BACKGROUND

Inclusion and diversity are urgently needed in all aspects of clinical trials to generate evidence that is generalizable to and trusted by the populations who are most likely to benefit from the practices or products being studied. Fostering an inclusive environment that engages a diversity of participants, sites, staff, and investigators is vital. In this DCRI Think Tank workshop, participants discussed structures and practices that promote inclusivity and diversity to identify actionable steps that drive meaningful, sustained change in clinical trials and practice.

WELCOME AND OVERVIEW

Co-hosts Gerald Bloomfield (Duke University) and Bray Patrick-Lake (Evidation) welcomed the attendees and introduced DCRI Executive Director Adrian Hernandez (Duke University). Dr. Hernandez recalled attending a conference several years ago where he found that most attendees were interested in improving inclusion and diversity in clinical trials but few were putting resources into making it happen. The co-hosts encouraged attendees to keep their focus on practical actions for making change, given the widely recognized lack of diversity in clinical research and its multiplicity of causes.

SESSION I: A VIEW OF THE ECOSYSTEMS FROM DIFFERENT PERSPECTIVES

Moderator Bob Harrington (Stanford University) introduced the session.

Panelist Jacqueline Corrigan-Curay (FDA) summarized the FDA’s commitment to increasing the diversity of clinical trial populations. She referred attendees to several guidance documents, including the 2020 guidance Enhancing the Diversity of Clinical Trial Populations. The guidance addresses broadening eligibility criteria, designing trials for accessibility, and improving recruitment practices. The FDA is also promoting transparency in efforts to support inclusion and diversity, such as Drug Trials Snapshots to highlight demographic characteristics of clinical
trial participants. “Decentralized clinical trials” may offer one model for increasing diversity. During the COVID-19 public health emergency, the FDA issued guidance encouraging sponsors to consider alternative methods for clinical assessments to improve diversity, such as phone contact and virtual visits.

Panelist George Mensah (NIH) offered a funding agency perspective, presenting on behalf of the NIH Community Engagement Alliance Against COVID-19 Disparities (CEAL), a trans-NIH initiative to lead outreach, engagement, and inclusive participation in racial and ethnic minority communities that have been disproportionately affected by the COVID-19 pandemic. Consistent themes in discussions with communities are trust, transparency, and truthfulness. When engaging communities about clinical research opportunities, researchers and institutions must prove themselves to be trustworthy and be transparent about adverse effects and potential risks or absence of benefits. It may be helpful or necessary to set recruitment targets that reflect the makeup of the community and to oversample minority communities when scientifically appropriate. It is also important to account for social determinants of health and barriers to participation, such as by compensating people for their participation, reimbursing travel and other expenses, and providing evening and weekend hours for recruitment and trial activities. Finally, researchers must address the “people like me” question: Do underrepresented groups see people like themselves represented in research leadership and participation? Research teams should model diversity and inclusion, reflect the diversity of the community, and pay attention to cultural and language issues.

Luther Clark (Merck) offered an industry perspective. Critical barriers to diversity and inclusion in clinical trials are well known: mistrust; lack of awareness of opportunities and benefits; access; logistical and resource constraints; lack of sites, networks, and investigators in underrepresented communities; and low levels of engagement of minority group members in the current landscape of clinical trial networks. Overcoming these barriers involves not just recruitment and enrollment, but also retention of participants, protocol compliance, and ensuring that participants have a positive experience. Complexity of study design and conduct can also be a barrier, which can be mitigated by making trials more patient-centered and integrating the research into clinical care. Meaningful partnerships and collaborations with trusted community leaders and organizations are key. Social and economic conditions hamper willingness and ability to participate in research. Many of these conditions can be addressed in clinical trial design and implementation. Collection of data on social determinants of health and barriers to participation is important for improving understanding and enabling change.

Amesika Nyaku (Rutgers University) described the Research With a Heart strategic initiative at the Rutgers New Jersey Medical School Clinical Research Center, which involves understanding the historical and social context in which the institution is trying to increase diversity in research participation. A strategic plan included a needs assessment focused on marginalized groups; community forums to understand community-defined needs for creating a more inclusive research agenda and inclusive research spaces; and building relationships with community leaders and organizations by collaborating with them and supporting their work. It will continue to be difficult to make progress without dedicated funding for community
engagement, alternatives to the per-participant funding structure often used in clinical trials, greater focus on participant retention, and study materials in languages other than English.

