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ESTABLISHING STRATEGIES TO IMPROVE DE+I IN CLINICAL TRIALS

Considering diversity, equity, and inclusion (DE+I) in clinical trial design and delivery is essential to properly measure treatment effectiveness and safety for therapies serving global patient populations. While the concept is nothing new to the clinical trial space and progress has certainly been made, increasing DE+I in clinical trials must remain an ongoing commitment for sponsors, clinical trial coordinators, and clinicians as well as community partners.

As part of this continuous DE+I journey, sponsors must be intentional when designing clinical trials, identifying site locations, and establishing patient screening criteria to ensure that patient populations best represent those potentially eligible for their therapies. This would require equitable representation of races and ethnicities as well as individuals from differing socioeconomic backgrounds, sexual orientations, gender identities, neurodivergences, and physical disabilities in the overall population.

History of DE+I and Clinical Trials

More than 80% of clinical trials are conducted in the developed world. The concentration of trial sites presents a problem for sponsors developing global therapies because developing countries represent the majority of the world's population and bear 90% of the worldwide burden of disease. In the United States, clinical trial populations have consisted mostly of white males. Even today, African American patients, for example, represent less than 10% of clinical trial participants. This representation imbalance has been significant in contributing to health disparities in minority communities, as treatments are tailored to only a narrow subset of the population and impede the quality of healthcare decision-making and even the development of more effective treatments.

As the industry turns its attention towards precision therapies, there's a risk of continued exclusion and outcome disparity if trials aren't designed with a broader view of recruitment factors. Considering race, ethnicity, sexual orientation, socioeconomic status, age, ancestry, and gender identity in clinical trials can yield broader inclusion and potentially new insights into drug efficacy. It also takes the industry one step closer to advancing health equity for historically underrepresented groups. Achieving health equity begins with each clinical sponsor and the actionable steps that they can take to expand DE+I in clinical trials.

Correcting Historical Health Inequities: Pre-Clinical Trials

Issues in past clinical trials, such as involuntary patient commitments and harmful management, have fostered distrust in many communities. These past issues still impact recruitment efforts and participation today as individuals choose not to opt into studies. There are steps that sponsors can take as they implement broader DE+I strategies for their trials:

1. **Leveraging Culturally Relevant Marketing**
   One means of bridging distrust is by utilizing culturally relevant marketing. This might mean

using language or imagery that connects with target communities in an authentic manner. A best practice for building this type of marketing is to work directly with members of the community to craft a message that will be fully embraced by the group.

It's also important to be aware of where marketing will be the most effective. Working with community leaders to understand certain places that are central to a group is key. Whether these are recreation centers, religious institutions, or local shops, being able to place marketing in culturally important locations can be a catalyst to opening dialogue.

Ultimately, rebuilding trust in a community through marketing begins with awareness and is vital to help potential participants feel safe. When it comes to culturally relevant marketing, it's important for organizations to know that this takes time, and developing these relationships with communities should occur before, during, and after the clinical trial process.

2 Building the Patient Relationship

It's crucial for sponsors to be mindful of the need to establish strong clinician-patient trust. Recruiters should have an understanding of the local community, any common barriers to participation (e.g. site access and trust), and an ability to explain the purpose of the trial in the context of its potential benefit to the community. Often the best clinicians for target groups are those who are members of that group themselves. This is important because patients may feel more comfortable participating with those who have shared experiences, being honest throughout the trial, and voicing concerns they may have.

A diverse clinical staff can also have insight into a culture that would otherwise be overlooked. This means recognizing, understanding, and addressing implicit biases that may skew patient interaction. Further, sponsors can partner with diverse clinical trial primary investigators (PIs) in addition to contract research organizations (CROs) with recruiting capabilities within diverse populations. These should be people that understand minority hesitancies and can effectively build trust through shared experience and educational programs.

Additionally, removing language barriers is a critical factor in building relationships Those who do not speak the primary language used in the testing protocol as their native language may feel uncomfortable participating or hesitant to voice their concerns. Sponsors must be mindful of their clinical research teams' backgrounds and demographics to ensure patients feel seen, represented, and heard.

3 Educating Communities

Issues of past unethical trials and ongoing experiences of bias in the delivery of care to marginalized communities are barriers to trust that sponsors will need to work to overcome. Broadly educating communities about the benefits of diversifying trials can begin to build a

bridge of cooperation. Training recruiters to include messaging about how the study may positively impact the community to which a potential patient belongs may persuade them to participate and even advocate for the trial to others.

