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RESEARCH

Increasing Diversity in Clinical Trials

Overcoming Barriers to Make Clinical Trials Truly Inclusive

Nitish Mittal, Partner
Chunky Satija, Practice Director
Nisarg Shah, Senior Analyst

Contents

Executive Summary

The evidence and insights from clinical trials form the backbone of care delivery, as regulatory bodies use them to approve drugs and physicians use them to decide clinical interventions and make prescription decisions. In an ideal world, clinical trials would have adequate representation from all sections of the population, regardless of ethnicity, gender, geographical location, and socioeconomic status, to ensure robust evidence for all population groups. But, in reality, clinical trial populations are significantly less diverse than the actual population of the people the medicines are intended to treat.

Though the life sciences industry acknowledges this lack of diversity in clinical trials, there has not been significant progress to address this important issue. The industry needs to move from having a few pockets of excellence in limited clinical studies to a more collaborative effort that involves different industry players, such as study sponsors, CROs, regulators, clinical trials sites, physicians, patient advocacy groups, and technology providers.

Technology investments and co-innovation with technology vendors will play a key role in enabling stakeholders to tackle the diversity challenge. Technology interventions that can be deployed across the clinical trial value chain, right from trial design to trial close-out, can help overcome barriers to increasing diversity. Technology can help stakeholders take a patient-centric approach through interventions aimed at minimizing minority patients' burden in clinical trials, alleviating existing stigma or fear through patient education and support, and building trust by regular communication about trial progress and conduct. Solutions geared to analyze minority population performance and monitor safety can also improve regulatory reporting and fast-track the drug approval process.

Virtualized trials hold immense potential in improving the diversity landscape, as their patient-centric nature directly addresses existing diversity barriers. Their virtual mode of conduct reduces physical barriers and helps target larger populations; their custom-built solutions support native languages and eliminate linguistic barriers, and their patient engagement functionalities increase trust.

To achieve the right mix of diversity in clinical trials, it is important that all stakeholders tackle the challenge together through appropriate metrics and governance mechanisms. Analyzing performance and progress and developing the right set of initiatives and best practices will be crucial to making clinical trials truly diverse and improving clinical trial data quality and integrity, while delivering a holistic view to regulators and physicians.

The current state of diversity in clinical trials

Regulatory bodies, patients, and caregivers expect therapies to be rigorously tested in clinical trials and have a rich body of evidence supporting safety and efficacy before a physician prescribes them. Turns out, the evidence from most clinical trials is not as rich and diverse as would be desired. This is because, while the world we live in is diverse, our clinical trial participant population is not.

Diversity in clinical trials refers to adequate representation of all sections of the population, regardless of ethnicity/race, gender, geographical location, and socioeconomic status.

The lack of diversity in clinical trials can have serious ramifications for the health and safety of underrepresented populations, as the lack of a therapy's evidence on a minority population can result in physicians prescribing a therapy without fully understanding how the patient would react to it. For instance, in 2014, the state of Hawaii sued two manufacturers of a blood thinner approved by the FDA. This was because the product was not effective in treating 50% of Asians and 75% of Pacific Islanders, who lacked the enzymes required to activate the drug. Patients representing these populations were not represented in clinical trials, and, therefore, this data was uncovered only after FDA approval. While there is widespread agreement about the need for greater diversity in clinical trials, the current numbers show that we are far from reaching the goal.

Understanding diversity by numbers

The US and Europe account for approximately 65% of the world's clinical trials, which effectively means that most trial volunteers are white. Exhibit 1 illustrates the distribution of clinical trials worldwide in June 2019.

EXHIBIT 1

Clinical trials conducted worldwide

Source: Clinicaltrials.gov

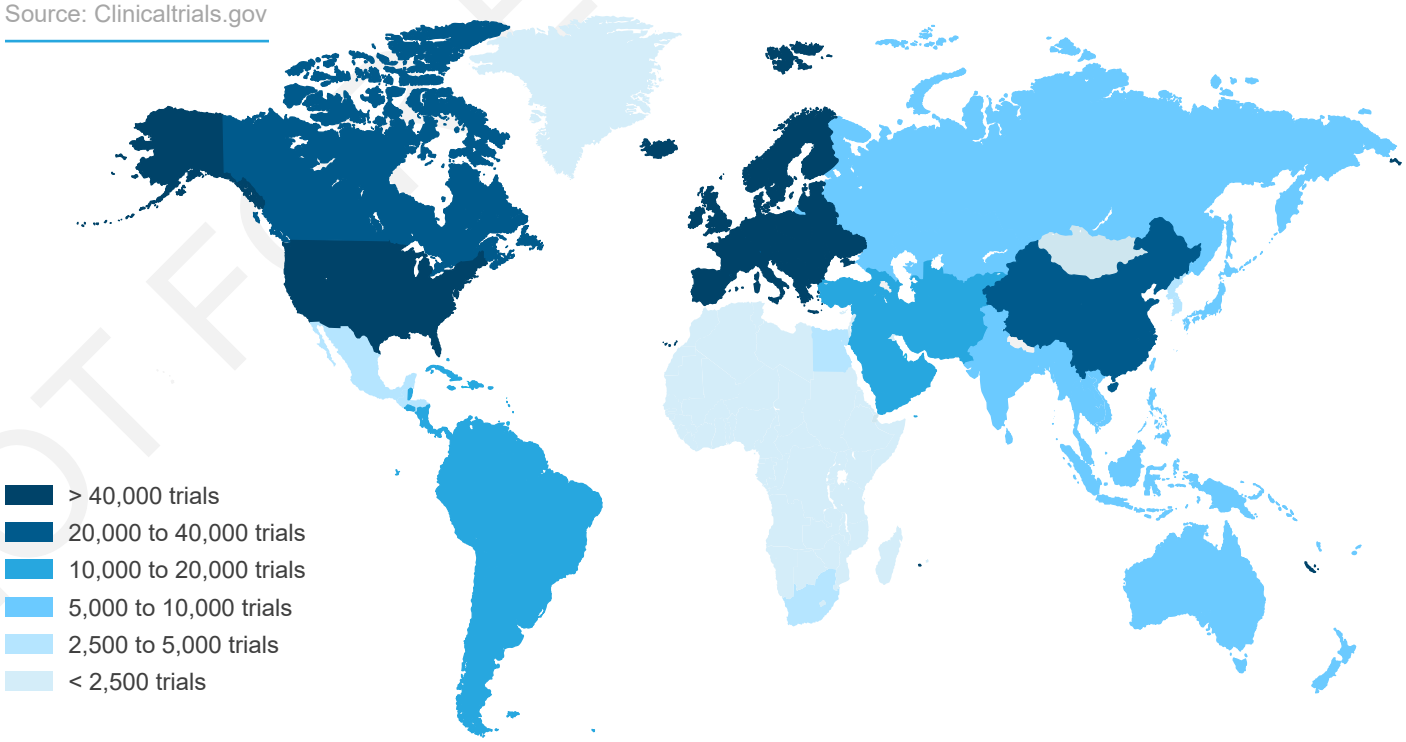


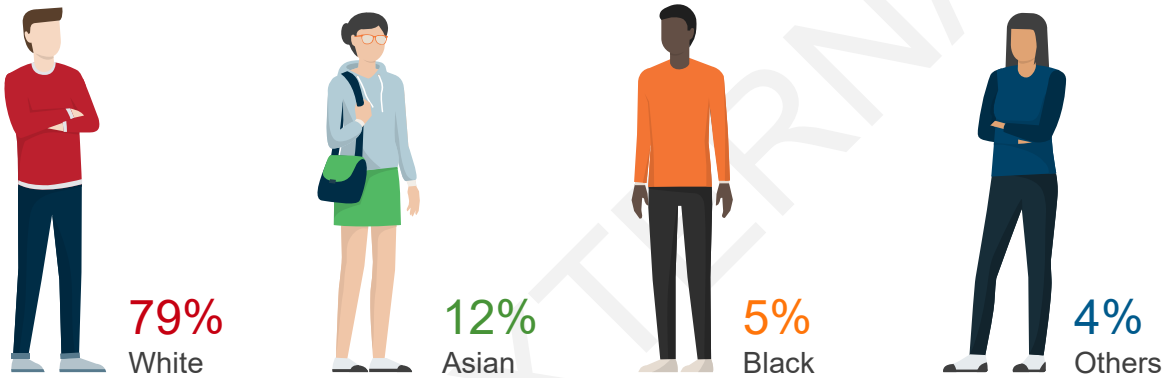
Exhibit 2 showcases trial participation by race and gender and reveals that approximately four-fifths of trial participants (in 2015-16) worldwide were white, whereas only a fifth of the participants belonged to Black, Asian, and other races, thus posing an ethnic and racial diversity challenge. The US, with approximately 4% of the world's population, represented nearly a third of the trial participants in 2015-16. However, the whites dwarfed involvement from minority communities, including African American, Asian, and Hispanics. In fact, while minority communities accounted for 19% of trial participants in the US in 2016, they accounted for nearly 40% of the overall US population.[1]