Attendees discussed the importance of focusing on the right problem: access to research opportunities for underrepresented communities. One answer is putting the research in the community. This means not simply developing full-service research sites, but understanding that patients are receiving their care in the community and that is where research activities should be happening. Community sites must be adequately supported and incentivized, but they often are under-resourced. Community sites also are better situated than typical sites, such as academic centers, to address social determinants of health, which often overlap with barriers to clinical trial participation. Meaningful community engagement has not been a priority for the clinical research enterprise.

Dr. Nyaku focused the conversation on identifying the bottleneck in research participation by underrepresented groups. The fundamental issue is not whether people want to participate in research but whether the research is relevant for them and their self-identified or geographic communities. There are fears about being used for experimentation and a lack of awareness about what it means to participate in research. Addressing these barriers will require systematic and meaningful investment and engagement, rather than simply opening new sites in new locations.

Finally, Rob Califf (Verily and Google Health) raised a concern about whether optimizing the clinical research enterprise for the US context comes at the expense of the rest of the world. Attendees discussed the importance of both supporting better research infrastructure in US communities and meeting the needs of the developing world.

SESSION II: PARTICIPANT ENGAGEMENT, RECRUITMENT, AND RETENTION

Moderator Raolat Abdulai (Sanofi) introduced the session and encouraged attendees to think of participants as partners in clinical research.

Patrick Gee (iAdvocate) shared a participant viewpoint on engagement and clinical trial recruitment. He noted that, although the Tuskegee syphilis experiment is commonly referenced as a source of Black communities’ mistrust of clinical research, the problem is deeper and should not be reduced to this single example. One source of mistrust: no one asks about participation. How many clinical trialists work in or with underserved communities and ask people in those communities if they are interested in participating in clinical trials? The failure to ask is itself a source of mistrust. People want to see partnership, but they feel excluded. Dr. Gee summarized 5 key social determinants of health: economic stability, education, community and social contexts, health and health care, and neighborhood and built environments. He then summarized the 4 dimensions of racism: institutional racism, interpersonal racism, structural racism, and internalized racism. The dimensions of racism
intersect with the social determinants of health and highlight the need to humanize clinical trial participants and the clinical trial experience.

Elizabeth Cohn (Hunter College) referred attendees to the CDC’s Principles of Community Engagement. A community-engaged approach increases trust, deepens understanding of cultural perspectives, strengthens the science, and improves the health of communities. It is important to view our research through the eyes of participants. How do we repair the fractured relationships that research institutions have with communities? How can better access to clinical research and diversification of researchers and teams improve patient care? Dr. Cohn posed several key questions for researchers and institutions to ask themselves: What is the reputation and involvement of your work and of your institution in the community? Will the outcome of the study benefit health in the community? At what points did you ask the community for input into the research? When and how will you return results to participants and the community? Are you a trusted and generous community resource? Two metrics for success include: Did the health of the community change? Did the research change because of your engagement with the community?

Judy Seward (Pfizer) described a recently published commitment by Pfizer to ensure that participants fully reflect the diversity of the countries and communities where they conduct their trials. She summarized 3 lessons from efforts to fulfill this commitment. First, build trust and awareness by “meeting people where they are.” This means ensuring that materials and other resources are culturally appropriate, soliciting input on study design and study materials, and working with patient advocacy organizations to co-create communications and provide clear information. Second, reduce barriers to participation by selecting sites where diverse communities can participate, addressing transportation challenges, and finding ways to bring trial activities to the participants. Third, participant experience is largely shaped by the site they go to. Choose sites that share in your commitment to diversity and equity. Think about the unique considerations of the community and the best ways to engage the community.

Attendees discussed the importance of early engagement with potential research participants. Researchers should solicit input from potential participants regarding visit schedules, study design, and materials. Consider how eligibility criteria can disproportionately exclude some groups. Once the protocol is finalized, consider what participant support services are in place and solicit feedback on this ahead of time.

Decentralized clinical trials offer the potential to improve participant engagement and recruitment, especially after experiences with the COVID-19 pandemic. Therefore, it is important to acknowledge equitable access to digital health tools as part of the challenge of diversifying clinical trials.

Finally, participants returned to Dr. Cohn’s recommendation to consider the history of the research institution in the community and how the institution’s reputation may affect community trust. These relationships may require repair.
FIRE SIDE CHAT: WHAT MATTERS FOR FUTURE TRIALS?