DE+I in clinical trials has tangible benefits for treatment success. As more groups are represented, researchers are better able to understand how the treatment affects the broader population. Improving clinical trials begins with a sponsor's awareness of making conscious choices to develop relationships within new communities, increasing the diversity of staff to expand thought and approaches, and working with the clinicians themselves in understanding the past and how to best approach different communities.

Considerations for Clinical Trials Design to Improve DE+I

DE+I within clinical trials goes far beyond just including more diverse individuals in the trials themselves. Engaging underrepresented groups often means rethinking entire strategies for designing clinical trials. To achieve clinical trials that are more representative of the overall population, sponsors and clinical trial coordinators must partner together on efforts for site location and patient selection and recruitment. The protocol should be reviewed to consider several dimensions:

Considerations for Site Selection

Location

Sponsors can consider opening a greater number of smaller locations to better distribute care sites geographically in target communities. Areas that are central to a community like recreation centers, places of worship, or shopping centers can often serve groups that are distant from medical centers and enable greater participation from previously excluded groups. Creating local partnerships through community-based locations can establish a more permanent partnership and presence within the community while also being economically friendly.

Accessibility

Clinical trials have historically been clustered around wealthier geographic regions because that's where hospitals with trained PIs have tended to congregate. This means that members of lower socioeconomic classes were often excluded due to an inability or unwillingness to commute to the test site. Sponsors can actively address this inaccessibility by selecting testing locations within target regions and engaging with trained PIs who represent these populations.

The pace of technology may also allow some clinical trials to be conducted remotely. Decentralized trials have enabled new capabilities, such as video conferencing tools

working in tandem with remote, data-collecting wearable device, which can effectively bridge the gap for individuals who otherwise couldn't participate. This has been especially bolstered with the rise of faster connectivity through 5G. However, there are other factors that also need to be considered and designed for in testing approaches, as certain populations may not have access to that technology in the first place.

Accessibility goes beyond just the physical location of a clinical trial site. Sponsors should also consider:

- ? What are the hours and days that trial sites are available to patients? Are your patients always working when the clinic is open?
- ? What are the commuting patterns of the area? Can people reasonably get from home or work to the site for check-ups?
- ? If the trial uses technology, will the participants need to be trained to use it? Will they have reliable broadband?
- ? Is hybrid data collection necessary? If so, are there funds to pay for the technology used?

Resource Support

Beyond considering trial site locations, sponsors can support patients by working with needs on a case-by-case basis. If it's unlikely that a clinical trial site will be moved from a location that is only accessible by car, then sponsors may consider arranging transportation or reimbursing travel costs. For example, most areas have access to ride sharing services such as Uber and Lyft, so visits to and from the site can be paid for.

Considerations for Patient Selection and Recruitment

Eligibility Requirements

For those who are willing to participate, sponsors must actively consider how to approach screening. One such consideration is basic eligibility requirements. Expanding the criteria for who can participate may include widening age limits, seeking more diverse participants and women, and examining patients with comorbidities on a case-by-case basis. Sponsors should examine common factors that may have led to historically high rejection rates for certain groups and reevaluate whether they're appropriate.

Social Determinants of Health

Health and treatment outcomes are often affected by social factors like employment, living environment, access to transportation, family education, and more. These social determinants of health (SDOHs) are often linked to systemic racism and can be seen

through inequality in education, healthcare, and residential neighborhoods. SDOHs are extraneous factors that can affect health and outcomes from a clinical trial. For example, some participants of a study may live in a heavily polluted region, which poses added risk for undergoing the treatment. These factors can be extremely wide-ranging, so it's up to firms to fully evaluate uncommon factors to determine risk and accurate results.

As a result of SDOHs, the health outcomes of clinical trial participants can be wildly different even amongst those who appear to be inherently similar. For example, multiple individuals of the same sex and pre-treatment health may have different education or employment that drastically alters results. This can be both dangerous for sponsors and the patients themselves because certain effects of the SDOHs are not anticipated.

Real-World Data

Diagnostics – or the lack thereof – is something sponsors need to keep in mind when it comes to increasing the diversity of patient population within clinical trials. There may be patients who don't realize they're eligible for a clinical trial because they haven't yet been diagnosed with the illness and that diagnostic information isn't available to them. As a potential solution, sponsors should leverage real-world data (RWD) – or data relating to patient health status and the delivery of healthcare routinely collected from a variety of sources – to better support clinical trial designs and ensure patients who do qualify are considered.

According to the FDA, RWD sources typically include more diverse study populations as compared to data collected in traditional clinical trials. Through RWD, sponsors have access to a database of real-world clinical observations and measures that would be otherwise difficult to obtain. This information can be used to drive their research further and identify clinical patterns under real-world conditions.