EXHIBIT 2

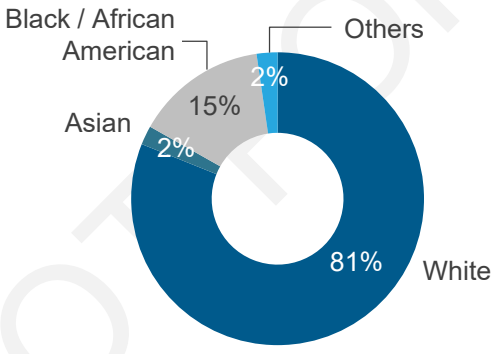
Trial participation by population group and gender

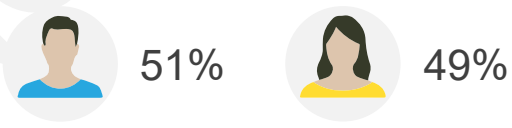
Source: FDA global participation in clinical trials report, July 2017 (For the year 2015-16)

Global participation in trials by race (2015-16; percentage)
100% = 131,749 participants

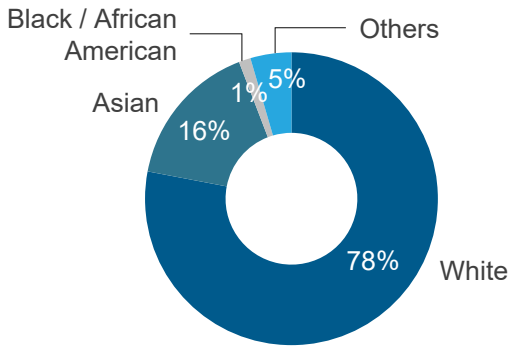


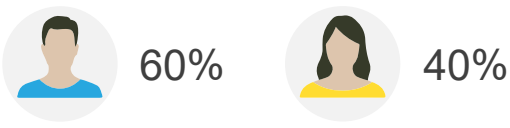
United States (2015-16; percentage)
100% = 40,835 participants





Rest of the world (2015-16; percentage)
100% = 90,914 participants





1 Statistica.com records for 2016

Similarly, trials in the past have predominantly focused on men. While the US has maintained a balanced male to female ratio in clinical trials, trials in the rest of the world still lack women's participation.

Income disparities also influence clinical trial participation, as lower-income patients are more sensitive to financial expenditures and associated costs of clinical trial participation. Studies show that patients with an annual household income below US$50,000 have 32% lower odds of cancer clinical trial participation when compared to higher income patients.[1] The situation is aggravated by physical limitations, as more than 70% patients live more than two hours away from the nearest clinical site.[2] Also, the uptick in precision medicine limits generalizability and availability of genomic-based therapies to all patients and therefore, diverse population representation is crucial to ensure efficacy of treatments developed using the precision medicine approach. Therefore, the biopharma industry still has roadblocks to overcome before it achieves diversity in clinical trials.

The pandemic and the lack of diversity in COVID-19 trials

COVID-19 has had a rather disproportionate impact on the world's population. It is already clear that older population (aged above 60 years) or those with underlying health conditions (such as heart disease, diabetes, or immune system disorders) are more vulnerable to COVID-19.
Another group particularly vulnerable to the virus is the minority population, especially Black Americans. Exhibit 3 shows that Black Americans continue to experience the highest mortality rates, more than twice as high as those for whites and Asians.

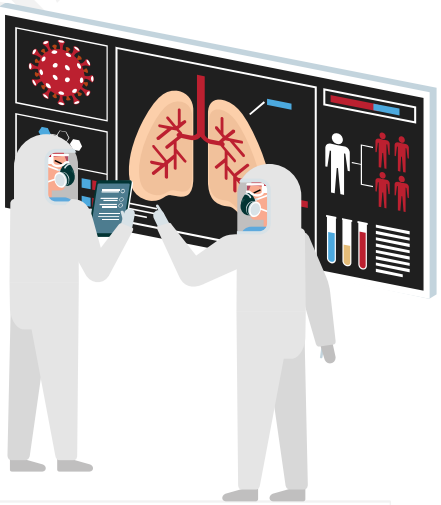
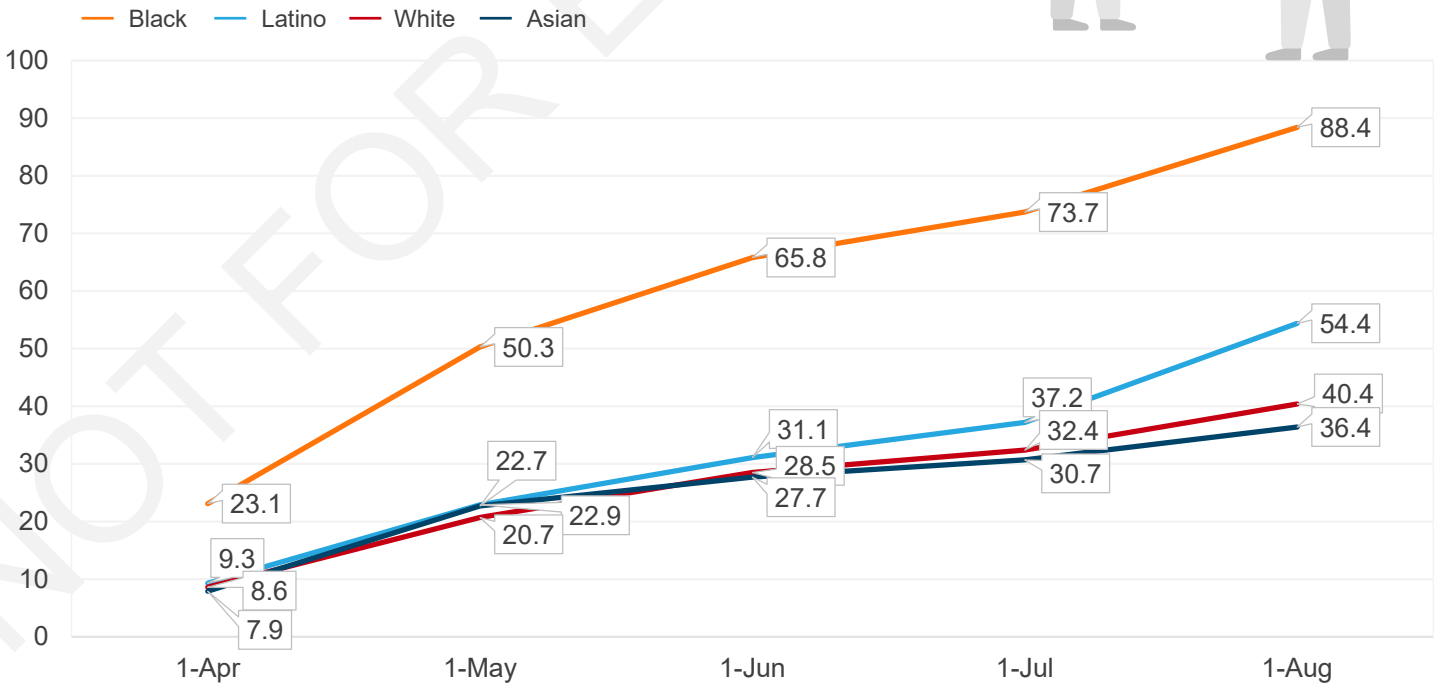


EXHIBIT 3

Cumulative actual COVID-19 mortality rates per 100,000 in the US by race and ethnicity, April-August 2020

Source: APM Research Lab



1 JAMA study on patient income level and cancer clinical trial participation, 2015
2 Roche internal review of trials

However, COVID-19 vaccine clinical trials have failed to enroll diverse populations to reflect the disproportionate impact on older and minority populations. Data published by the Oxford University/ AstraZeneca vaccine group reveals that over 90% of the 1,077 healthy volunteers in Phase I and II trials were white. A similar lack of diversity was found in the Moderna Phase I trial and Pfizer and BioNTech's Phase I and II study.