Dr. Hernandez facilitated a discussion with Cartier Esham (Biotechnology Innovation Organization), beginning with a question about important lessons from the COVID-19 pandemic. Dr. Esham noted that the experience has shown the power of collaboration and how it can be operationalized quickly to simultaneously test many tools and approaches, including using real-world evidence in real time to understand outcomes. Use of master protocols and pragmatic approaches was also important.

The success of vaccine development has brought into relief the challenges of developing therapies for COVID-19. The difficulty of scaling up drove prioritization in therapeutics development. There has long been a lack of a good economic model for bringing infectious disease therapeutics to market. One solution might be to build a library of therapeutics that can be repurposed for other uses to speed development in future emergencies. We also need to address capacity for manufacturing.

The experience of continuing recruitment in COVID-19 vaccine studies to ensure diversity has highlighted how we can make better decisions in the future and the importance of early community engagement. Research infrastructure and systems should be built around community engagement and developing relationships with community leaders. Clinical trial research networks also need to be more inclusive, in terms of trial sites, investigators and research staff, and decentralized approaches that meet regulatory requirements. Companies need a different incentive structure to prioritize diversity. A key reason for ensuring diversity is to better understand health outcomes for all patients.

There are concrete actions we can take to achieve these goals and hold each other accountable. First, develop information sharing strategies that enable ongoing exchange of best practices for setting goals and achieving diversity. Companies may need to restructure internally to achieve these goals. On the policy side, there is a need to build an infrastructure around new approaches to make them sustainable.

SESSION III: SITE NETWORKS

Moderator Rob Mentz (Duke University) introduced the panelists.

Minnow Walsh (Ascension St. Vincent Heart Center) focused on 3 points related to diversification of clinical trial sites. First, clinical research needs more representative geographic diversity. Second, what limits site selection is not what you know but who you know. Previous site performance and whether the site has worked with the principal investigator or institution before largely determines repeat selection of the site. This reliance on existing networks makes it difficult for new or less experienced investigators to participate. Third, diversification of sites requires diversification of investigators, which will lead to diversification of research
participants. There are too few women and racial and ethnic minority investigators in clinical research leadership, which limits the questions that are asked and has negative implications for clinical research. Dr. Walsh referred attendees to Upping Your Game, a diversity and inclusion initiative of the American College of Cardiology. The program aims to increase the number of persons underrepresented in cardiology who serve in clinical trial leadership roles.

Chris Komelasky (SiteBridge Research) described efforts by SiteBridge to drive innovation in site and patient access. Because there is systemic bias in site selection, it is important to be intentional about removing barriers in each component of the clinical research process. SiteBridge is focusing on 5 approaches. First, build a national site network that reaches further into communities and clinical practices that have not typically been part of research (such as small and medium physician practices, community hospitals, and Federally Qualified Health Centers). Second, reduce administrative barriers by creating a “trial in a box” approach that offers functional expertise in every aspect of clinical research. Third, develop community engagement strategies that rely on trusted messengers, relationship building, and listening to local communities to understand needs and challenges. Fourth, set explicit targets and find the physician key opinion leaders who can champion this cause and make it a priority for clinical research. Fifth, better use real-world data and real-world evidence to create a scalable way to match studies to sites, build registries as foundations for clinical studies, and help make the business case for industry and payers to invest in sustainable approaches.

Kendal Whitlock (Boehringer-Ingelheim) described a new initiative at Boehringer-Ingelheim to work with a digital technology company to launch 1 of 12 decentralized clinical trials using a “meta-site” model. The intention is to address access to research sites in nontraditional ways and increase patient opportunity and readiness to participate in research. The structure of patient enrollment can shape patients’ awareness and ability to participate in research. There are many places and spaces where conversations about clinical research are not occurring, which restricts health literacy, awareness, and access in underserved communities. One approach of meta-sites is to engage investigators who already have diverse patient populations. These sites and their patients become trusted sources of information in their own communities.

Attendees further discussed the need for leadership pipeline development and programmatic changes so that clinical researchers do not continue to rely on the sites they have always used. Research teams can be diverse only insofar as clinical teams are diverse, so work is also needed to improve diversity in clinical teams. Mentorship is also important. Many investigators from underrepresented groups do not have mentors, which limits access to professional and research networks. In this sense, mentors are a form of gatekeeper, and limited mentor pools restrict access to professional development and leadership opportunities.

