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Clinical trials have ‘much work to do’ in boosting diversity

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A veteran with more than 20 years of experience talks about the vitality of recruiting an inclusive patient population, and the perils of falling short.

Clinical research professionals often voice concern about the need to increase the diversity in the pool of patients they recruit for their studies. Regulatory bodies concur, with agencies like the US Food and Drug Administration (FDA) issuing guidance documents and challenges to ensure certain groups aren’t underrepresented—but there is still a great deal of room for improvement.

Outsourcing-Pharma (OSP) recently spoke with Aman Khera (AK), global head of regulatory strategy at contract research organization (CRO) Worldwide Clinical Trials, about the importance of recruiting diverse patient populations, and how trial teams might come closer to their diversity goals.

OSP: Could you please tell me about Worldwide Clinical Trials—who you are, what you do, who your key client base is, and what sets you apart from the competition?

AK: Founded by physicians committed to advancing medical science, Worldwide is out to change how the world experiences CROs – in the best possible way. From early phase and bioanalytical sciences through late phase, post-approval and real-world evidence, we provide world-class, full-service drug development services.

With infrastructure and talent spanning 60 countries, we execute predictable, successful studies with operational excellence across a range of therapeutic areas, including central nervous system, cardiovascular, metabolic, general medicine, oncology and rare diseases.

As a midsize CRO, Worldwide is uniquely able to flex, balance and respond to sponsors’ needs. We help pharmaceutical and biotech companies complete their trials successfully, on time and on budget. We never compromise on science or safety. We’re never satisfied with the status quo. We’re the Cure for the Common CRO.

OSP: How have clinical trial sites and sponsors typically viewed patient population diversity and inclusivity? Is that a factor they have failed to consider in the past?

AK: I’ve been in industry for over 23 years, and historically patient population diversity and inclusion initiatives have generally been considered a “nice to have” rather than an imperative. The issue has not had the momentum needed to bring about real change. There have been many worthy initiatives in this space, but they have been fragmented and fallen short.

Every year, the FDA issues a Drug Trials snapshot report. Last year only 26% of clinical trial participants were the age of 65 or older, 72% were White, 18% Hispanic, 9% Black or African American and 9% Asian. Last year, the FDA also introduced draft guidance to enhance the diversity of clinical trial populations, encouraging trial teams to broaden eligibility criteria, use adaptive clinical trial models and to consider enrollment challenges that potential participants may face.

OSP: What are some of the risks associated with failing to recruit a diverse/representative patient population in a study?

AK: Disease and illness do not discriminate. However, our age, race and ethnicity DO play a part in determining how certain conditions and medical treatments affect us.

The fundamental concern is that you are undertaking clinical research in a patient population that is not representative of the treatment's true intended patient population in the market. If it's approved for market, you have a problem.

There are many elements to diversity in clinical research: age, race, gender, ethnicity, genetics, comorbidities, concurrent medications, social determinants of health and environmental factors. These dimensions of diversity are not independent variables but rather have intersections.

We still have much work to do in exploring the basic elements of diversity before we conquer the various intersections at play.

OSP: If you can think of any, please share an example of an instance in which failure to recruit a suitably diverse population led to less-than-favorable results in a study (or, heaven forbid, a drug that made it to market).

AK: The variations in disease manifestation and treatment responses demonstrate why it is important to consider diverse populations. For example, racial differences in skin structure and physiology can affect responses to dermatologic and topically applied products.

Another example is that the frequency of CYP2D6 poor metabolizers, which is important in beta blockers, antidepressants, antipsychotic beta blockers, is higher in Whites, Blacks and African Americans than the Asian population.

The FDA has been looking at approved labelling that is related to specific races and ethnicities.

- Carbamazepine has a boxed warning that describes the risk of serious and sometimes fatal dermatologic reactions, a risk that is higher in people of Asian ancestry.
- ACE Inhibitors are associated with a higher rate of angioedema in Black than in non-Black patients. First-line therapy in African American/Black populations is often less effective than in non-Black patients due to a lower renin profile in the population.

