PEER REVIEWED

Who Cares About Diversity in Clinical Trials?

The imperative to obtain a diverse body of clinical trial participants has been stressed in public statements for decades, including formal promotion by the U.S. National Institutes of Health (NIH), regulatory authorities such as the U.S. Food and Drug Administration (FDA), and recently, with the Consolidated Appropriations Act of 2023, even the U.S. Federal Government.[1–4] Despite the duration and high profile of this issue, however, parties executing clinical trials, including sponsors, clinical research organisations (CROs), and academic centers, have remained insufficiently effective in addressing it. According to the 2020 U.S. Census, an estimated 33% of people in the U.S. identify as members of racial or ethnic groups that are underrepresented in medicine.[5] However, between 1997 and 2014, only 4 to 5% of participants in trials of drugs submitted for approval by the FDA were from these groups.[6] In 2017, non-Hispanic Whites of European ancestry still comprised more than 90% of participants in clinical trials[7] and even in 2020, the year during which the first Covid-19 vaccines were developed, and issues of racial diversity were prominent, 75% of clinical trial participants remained White.[8] Although demographic variables other than race, such as gender, socioeconomic status, stage of disease, and residential location, are known also have critical impacts on medical outcomes and have also been mentioned in FDA Guidance, enrollment of diverse clinical research participants in these respects has received even less attention.

This state of affairs has persisted despite assertion by the vast majority of research professionals that DEI (Diversity, Equity, and Inclusion) is important. In the 2020 WCG Avoca Industry Survey, in which clinical research professionals were asked to provide confidential opinions about the importance of diversity among clinical trial participants, 81% of 215 respondents felt that at least one aspect of diversity (e.g., race, gender, socioeconomic) was important or critically important, including 40% who endorsed diversity as "critically important," the extreme of the scale.[9–10] This result was replicated in 2021 (75% and 37% of 101 respondents, respectively). [11] Similarly, in a survey conducted at a 2020 meeting of the Clinical & Translational Science Awards (CTSA) consortium leaders (funded by the NIH National Center for Advancing Translational Sciences), 94% of 231 respondents said they believed DEI in clinical and translational science to be "important," and 86% were "committed" to making changes in CTSA processes to improve DEI.[1] Clearly, there is a disconnect between what the vast majority of professionals voice to be important and the results their enterprises have actually achieved.

The present study seeks to gain insight into this disconnect by performing a detailed analysis of data regarding the DEI-related values and motivations of individuals executing clinical research projects. Herein we revisit the data from the 2021 WCG Avoca industry survey, asking specifically who cares (and does not care) about diversity in clinical research participation and why, rather than simply how many and how much. Our working hypotheses are (1) that there may be systematic motivational differences across clinical research professionals that result in DEI-related decisions not being made in a manner that reflects the values of the wider group, and (2) that beliefs about why diversity is important (i.e., ethical vs scientific vs regulatory) may impact how critical to research quality diversity is felt to be. Although the authors fully recognise the challenges associated with enrolling diverse participants (and have discussed these at length elsewhere[9–11]), we believe that the values and motivations of acting parties – and not just forces beyond their control – play a role when it comes to making difficult decisions about practices that impact the DEI results achieved.

Methods and Respondents

The 2021 WCG Avoca Industry Survey was designed to gain deeper comprehension of respondents' values, views, and experiences regarding diversity in clinical research execution and clinical research participants.[11] An open invitation to participate was extended to attendees at the 2021 WCG Avoca Quality & Innovation Summit, sent to contacts in the company's database, posted on its website and on LinkedIn. Data were collected during the four-month period from September to December 2021.

The 101 respondents included clinical research personnel from 64 sponsor companies, 35 providers, and two academic research organisations. Approximately 38% of respondents held positions within clinical development/operations, 34% within quality assurance, and the remainder within a wide spectrum of management and functional roles. Thirty-seven percent of respondents represented companies that sponsored or conducted more than 50 clinical trials during 2021, and 20% represented companies that sponsored/conducted five or fewer. Most respondents worked for companies headquartered in the U.S., but approximately one-third represented companies headquartered in Northern/Western Europe (19%), Japan (5%), or other parts of the world (9%). Most (78%) of the respondents resided in the U.S.