This situation is not just true for the US. In August 2020, UK's National Health Service (NHS) launched a fresh attempt to recruit volunteers from the British Asian community after enrolling less than 10% minority patients with a British Asian background out of the 112,000 patients registered.

However, companies are now focusing on increasing diversity in their Phase III trials. Moderna's CEO, Stephane Bancel, said on September 4, 2020, that they were slowing enrollment slightly in its Phase III vaccine clinical trial to ensure sufficient representation of minorities, thereby incorporating a small delay to ensure better trial quality in the long run. He also mentioned that the company's goal for enrollment is to line up with US Census Bureau numbers.

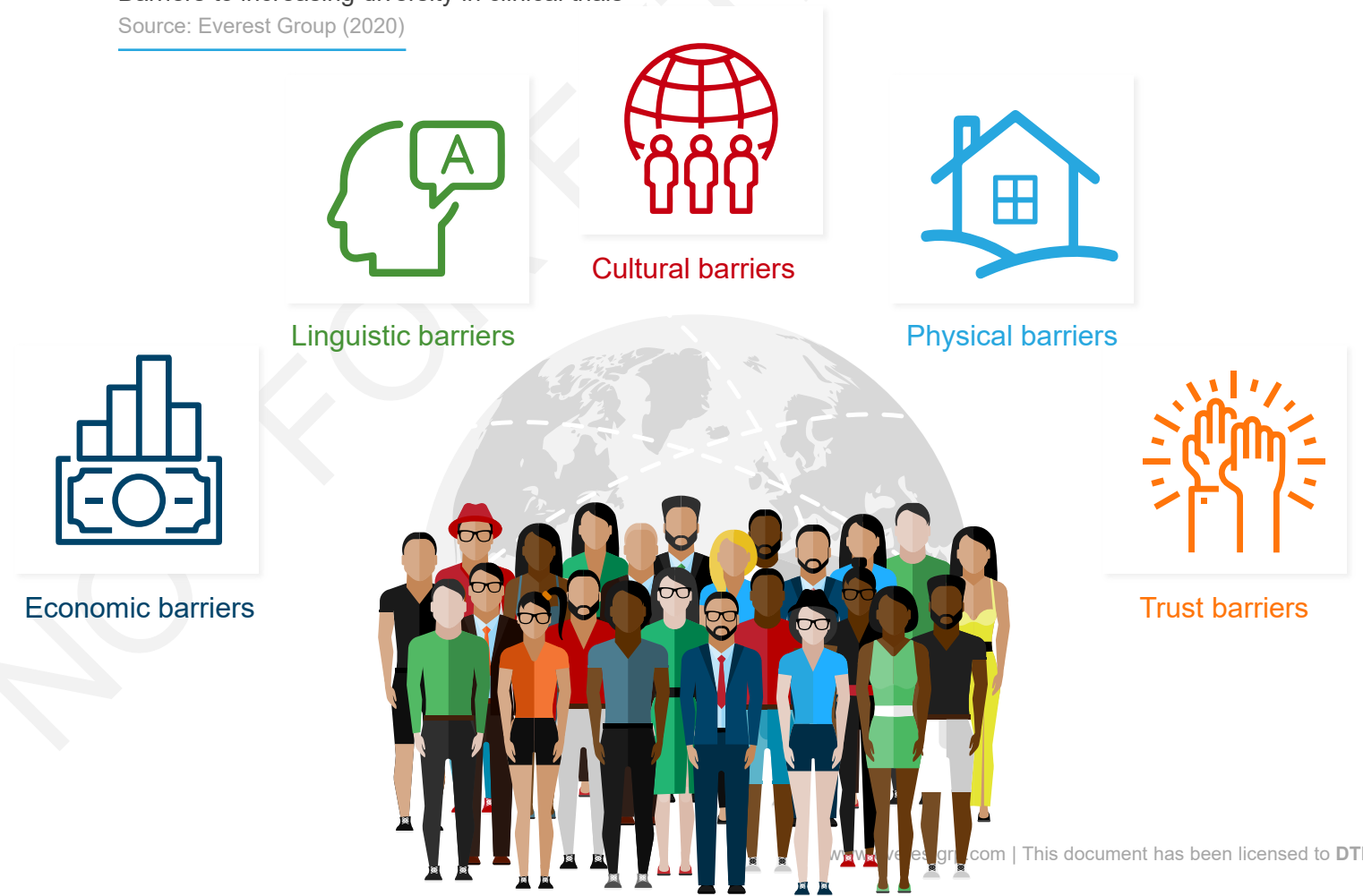
Barriers to increasing diversity in clinical trials

There are many barriers to ensuring diversity in clinical trials. Prominent among them are barriers that deter people from participating in clinical trials, as highlighted in Exhibit 4. Ethnic/racial minorities are disproportionately impacted by these barriers.

EXHIBIT 4

Barriers to increasing diversity in clinical trials

Source: Everest Group (2020)



- **Economic barriers:** Patients from minority communities may not have the financial resources to continue participating in clinical trials, especially when trial-related out-of-pocket expenses, such as patient lodging and transportation, can get expensive and may not be reimbursed by the sponsor
- **Linguistic barriers:** For a lot of minorities, English is not their first language. Also, comprehending complex information creates linguistic barriers for minority participation in clinical trials. Similarly, a lack of understanding about how to participate in clinical trials also plays a role in limited enrollment
- **Cultural barriers:** A Lack of information about clinical trials, coupled with the stigma around clinical trial participation, can deter minority patients from participating in clinical trials. Prior experiences with racism can also stymie enrollment rates
- **Physical barriers:** Physical barriers can limit participation, especially when patients live away from clinical sites. The situation is exacerbated by sponsors' tendency to select trial sites that are rich in patients but lack diversity
- **Trust barriers:** Inequities in healthcare and insurance access, and limited involvement with the scientific community can result in a general lack of trust that impacts minority communities' trial participation

Industry efforts to increasing diversity

The US FDA started the Drug Trials Snapshot Project in 2015 to provide information on the sex, age, race, and ethnicity of clinical trial participants for an approved drug. Thereby, the FDA made diversity information more transparent to the public, in a bid to track and improve the statistics over time. In June 2019, it also released a draft guidance to improve diversity in clinical trials, in which it recommended initiatives for sponsors such as broadening the eligibility criteria to include the minority population, considering adaptive trials so as to start with a small population and increase it gradually to a wider population. This was aimed at making trial participation less burdensome for patients through initiatives aimed at reducing trial visit frequency and financial reimbursements for visits.

At their end, pharma companies are also trying to tackle the diversity challenge. While some companies are carving out a separate role – the Director of Diversity and Inclusion in Clinical Trials – others are broadening the role of the Chief Patient Officer to focus on diversity initiatives. Through minority-focused news media and by connecting with minority physicians in local communities, pharma companies and investigators are establishing meaningful connections to boost minority participation in clinical trials and keep patients engaged across the trial life cycle. For instance, Janssen partnered with the Society for Clinical Research Sites (SCRS) to develop an awareness and best practice program for clinical trial sites – this includes tools, webinars, and live seminars to assist clinical research site leaders in best practices for diverse patient engagement efforts in clinical research. The firm also has an internal, cross-functional working group focused on increasing diversity in clinical trials. One company is working with ambassadors to raise awareness and provide access to information about clinical trials in the communities that it serves.