The discussion turned to expanding the notion of what counts as a research site. For example, a hypertension study conducted in Black barber shops, and other studies that have gone to Black churches, offered a community-based approach that could be replicated. These examples illustrate that clinics are not always the best places to build relationships and recruit patients.
Access in the community means going where people are, and research participants recruited in this way can become trained as community educators.

Drs. Harrington and Califf discussed the need for better clinical research infrastructure to support alternative approaches. Instead of a sustainable national infrastructure, the current system builds the research infrastructure on a trial-by-trial basis, which forces shortcuts like relying on personal and professional networks that limit diversity. Dr. Califf noted that many of the ideas raised by the workshop attendees would be difficult to implement, given how clinical research is currently organized and funded, and that such innovation would be financially adverse to the clinical research and health care systems that currently control most traditional research sites.

SESSION IV: APPROACHES IN DIGITAL TO INCREASE DIVERSITY AND RETENTION

Moderator Christoph Hornik (Duke University) introduced the panelists.

Silas Buchanan (Institute for eHealth Equity) works with underserved communities to increase literacy about the benefits of digital technologies to improve health, as well as with the innovators of digital health technologies to ensure they develop tools in culturally appropriate ways that benefit communities of color. Most of the work occurs in faith- and community-based organizations to build digital platforms as social networks that enable equitable partnerships with research organizations. For example, see AMECHealth.org and ShepherdsConnection.org. In the community, historical context is important. Community organizations often do not have confidence that health care and research institutions truly care about them. Trust comes from equitably sharing ideas, money and resources, data, and power. In a recent Alzheimer disease awareness campaign, it was important to co-create the campaign. For example, the invitation to the online community event identified the church as the lead, and the speakers for the event were church and community leaders. Driving messaging through the national AME Church’s social media channels and those of their individual churches also made it possible for the church to strengthen its own relationships with the communities and build channels for the individual churches that lacked them. Actionable steps for lasting change include acknowledging and understanding histories of marginalization and mistrust, co-creating strategies for engagement, and serving the interests and building the capacity of underserved communities.

Rob Califf (Verily and Google Health) noted that almost everyone engages with a cell phone and that individual users have particular channels they use repeatedly. Messaging and engagement through these channels can influence enrollment and retention. Total virtual trials are possible and may be desirable in some situations. But there are problems with digital approaches. Most serious clinical trials in serious diseases need research sites where experts can broker information about risks and benefits. Most new therapies in clinical trials have no benefit or have greater risks than benefits. Yet our language has changed such that we talk about clinical trial participation itself as a benefit rather than as a risky activity in which participants need
protection. Digital approaches can be helpful in matching the right trials for the right people and can set up the right discussions between potential participants and their clinicians.

Solomon Howard (Evidation) discussed how diversity, equity, and inclusion–focused adaptations to existing workflows can improve community engagement. Although digital tools and approaches can reduce trial burden and improve reach for underrepresented populations, development of digital approaches still must include co-design of trials with communities to optimize protocol design, recruitment, retention, and value. Product design should be approachable and relevant for target populations. Tools should be accessible to or already in the hands of minority participants. Protocols, consent documents, communications, recruitment and retention plans, and trial experiences should be optimized for diverse participants. Study activities and mechanisms of support should be designed to meet the needs of diverse participants. Ultimately, digital tools and approaches are not a shortcut, but they can facilitate a switch from transactional approaches in clinical trials to foundational engagement powered by participant insights and rooted in values aligned with community priorities.

Attendees discussed whether money spent on investments in digital approaches would be better spent on building a less fragmented health care system and a data infrastructure that links clinical care with research. Silas Buchanan noted that health disparities will continue until the clinical research enterprise more systematically uses culturally specific interventions and engagement. This starts with acknowledging the history of clinical research institutions in communities of color, building networks of community-facing organizations that help them connect and that build community capacity, then inviting stakeholders who can present opportunities for participation in clinical research. People will participate if they are asked, and the messenger often matters more than the message. Community organizations are trusted in their communities, but many need help building capacity and accessing technology to become more effective messengers.

WRAP-UP

Dr. Hernandez thanked the attendees for their participation. Co-host Bray Patrick-Lake noted that attendees will be invited to participate in drafting a white paper from the workshop.