Data analysed for the present study derived from two key questions in the 2021 survey. Survey respondents were asked to rate the importance of different types of diversity (i.e., racial/ethnic, gender, socioeconomic, etc.) to clinical research quality on a scale of 1 (no importance) to 5 (critically important). They were then asked to indicate whether their importance ratings were driven mostly by scientific, regulatory, ethical, or marketing and sales considerations. The impacts of "demographic" variables including respondent age, time in company, time in role (irrespective of company), functional area, and location were then investigated using multiple regression and ANOVA techniques.

RESULTS

Respondent Traits vs. Importance of Diversity

Figures 1 and 2 and Table 1 depict the average "importance ratings" (on a scale of 1 to 5) across respondents for each of five different types of diversity, as well as the statistical relationships between the quantitative respondent characteristics and these ratings. Of these variables, time in role demonstrated the most robust correlation with importance ratings across all of the diversity categories and was the only respondent characteristic to bear a statistical relationship to diversity importance ratings if corrections for multiple tests were applied. Specifically, the more time participants spent in their roles, the less important they generally rated every type of diversity. On

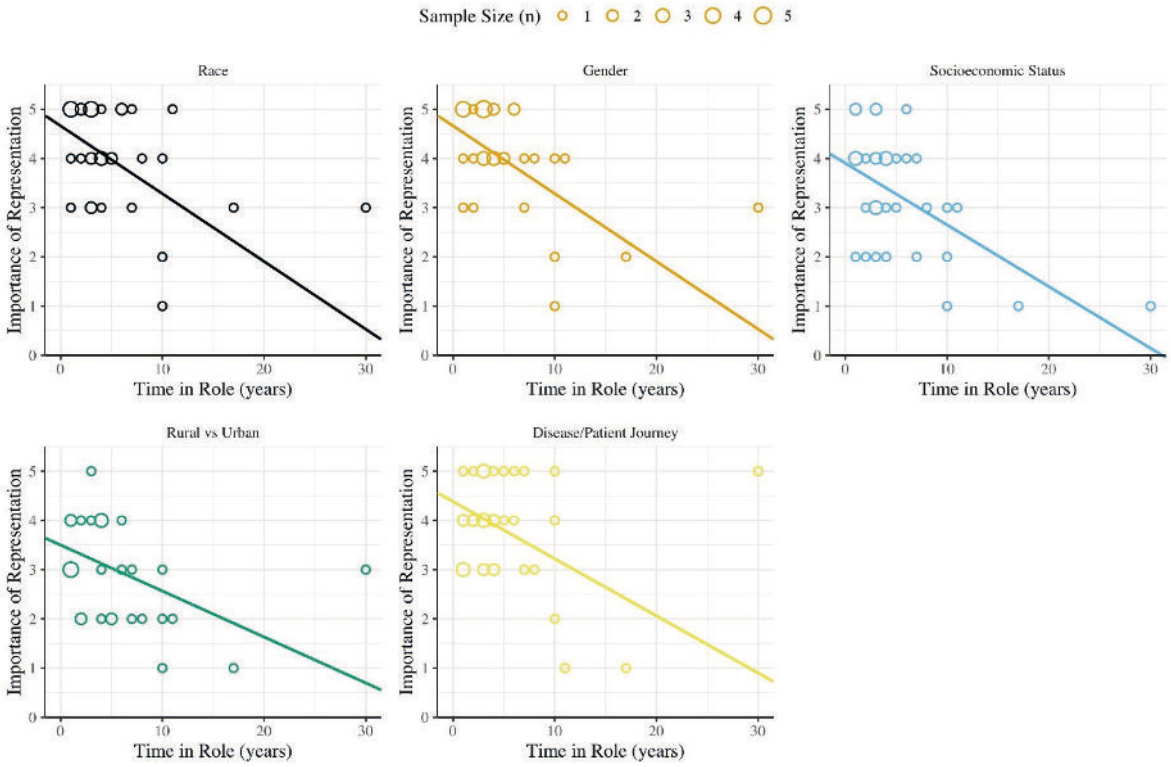

Figure 1. Importance Ratings for Diversity in Clinical Research Participation vs. Time in Role