Exhibit 5 (on the next page) shows what various organizations are doing to improve clinical trial diversity

EXHIBIT 5

Initiatives taken by the industry to increase diversity in clinical trials

Source: Everest Group (2020)

Participant(s)	Initiative
Clinical Research Pathways and Morehouse School of Medicine (MSN)	Funded by Clinical Research Pathways, MSN will launch a three-year program wherein minority physicians will be recruited to conduct clinical trials. MSN will educate and mentor the recruited physicians. The goal is to encourage more minority patients to participate in clinical trials by taking trials directly to minority patient populations
Clinical Research Pathways and WellStar Health System	The two organizations will develop strategies to enroll more minority patients in oncology trials. They will work to strengthen the minority clinical investigator workforce, which plays an essential role in patient recruitment. Clinical Research Pathways has awarded a US$20,000 grant to WellStar to support these efforts
The Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard (MRCT)	The MRCT Center Diversity Workgroup was formed in February 2018 to advance the goals of diverse participant representation in clinical research. The workgroup aims to substantiate the value of diversity, inclusion, and health equity; identify and analyze barriers that limit diverse participation; and develop and disseminate guidance materials, tactical strategies, and tools to advance required changes to conceptual, organizational, and operational challenges
Pfizer	The company has launched multiple initiatives for the creation of a real-time dashboard for recruitment tracking, new investigator training programs, and a collaborator network to help establish diversity as a key scientific variable across its research portfolio
Eli Lilly	The company requires that for large studies (using at least 25 sites), a minimum of 2 sites must be “diverse disease sites,” which the company defines as having at least 25% of its population as non-Caucasian
Sanofi	Sanofi engages the patient community directly to better understand how to remove barriers for participation and also partners with patient organizations. The company launched an online guide to understanding clinical research that sites and partner organizations can access when working with patients

Besides, Integrated Research Organizations (IROs) partner with healthcare organizations to provide clinical research infrastructure. They use data and analytics to align trials with population health initiatives to serve patient needs and embed clinical trial navigators within healthcare organizations to work alongside providers and patients to increase clinical trial participation.

Trial navigators also play a key role in assisting patient volunteers in their clinical trial journey, thereby making IROs a direct-to-patient model centered on improving patient access to clinical trials. IROs can work with CROs and sponsors to provide benefits such as rapid site activation, enhanced enrollment and retention, and access to diverse patient populations. IROs can especially boost diversity rates where minority community physicians do not have exposure to clinical trials in progress.

Challenges with diversity initiatives today

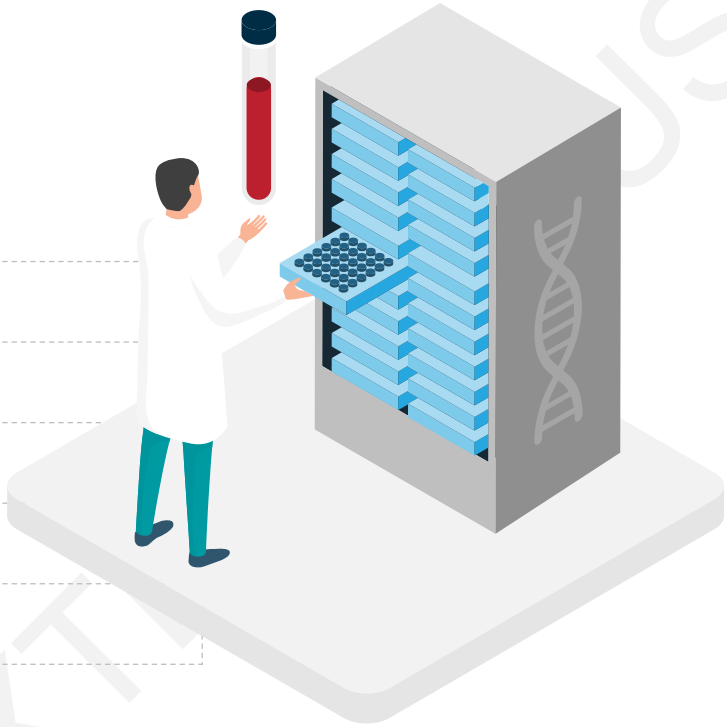
What's missing in current approaches?

Though regulatory agencies and the industry have taken several proactive measures to increase diversity in clinical trials, there are several factors that are hampering the goal of diversity, as illustrated in Exhibit 6.

EXHIBIT 6

Challenges with diversity initiatives today

Source: Everest Group (2020)



- **Disjointed approaches**
- **Lack of a shared vision**
- **Absence of incentives**
- **Minimal technology investments**
- **Lack of a global approach**

- **Disjointed approaches:** Current approaches to tackle diversity challenges are highly disjointed, and, as revealed by Exhibit 5, highly specific to a company's needs. Different stakeholders, such as sponsors, CROs, physicians, and patients, are each taking their own approach to resolve diversity requirements in clinical trials. For instance, sponsors expect high-performing sites to recruit minority patients, which might not always be possible. CROs lay heavier emphasis on certain minority communities. Physicians serving the minority communities are not involved in CROs' and sponsors' recruitment efforts. The result is a diluted and inefficient approach that lacks the synergistic benefits of all stakeholders working in unison to enhance diversity
- **Lack of a shared vision:** While the FDA published guidance on enhancing diversity of clinical trial populations in June 2019, the stakeholders are not bound by these guidelines. These guidelines also do not address aspects such as the lack of a shared vision among stakeholders to resolve diversity-related challenges. The industry does not have a clear definition of diversity to follow, nor any recommended guardrails to ensure diversity in clinical trials. Limited progress in improving diversity can also be attributed to the absence of recommended industry standards for diversity, for example, the minimum percentage of minority populations to be enrolled in a trial so that the trial qualifies as a diverse trial or the minimum representation of patients by gender and socioeconomic status for trials
- **Absence of incentives:** The lack of incentives or regulations also creates a challenge because there is no mandate to tackle diversity issues. While regulators require sponsors to report diversity information in clinical trials, this is currently only being used for analytical and reporting purposes. Instances of denying drug approval on the basis of lack of patient diversity are rare, if not absent.

As incentives drive outcomes, the present scenario does not offer much to stakeholders to resolve diversity challenges in clinical trials, as neither the regulators nor the sponsors incentivize (or even disincentivize) the inclusion of diverse patient populations in clinical trials

- **Minimal technology investments:** A key aspect is the lack of awareness of technology's potential to resolve the diversity challenge. This is where software providers come into the picture – the current landscape of clinical trial solutions offers only a point solution approach to tackle diversity challenges. These solutions are largely aimed at patient recruitment, eConsent, and site selection. However, to unlock the full potential of technology, stakeholders need to adopt a holistic approach across the clinical trial landscape. An end-to-end clinical trial platform will provide various stakeholders with a common set of functionalities to address diversity challenges. As data silos and process inefficiencies are eliminated, stakeholders can effectively collaborate and track the progress of diversity initiatives
- **Lack of a global approach:** Most diversity initiatives are concentrated in the US and Europe. However, as highlighted in Exhibit 1, 35% of trials take place outside these locations; these measures need to percolate to the rest of the world to improve the diversity of clinical trials across the globe

