, aligning incentives and choosing wisely where to sponsor trials will enable sponsors to achieve diverse and targeted populations in their clinical trials and to facilitate timely and cost-effective trials that will benefit all patient populations.

As the number of clinical trials being conducted continues to grow, therapies become more complex, the clinical trial landscape becomes more competitive and new legislation that promotes diversity within clinical trials is introduced, all four of the above components must be intertwined to create a longitudinal clinical trial network.

Putting patients first through cultivating long-term relationships, using tailored communication and implementing patient-centric monitoring will improve patient enrollment and retention, thereby reducing trial length and cost.

Intentionally cultivating the site ecosystem entails implementing a proactive approach to engage with existing and emerging trial sites to reduce the time necessary to initiate a new clinical trial. Additionally, experienced trial sites can be valuable resources when developing protocols for new trials.

Aligning incentives is critical to streamlining the clinical trial process at chosen sites and ensuring proper infrastructure is in place. And last, selecting wisely where to sponsor clinical trials ensures that sponsors are positioned as the medical and scientific leaders of trials and that data is handled in an efficient manner.

Integration of all four key components in an intentional and proactive manner drives solutions that achieve diverse trial populations in a cost- and time-efficient way, providing benefits to both diverse patient populations and trial sponsors.

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Endnotes

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