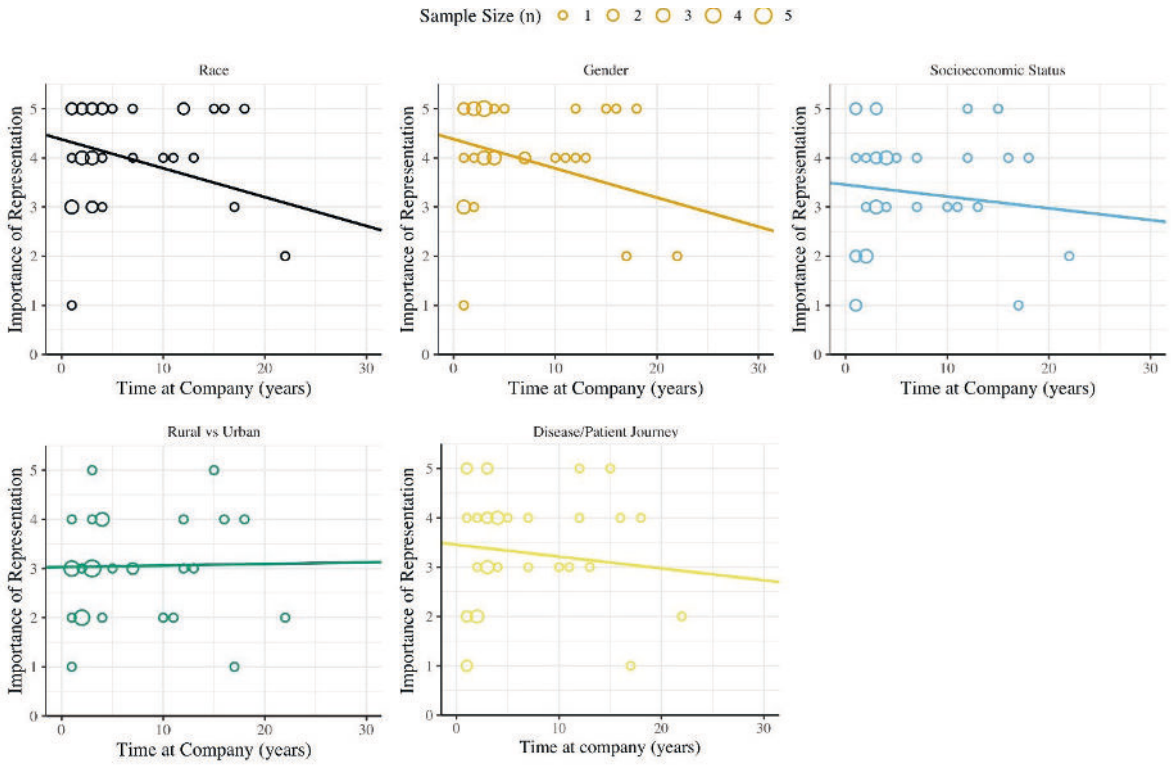

Figure 2. Importance Ratings for Diversity in Clinical Research Participation vs. Time in Company

average, respondents who had worked less than 10 years in their current roles rated the importance of the various diversity categories between 3.3 and 4.3; for participants who had worked more than 10 years in their roles, in contrast, average ratings ranged between 2.1 and 3.0. This relationship could not be explained by age and/or tenure within respondents' companies (Table 1). Separately, we examined the possible impacts of respondent functional area and location; neither of these either bore independent statistically significant effects on importance ratings or covaried with the continuous variables in a way that would confound the results.