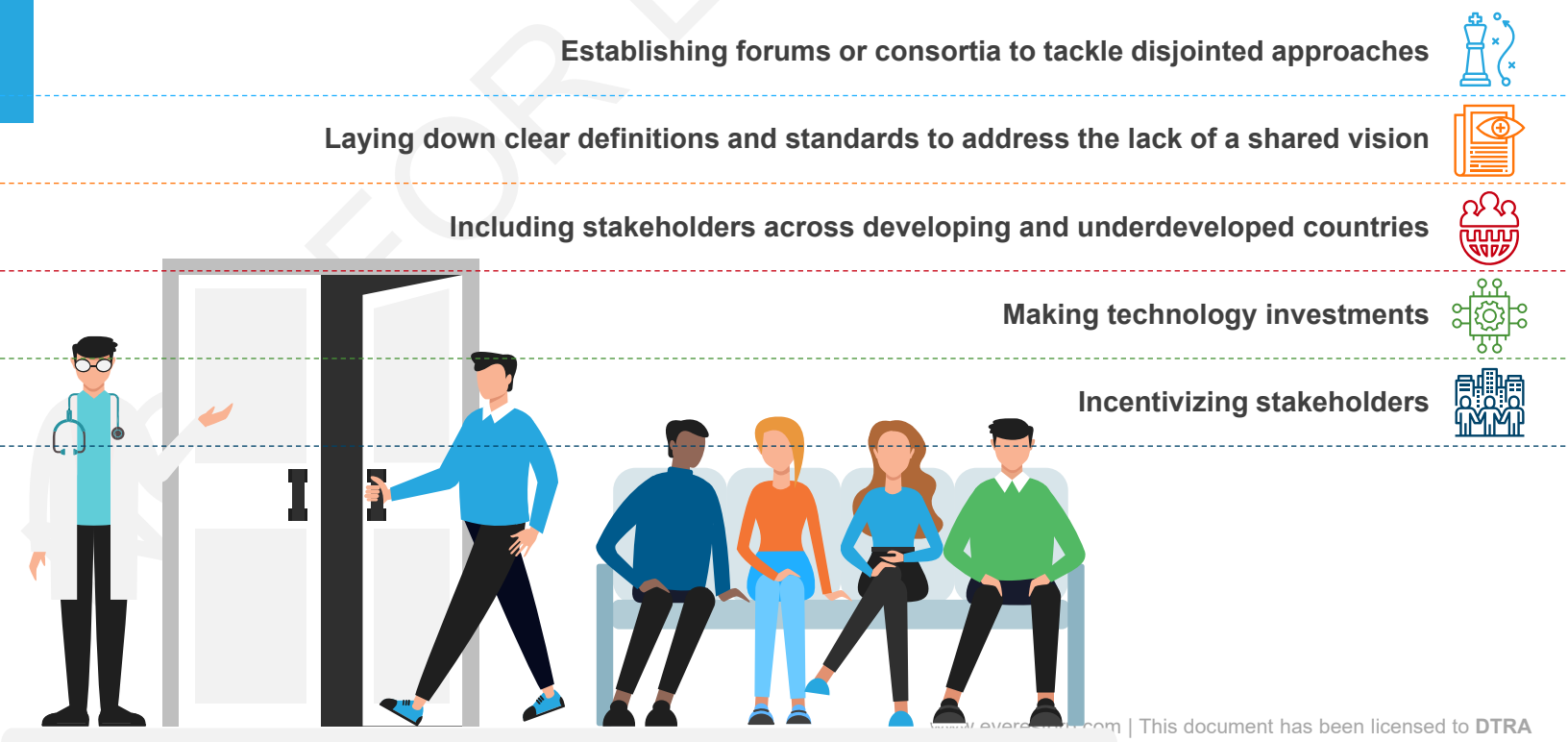
Initiatives needed to plug diversity gaps

It is evident that the current set of initiatives to address diversity challenges are not enough – there is a need for a unified approach and all stakeholders need to be in agreement about what diversity in clinical trials truly entails. To gauge the upside of adopting a technology-led view, stakeholders need to co-innovate and adopt solutions across the end-to-end clinical trial landscape and not just in the trial start-up phase because diversity challenges loom large even during a trial's conduct and close-out phases. Exhibit 7 lists initiatives that can address the gaps in current diversity approaches.

EXHIBIT 7

Initiatives needed to increase diversity in clinical trials

Source: Everest Group (2020)



- **Establishing forums or consortia to tackle disjointed approaches:** Such forums will consist of representatives from all stakeholder groups – sponsors, CROs, minority patient communities, regulators, and physicians. Existing forums or consortia can also include diversity in clinical trials to get started in this area
- **Laying down clear definitions and standards to address the lack of a shared vision:** It is important to establish clear definitions of diversity and identify guardrails of significance when looking at diversity in clinical trials. While each drug would have a different composition of diverse patient populations, it is important to have a set of standards that earmarks certain criteria to be met when striving for diversity in clinical trials
- **Incentivizing stakeholders:** Efforts should be made to discourage the lack of diversity through stricter regulator scrutiny. Also, stakeholders should be incentivized, for example, physicians for their time spent in referrals, CROs for diverse site selection, and patients through reward programs, to improve clinical trial diversity. Instituting rewards and sharing of best practices should also be encouraged
- **Making technology investments:** Trial management platforms should be embedded with functionalities to improve diversity. Firms should co-innovate with leading product vendors to develop a mature solution capable of supporting diversity functions across the clinical trial value chain
- **Including stakeholders across developing and underdeveloped countries:** Stakeholders should support the adoption of best practices in developing and underdeveloped countries and encourage the adoption of solutions with inbuilt functionality for enabling diversity

A technology framework to increase diversity in clinical trials

Current and future state of technology landscape for diversity and inclusion

Undoubtedly, technology will play a major role in resolving diversity challenges. However, current technology leverage is limited to using data analytics to identify highly diverse sites, developing patient-facing applications to simplify onboarding operations and improving patient engagement, and using data analytics to build dashboards to display performance metrics on diversity. These are purpose-built technology applications designed to help resolve diversity challenges in clinical trials.

But, we believe, that the technology to increase diversity in clinical trials will evolve in three phases:

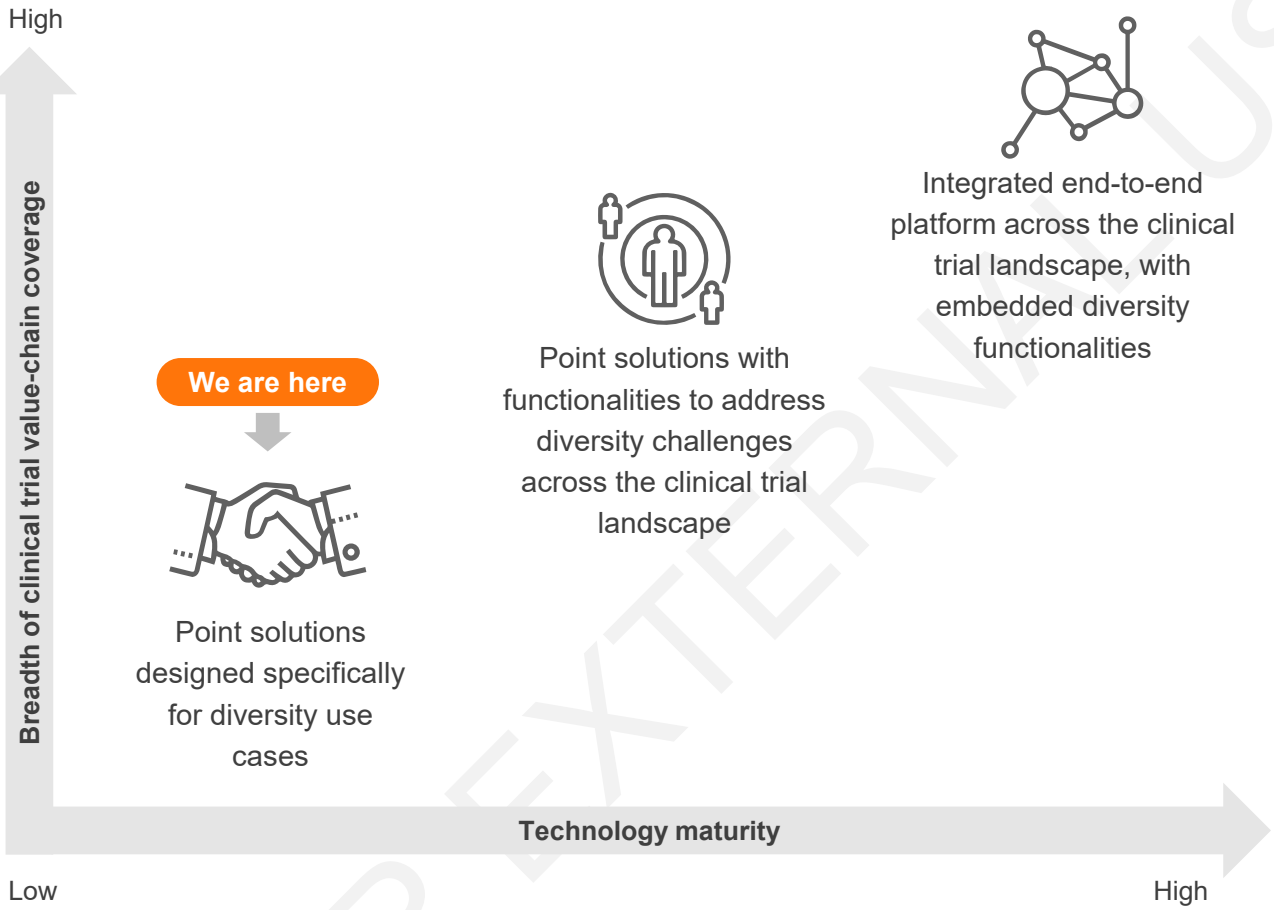
- **Bespoke solutions:** The life sciences industry is currently adopting point solutions that are purpose-built for the diversity challenge and cover mostly the trial start-up value chain
- **Solutions with integrated diversity-enablement capabilities:** To get to the next wave of innovation, diversity solutions need to cover the end-to-end clinical trial value chain. Diversity enablement functionalities will be embedded in existing clinical trial solutions, such as Clinical Trial Management System (CTMS) and Regulatory Information Management (RIM) systems
- **Interoperable and end-to-end solutions for clinical development:** The final wave of innovation will happen when the solutions integrate into an end-to-end modular and interoperable platform. The platform will cater to diversity requirements, along with other clinical development functionalities