Recruitment

Sponsors and clinical trial coordinators most likely have a diligent process and strategy when it comes to selecting and recruiting patients. However, it's important to keep in mind that the resources, agencies, or tools used in the past to increase diversity in trial participants may not be the best approach for the next time, as DE+I initiatives must be continuous and evolving. As sponsors and clinical trial coordinators pursue different marketing and recruiting strategies, they'll need to layer in these considerations from a DE+I perspective and not solely rely on tactics used in the past.

Proper screening and selection are vital to improving DE+I within clinical trials. This includes expanding eligibility requirements, understanding the history, and taking an active approach to recruit wider range of individuals – all important factors in creating health solutions that address broader populations and reverse historical inequities. Ultimately, DE+I within clinical trials begins with reevaluating design strategies and giving active consideration to all facets of a trial.

One Step Further: Retention Strategies in Clinical Trials

Now that you've taken into consideration a number of factors for clinical trials design and are in the active phase of the trial, what's next? Considering DE+I within clinical trials is not simply a task for when the trial is ongoing. To properly expand the range of clinical trial participants, sponsors must consistently build trust within communities before, during, and after trials. Maintaining the trust of trial participants or the communities to which they belong begins with retention strategies.

Retention Strategies

Community Investment: Making permanent investments into communities can be vital to retaining participants. This might include construction of new buildings, healthcare facilities, or educational centers that will bolster and further engage the community. It could also mean sponsoring programs, events, local charities, or even scholarships. Regardless of what the investment is in, sponsors can create long-term relationships with communities by demonstrating their commitment.

Support: Many groups that have historically been excluded from clinical trials are also affected by socioeconomic inequities. While support can come in the form of education and investment, sponsors should also consider how they can impact communities in non-traditional ways. One means of connecting with a group is by committing to open conversations about any concerns that they may have. This allows them to have a voice in a space that has been historically closed to them.

Patient-Centric Approach: Sponsors and coordinators must take into consideration the overarching patient experience and how they can improve or optimize it. One initiative would be to allocate funding and plan for ancillary treatments and diagnostics as well as set aside funds for any complications which occur as a result of the trial. This commitment to a patient-centered approach should start from the beginning but remain constant after the trial ends in order to both address ethical concerns and work toward a future of greater trust.

Long-Term Partnerships

Developing lasting relationships with community partners is tremendously important for building long-term trust. These organizations provide outlets for community outreach, education, and connection. Some of these partnerships may be with large, nationwide health organizations like the National Alliance for Hispanic Health. A few advantages of large partnerships might include greater resources, broader outreach, and reputability. Clinical trial sponsors, however, should also seek more local organizations within targeted communities. Smaller partnerships may be with a local religious center, recreation center, or school. While these organizations may not share the same resources as some that are larger, they are vital because of the trust that their communities have in them.

Sponsors should leverage their outreach not just to educate the community, but also to hear the community members' concerns. It's equally important to understand the hesitancies of a group so that they may be addressed rather than operating off generalized assumptions. Currently, the National Institute of Health (NIH) is making efforts to partner with community health organizations through their "All of Us" Research Program, aiming to diversify the individuals participating in their research. This includes women, members of the LGBTQ+ community, BIPOC, individuals with disabilities, among others, for the purpose of expanding the safety and efficacy of treatments.

Retaining communities and individuals for clinical trial participation is difficult, but sponsors must realize that improving DE+I in clinical trials is not just a short-term task. Rather, these relationships begin long before the trial and should continue well after.

The Future of DE+I In Clinical Trials

Ultimately, improving DE+I in clinical trials is a major part of bridging historical inequities in medicine. It's crucial for new products and treatments to best address the totality of the population rather than only majority groups. The primary challenge that companies currently face with bridging these gaps is a lack of a benchmark. It's difficult to predict the results or procedures of future clinical trials with expanded DE+I because there may be a lack of comparable studies that firms can use to support their predictions. While this does present obstacles, the solution is to simply create those benchmarks one by one. Consequently, every sponsor has a role to play in advancing health equity that begins with critically reevaluating current and future clinical trial execution.

It's also important for sponsors to remember that improving DE+I in clinical trials will be a continuous journey and an ongoing commitment on the part of sponsors, clinical trial coordinators, and clinicians alike. Strategies and initiatives will need to evolve as we gain a greater understanding of DE+I in clinical trials and the impact to patient care, treatment outcomes, and overall healthcare delivery. Firms must institutionalize this ability to address that understanding in their clinical trial design and delivery in order to work toward more meaningful, impactful, and sustainable change for all individuals.

Contact us to learn more about how we can help improve DE+I in your clinical trials operations. You can also learn more about our other DE+I services here.

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