We know that individuals of South Asian, African or African Caribbean descent in the UK are at higher risk of developing heart and circulatory diseases than white Europeans.

Much research reinforces the fact that lack of diversity in clinical research continues to allow patients from diverse populations to be ignored or not considered. Diversity in clinical research must become a business imperative for industry — if we do not include diverse populations in clinical trials, we absolutely run the risk of skewed or inaccurate results.

OSP: What obstacles do trial teams commonly face in reaching these populations?

Aman Khera, global head of regulatory strategy, Worldwide Clinical Trials

AK: These obstacles are often multifaceted and multi stakeholder related. Let's take a deeper look at obstacles at the sponsor and site level. Their lens of challenges includes the lack of patient advocacy, a fear of delaying the trial or increasing the cost of the trial.

From an investigator or clinical research staff perspective, they would probably speak to how eligibility criteria limits enrollment. Typically, patients are recruited from the same sites repeatedly. The benefit of this model is that investigators are knowledgeable and experienced; this also means trial teams may not open research naïve sites in locations that may hold more diverse patient populations.

There probably is inaccuracy at the site feasibility assessments level, which also needs to be looked at more carefully.

There are always recruitment, and just as importantly, retention challenges for trials. We must consider that there may be an institutional bias that directly results in a lack of diverse cultural understanding, paired with a lack of diverse staff at the site.

From a community and patient perspective, the obstacles that exist include:

- Distrust of research and clinical trials overall
- Lack of awareness and limited health literate education and communications
- Logistical issues of trial conduct; study design and procedures are burdensome
- Payment and other financial concerns

Additionally, there are no harmonized requirements for data collection. There is an inherent lack of data standards that results in inconsistent data analysis.. The take home point is that there are not just a few obstacles at certain levels, but that this needs attention from all stakeholders working together.

OSP: Can you talk about what sorts of tools and techniques might be available for trials to increase their engagement and recruitment with different populations?

AK: Sponsor companies must be open to change. We need to consider engaging with diverse patient communities even before having a protocol developed. Community and patient engagement are key.

Working with communities to improve information and access to clinical trials is not optional. The COVID-19 pandemic has demonstrated that overall public interest in clinical trials has increased but there is a lot

of work to do with engaging communities.

We need to think about how we reach out to research naïve sites and arm trial teams with training around inclusive language and behavior. We also need to consider offering translation or interpreter services.

We need to look at protocols with an assessment of the patient burden, to determine if steps can be taken to reduce the secondary and tertiary endpoints, potentially opening the pool of patients.

OSP: Are there any partnerships trials can take greater advantage of—i.e. community physicians, healthcare companies, advocacy groups, etc.?

AK: There are many partnerships and services available, and I'm pleased to say that our industry is making this a business imperative. The conversations in this space are finally in the mainstream, and there is no lack of help for all stakeholders wherever they are struggling.

I invite trial teams to discuss their obstacles with stakeholders, this is something that Worldwide is helping in. There are also service providers that have made it their core mission to break down the barriers and provide their experience and expertise, as well as specialized patient recruitment services to help sites identify eligible participants.

OSP: What about diversity at sites and at pharma companies—are those challenge areas in which improvement in inclusivity could lead to a difference in trial outcomes?

AK: Absolutely; we need to consider that if there is a lack of "diverse" voices at sites and biopharma companies, how are you able to understand the lens of the very patients you wish to enroll and eventually treat?

I can't emphasize strongly enough the importance of both acknowledging and understanding cultural competencies. This doesn't just come from training courses but instead having those voices represented at sites and companies.

In sites, we can all make an effort to support diverse teams that have the right intentions but may lack the experience. This is where we must work collaboratively to invest in clinical research sites for the present and for the future.

OSP: What else would you like to talk about regarding trial diversity and inclusivity that we might not have touched upon?

AK: When thinking about trial diversity and inclusivity, we need to think about the different dimensions of diversity: age, gender, ethnicity, socioeconomic status and many others. You need to take a step back.

There are many wonderful innovations occurring across our industry but ultimately, we must never forget why we do what we do: to make positive healthcare change for humanity – and that means all of humanity, not just select populations.

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