Exhibit 8 illustrates the phased maturity required in technological solutions to enable diversity.

EXHIBIT 8

Technology maturity of solutions to enable diversity

Source: Everest Group (2020)



Technology interventions for diversity across the clinical trial value chain

At present, most technology interventions exist in the trial design and start-up value chain, indicating that once a trial's diversity requirements are fulfilled, the focus simply shifts to continuity and trial management. However, interventions are also needed to maintain diversity in clinical trials during conduct and close-out because financial and economic barriers can result in a higher dropout rate for minority patient populations.

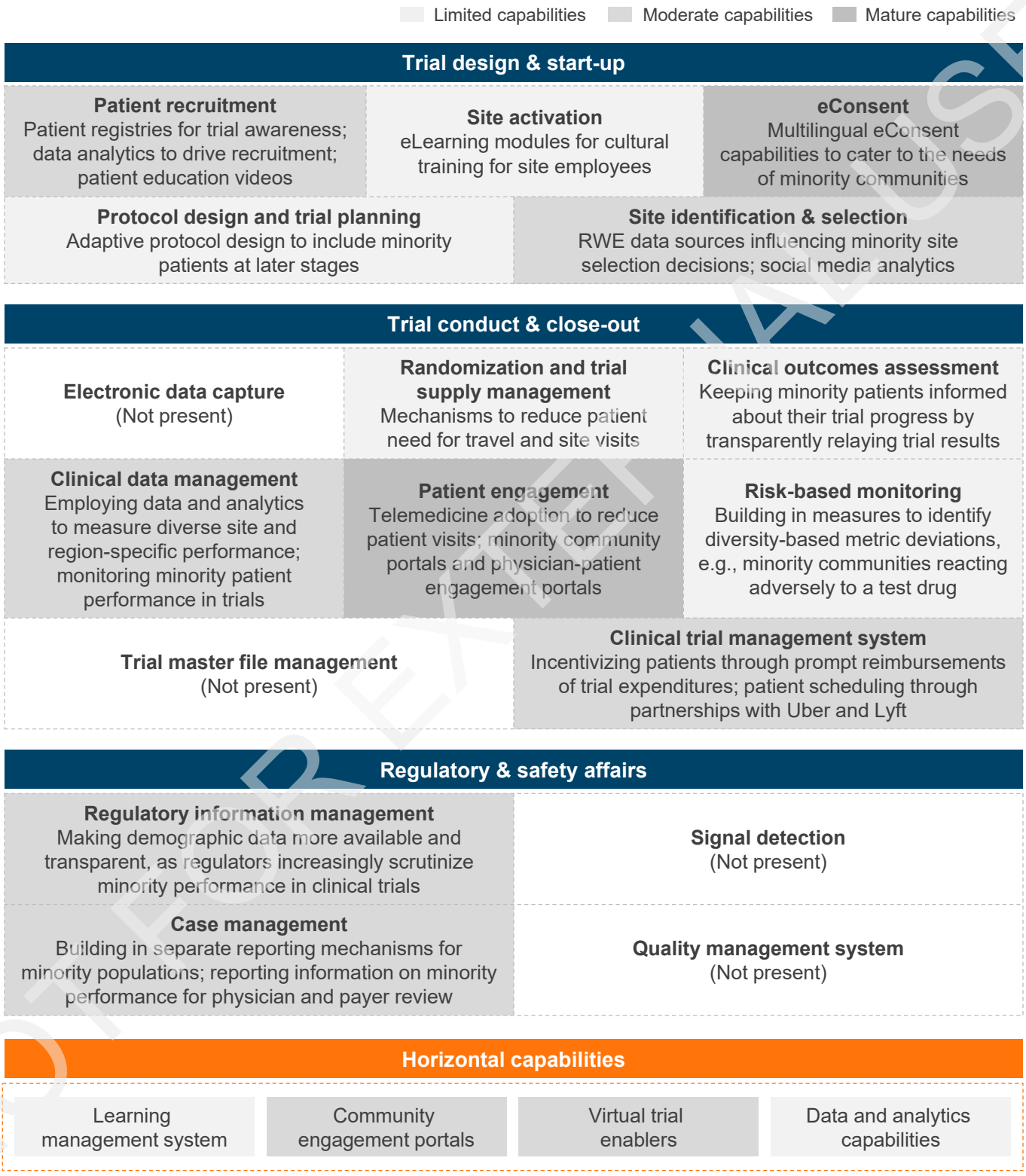
Also, low minority patient engagement can result in misinformation or limited information around their participation, which can drive minority patients to feel sidelined and disinterested in future trials. This is exacerbated when the results of a clinical trial are not communicated to the patients, which leaves them in the dark and deters future participation. Thus, it is important to design solutions that enable diversity in clinical trials, not only during trial start-up but also during trial conduct and close-out.

Exhibit 9 (on the next page) shows some technology interventions – both existing and forward-looking use cases – along with the degree of adoption in the clinical product ecosystem today.

EXHIBIT 9

Technology interventions to increase diversity across the clinical trial landscape

Source: Everest Group (2020)



Note: Limited capabilities indicate that the solutions include few capabilities that cater to diversity in trial requirements. Mature capabilities indicate that the solutions have capabilities that also cater to diversity requirements in clinical trials.

- **Interventions in the trial start-up technology landscape:** The trial start-up phase involves solutions that help sponsors discover sites that have access to diverse populations. Data analytics solutions that analyze sources of Real-World Data (RWD) and social media for patient recruitment are widely used to include diverse patient communities. Patient registries that store patient records, as well as information that enables patients to proactively locate sites with ongoing trials, can also serve as avenues for patient recruitment, while keeping patient engagement rates high. Such registries can also include videos to help patients understand trial-related aspects and reduce the stigma and aversion associated with clinical trials. The next stage involves solutions that enable minority patients to understand the trial process through e-learning modules and capture participation consent through multilingual eConsent capabilities. Only protocol design and trial planning offer limited visibility around such applications. To accelerate timelines, the FDA has suggested adaptive trials so that minority patients can be included in later phases, such as Phase II or even Phase III of a clinical trial. However, to avail this functionality, sites need to meticulously plan and design for the trials in advance
- **Interventions in trial conduct and close-out technology landscape:** The current solutions are geared to help engage minority patients and include telemedicine applications, which help reduce economic and physical barriers by enabling remote physician consultation. Solutions such as portals for community engagement with sponsors and CROs are also available so that sites can continue to engage with ongoing clinical trial patients and potential patients. Certain solutions also provide payment processing functionalities so that reimbursements for trial patients can be tracked better and approved faster. In fact, the need for reimbursement can simply be eliminated in situations where the sites can partner with mobility providers to transport minority patients. What is currently absent, however, is a mechanism to communicate with patients about trial progress and, in some cases, how their data influences trial decisions (often referred to as lay summaries). Solutions that can analyze a drug's performance on a minority community and flag any outlier cases or potential side effects are also currently limited currently. Risk-based monitoring solutions help detect outlier cases and can be used to observe a drug's performance on minority populations to detect any anomalies
- **Interventions in the regulatory and safety affairs technology landscape:** Regulatory and pharmacovigilance systems today have limited functionalities for diversity in clinical trials. However, as regulatory interest in this area increases, these solutions will have to evolve to report and screen details related to certain diversity guidelines. For example, in 2016, the FDA updated a few guidelines on reporting race and ethnicity data in clinical trials and submission of such data through applications electronically

Virtualizing trials to improve diversity metrics

Virtualized clinical trials are studies where certain parts of a trial are conducted outside of a clinical site, such as capturing of patient consent, data capture and monitoring through sensors or remote monitoring devices worn by a patient, and physician consultation through telemedicine platforms. This can deliver many benefits to life sciences companies, including cost savings, better patient recruitment and retention, and improved data quality. While virtualized trials are a widely debated topic, they have only recently gained attention, catalyzed by the COVID-19 pandemic. Of course, much of their success lies in the strength, viability, and rigor of the technologies that support them.

The benefits of virtualized trials are manifold, including:

- **Reduced costs:** Virtualizing a trial reduces setup, monitoring, and associated costs
- **Patient centricity:** Virtualized trials improve patient enrollment, as the need for frequent site visits is reduced. Due to improved patient engagement and reduced patient burden, patient dropout rates also decrease. Studies have also shown that 54% of potential patients would be willing to participate in a trial if it were virtualized[1]
- **Improved resource utilization:** Such trials present numerous advantages to trial sites – with improved recruitment and retention, sites can focus on value adding activities such as patient safety monitoring and patient engagement. Also, as the site staff spends less time with each patient, sites can leverage their resources more efficiently and manage more trial activities simultaneously

> "We (the FDA) believe that more accessible clinical trials can facilitate participation by more diverse patient populations within diverse community settings where patient care is delivered, and in the process can generate information that's more representative of the real world and may help providers and patients make more informed treatment decisions."
>
> - Scott Gottlieb, Former FDA commissioner

The same reasons also make virtualized trials suitable for improving diversity in a clinical trial. Their patient-centric nature significantly reduces the barriers to minority participation in a clinical trial. As highlighted in Exhibit 10 (on the next page), virtualized trials, backed by technologies such as the cloud, remote monitoring, and mHealth, address almost all the barriers that a patient belonging to a racial or ethnic minority can face.

The virtual mode of conduct increases the horizon of eligible patients, as patients farther from a site can also participate due to reduced or limited travel requirements to clinical sites. Therefore, sponsors can select sites that can recruit patients from diverse communities rather than relying on best-performing sites, which may not have access to diverse patient populations. This makes virtualized trials highly inclusive.

Right from the onset, virtualized trials provide the capability to link patients and healthcare staff through telemedicine to establish an authentic, human connection with patients who have limited access to care facilities, thereby reducing physical barriers. These telemedicine consultations can be scheduled as per the patient's schedule, and, thus, patients need not take time off from work or family obligations. Through the design of patient-facing applications, trial sites and sponsors can design consent forms for minority patients in various native languages and accept the consent electronically. To help patients to understand the trial process, various documents and videos can be presented in native languages to keep cultural and linguistic barriers at a minimum. Most virtualized trials leverage remote monitoring devices such as wearables, sensors, or smartphone applications, making it convenient to track adherence to drug regimens and alert sites and patients about any vital parameters that merit attention or adverse reactions.

1 Pharmaceutical processing article on "Are Site-less Trials the Future of Clinical Research?," May 2018

As data is relayed directly to the cloud from such devices, the data capture quality is very high. Keeping minority patients updated on their trial performance and educating them about how their participation contributes to trial progress reduces trust barriers and improves their experience during the trial. For trials that require the measurement of vital parameters – which cannot be performed through wearables, sensors, or by the patients themselves – trial sites can capture them through home health nursing services, as part of which nurses visit the patient's residence to track the parameters. This facility significantly reduces the need for the patient to travel. Virtualized trials hold immense potential to revolutionize the clinical trial landscape, especially for aspects such as diversity and inclusion in clinical trials. All that is needed is for product vendors and the clinical trial community to build resources and functionalities that enable minority patient participation and engagement in clinical trials.

EXHIBIT 10

How virtualized trials and technologies address various diversity barriers

Source: Everest Group (2020)

Applications for monitoring adherence	Telehealth and mHealth applications	Wearables for continuous data collection	Cloud-based data collection	Electronic patient reported outcomes	eConsent

Role of virtualized trials in addressing various diversity barriers

Economic barriers	Linguistic barriers	Cultural barriers	Physical barriers	Trust barriers
Prompt reimbursements and rewards for participation in clinical trials; remote monitoring to reduce minority patient burden through reduced need for visits; sponsor-provided tablets or smartphones with in-built trial management applications to allow for virtual mode of trial conduct	Design of consent forms in native languages and remote submission of eConsent; use of patient-facing applications in patients' regional languages; contact centers with native speakers to address patient issues and queries regarding trial progress	Matching of patients with physicians of the same culture and race during remote consultations	Reducing frequency of visits through telemedicine and remote consultation applications; functionality to book rides from ride services companies directly from patient-facing applications for hassle-free travel to sites	Sharing lay summaries and trial performance updates frequently and directly with patients through patient-facing applications; encouraging minority participation in clinical trials through in-app educative campaigns, promotional seminars with native influencers, and eLearning videos

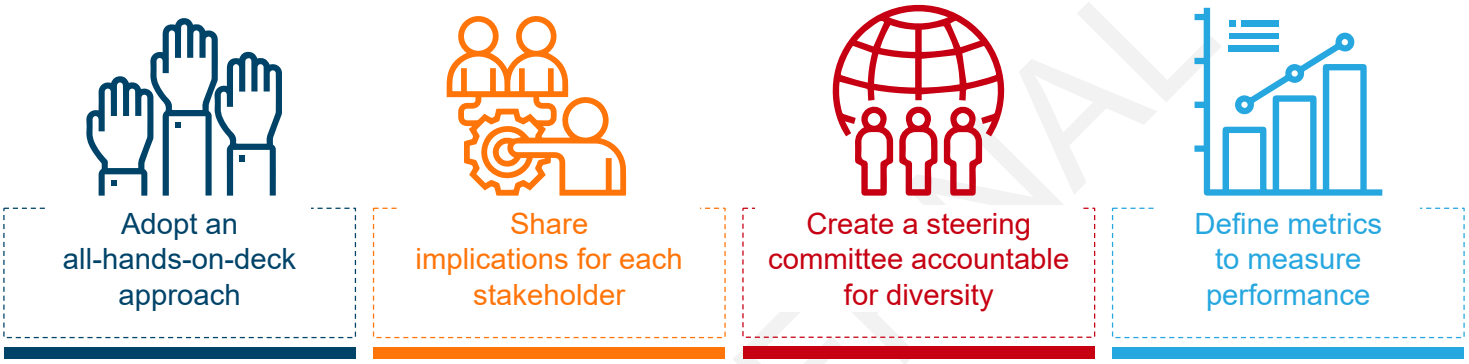
Preparing a blueprint for success

The journey to success begins when all stakeholders are on the same page and know their individual responsibilities. It can be significantly improved by setting up a steering committee accountable for ensuring diversity in clinical trials and agreeing on metrics that can be tracked to measure performance. Exhibit 11 proposes the action items for stakeholders to help address diversity challenges in clinical trials.

EXHIBIT 11

A blueprint for success

Source: Everest Group (2020)



Bringing the ecosystem together

To accelerate the diversity conversation, stakeholders need to adopt an all-hands-on-deck approach. There are different implications for each stakeholder and only if each performs their part, can the industry get past the diversity challenge. The ecosystem has five major players that can bring about meaningful change to the current diversity situation: patients, pharma sponsors, clinical trial sites or investigators, physicians and health systems, and regulators.

- **Patients:** While the onus is not on patients to drive diversity in clinical trials, patients can contribute to diversity by proactively looking for participation opportunities, being open to community engagement initiatives organized by various organizations, and placing faith in the regulatory and trial conduct ecosystem
- **Sponsors:** To involve diverse communities, clinical trial sponsors should partner with racial and ethnic minority communities. This can be done in conjunction with minority-serving organizations and minority influencers to spread awareness about diversity in clinical trials. To further these campaigns, sponsors should develop educational material in minority-native languages to maximize retention and reception. Also, besides targeting communities, sponsors should intentionally select research sites that are rich in minority communities and not restrict themselves to the traditionally best-performing sites, which may not be rich in diversity. This step might incur additional costs in the short term in the form of additional resources to support site recruitment, documentation to support minority communities, as well as extra effort on ensuring retention of such patients. However, these efforts are necessary to achieve diversity in clinical trials. While trial sites can offer virtual trial options to patients, it should be noted that minority patients face additional hurdles such as limited access to WiFi or cellular plans, and, therefore, the costs of enabling these functionalities should be factored in by sponsors. All these initiatives will not take off unless backed by a steering committee comprising senior leadership from

the sponsor organization, which can oversee progress and financially commit to diversity improvements in clinical trials. It is also important to remember that clear communication of diversity goals and transparency in reporting is vital between sponsors and trial sites

- **Investigators:** The most important task for clinical trial sites is to build trust with minority communities. This requires building reciprocal and long-term relationships with various community stakeholders. Effective ways of building trust include the involvement of minority stakeholders in identifying minority patient needs and interests, and then designing recruitment and retention strategies so as to minimize patient dropout. Trial sites should also establish themselves as trusted information sources by frequently updating participants about trial progress. To perform well, it is important that sites provide cultural training to their staff so that they are aware of the implicit biases and ways of effective communication with minority patients. The sites can also coordinate with physicians that serve minority communities to establish robust referral programs and encourage them to refer patients for clinical trials. As a final step, the sites can hire staff from minority communities so that patients can engage best with them and feel a sense of connectedness
- **Physicians:** Physicians are often best placed to help minority patients understand the requirements of a clinical trial and how patients can benefit by participating in such trials. They are also the first point of contact in the patient journey for care and, therefore, can influence minority participation in clinical trials happening nearby. However, physicians need to be compensated for spending time in processing the referrals and should be provided with adequate resources so that they can educate patients about participating in clinical trials
- **Regulators:** Regulators, being the utmost authority, directly influence clinical trial diversity. While the FDA has been vocal about diversity and recommended guidelines to improve it in trials, it also needs to roll out a common framework defining diversity and indicative metrics to satisfy diversity requirements in different clinical trials. Regulators should examine trial data submission with greater emphasis on diversity metrics, especially for drugs meant to be sold to a large population set. They should also make available resources that make the minority population aware about the importance of diversity in clinical trials
- **Software vendors:** A community that often gets excluded from diversity discussions is software vendors, which orchestrate the platform that brings together all stakeholders on the same page. A co-innovation model driven by feedback from the stakeholder community will help improve the current ecosystem of diversity technology solutions

Measuring success and governance mechanisms

The management adage “What gets measured, gets done” is particularly relevant for diversity and inclusion in clinical trials. This is because it takes more than well-intentioned policies and programs to shift industry mindset toward increasing diversity in trials. Measuring performance and metrics helps steering committees stay on track, helps identify challenges and biases, and prevents stakeholders from going back to habitual patterns that eventually limit the overall progress.

Exhibit 12 (on the next page) lists the key metrics to track for ensuring diversity in clinical trials.

EXHIBIT 12
Key metrics to track for ensuring diversity in clinical trials
Source: Everest Group (2020)

Ease of uptake, access, and maintenance of technology used by minority patients	**Enrolment rates by minority population race and ethnicity**	**Number of diversity-rich sites selected**	**Dropout rates of minority population and top reasons for dropping out**	**Number of minority communities engaged with and number of campaigns run**	**Reception of training and educational material by minority patients**

Tracking these metrics will help improve the overall diversity scenario and prevent a return to traditional ways of functioning. Ultimately, the metrics look at sponsor performance in intentionally selecting diversity-rich sites even though they may require additional efforts in activation. Once activated, a site-wise tracking of the minority population's enrollment and close monitoring of dropout rates serve as site performance indicators for diversity. It is also important to understand minority patients' major reasons and concerns when dropping out from clinical trials, so that sponsors and sites can alleviate the challenges through technology or other appropriate measures.

The overarching consideration when setting meaningful metrics is that they must map progress to each sponsor's diversity goals. Each trial will have a different focus on patients, and sponsors need to agree on the diversity metrics to adhere to while conducting trials. Adhering to these baseline metrics will eventually require the assignment of responsibility and accountability. The steering committee will be primarily accountable for adherence to the agreed metrics. It should transfer the responsibility to on-field execution teams by creating appropriate scorecards based on the identified metrics.

Once the formal plan is developed, it is important to analyze and report the findings, agree on the frequency of convening, and the process for reporting the findings in a transparent manner. The steering committee can also consider incentives for execution teams and including outcome-based measures, such as improvement of diversity metrics when engaging with CROs, to emphasize the focus on diversity.

Tracking diversity performance entails two kinds of metrics – diagnostic metrics and progress-tracking metrics. Exhibit 12 shows key diagnostic metrics to track. Progress-tracking metrics track the progress of various stakeholders' efforts in achieving diversity and include participation rates in formal meetings, execution of initiatives stemming from analyzing diagnostic metrics, and recognition conferred to teams excelling in diversity metrics.

Conclusion: focus on the journey

Diversity-rich clinical trials – those that enroll adequate sections of the population from varying ethnicities/races, genders, geographical locations, and socioeconomic statuses – enrich the safety and efficacy data of clinical research.

While efforts are being made to ensure inclusivity in trials, they are highly limited – with top life sciences companies piloting initiatives aimed at improving the situation in certain studies. The lack of regulatory enforcement or penalties in this area do little to incentivize efforts in this field. The current suite of technology solutions, too, are not enough.

Technology can play a big role in improving the diversity situation in clinical trials. Clinical development solutions with in-built functionalities to enhance diversity needs can be deployed right from the trial planning stage through the trial close-out stage. In particular, virtualized trials, due to their patient-centric nature, have immense potential to significantly improve the quality of clinical trials by not only improving data quality and ease of trial conduct, but also directly addressing patient barriers to diversity.

However, to really address diversity gaps, all stakeholders need to work in unison. Bringing together all stakeholders, delineating responsibilities, setting up a steering committee accountable for ensuring diversity in clinical trials, and deciding metrics to track the success of initiatives would be essential to ultimately improve patient diversity in clinical trials.

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For more information about Everest Group, please contact:

+1-214-451-3000
info@everestgrp.com

For more information about this topic please contact the author(s):

Nitish Mittal, Partner
nitish.mittal@everestgrp.com

Chunky Satija, Practice Director
chunky.satija@everestgrp.com

Nisarg Shah, Senior Analyst
nisarg.shah@everestgrp.com