To determine whether the effect of Time in Role could be accounted for by time in any specific role, we looked separately at respondents in each of the two most-represented functional areas in the survey: clinical development and quality assurance. The statistically significant negative relationships between time in role and importance ratings for each aspect of diversity persisted for each of these functional areas taken separately, at least at the trend level (except in the case of race, within the group of respondents from Clinical Development). Again, the relationships could not be explained by confounding effects of age and/or tenure within respondents' companies.

	Race	Gender	Socioeconomic status (SES)	Rural/Urban	Stage in Patient Journey
Time in Company	0.56	0.56	0.03	0.005	0.03
Time in Role	0.0006	0.0004	0.00002	0.0001	0.0005
Age	0.26	0.31	0.26	0.65	0.03

Table 1. Statistical Significance Levels (p value) for Impacts of Respondent Characteristics on Importance Ratings

		Mean (N) Importance Ratings Type of Diversity				
		Racial/Ethnic	Gender	Economic	Rural/Urban	Patient Journey
Primary Reason Diversity is Believed to be Important	Mostly Scientific	4.1 (50)	4.0 (68)	3.4 (17)	3.4 (20)	4.0 (71)
	Mostly Ethical	3.9 (33)	3.9 (18)	3.5 (63)	3.1 (47)	3.9 (13)
	Mostly Regulatory	3.9 (11)	3.6 (9)	3 (3)	2.3 (3)	3.5 (6)
	Mostly Marketing	3.0 (1)	0 (0)	2.2 (12)	2.5 (25)	3.2 (5)

Table 2. Importance Ratings for Diversity vs. Primary Reasons Diversity was Considered to be Important

Why Diversity is Important vs. How Important It Is

We also examined relationships between the reasons participants felt that diversity was important and how important they felt it to be. Our hypothesis was that feelings about diversity's importance might be stronger if the propelling values were, e.g., scientific or ethical as opposed to regulatory or marketing. In general, this was found to be true. Across all aspects of diversity, respondents whose ratings were driven by scientific or ethical considerations felt more strongly about the importance of diversity than did those who felt diversity to be important primarily for regulatory or marketing reasons (Table 2).

Discussion

The goal of the present analysis was to better understand what drives differences across research personnel in how critical diversity among clinical research participants is believed to be. Understanding these differences and drivers may provide insight into motivational factors that underlie the disconnect between the stated importance of diversity (by groups of research professionals) and the DEI-related results actually achieved, and may thus inform efforts to improve performance in this respect. Of the variables we explored, time in role was, by a margin, the strongest predictor of the perceived importance of every aspect of diversity explored, with longer times in role associated with lower importance ratings for diversity. These effects were independent of the effects of age, functional area, location, and time in company, the last of which also bore independent negative relationships to diversity importance ratings in areas other than race/ethnicity and gender.

Responses to open-ended survey questions requesting the rationale for provided responses did not provide an explicit explanation for the observed relationships; however, they did shed light on important themes that may be at work. Most respondents described cultural difficulties and structural restrictions that posed challenges to incorporating DEI in clinical research, including "upper management stagnation" and hesitance to depart from "old ways." One respondent in clinical development implied a lack of open-mindedness at the senior levels at which decisions were made: "Top decision-making people have to fund, invest, trade… and for that, they first have to be open-minded…." Disincentives for doing things in new ways were also described, including the "old school sponsor mentality that it must always be done a certain way because that way has proven successful in the past. There is a place for risk management built in, yet the folks executing the trial have hoops to jump through…such that it becomes a disincentive to be a leader in the unknown…to be an innovative trial leader." One respondent mentioned the increased costs associated with DEI initiatives: "When it increases costs due to the need for more clinical sites to achieve diversity and/or it prolongs the time to enroll the target numbers in all subgroups, then sponsors and shareholders are going to need to be sold on this"; and another called for "education based on solid evidence that variability and flexibility [in clinical trial execution, that would support diversity] will be accepted by regulators."

It would stand to reason that those who have worked longer in their roles, particularly if they have also worked for a long time in their companies, are more likely to be entrenched in "old ways" of doing things; more likely to directly hold budget, timeline, and regulatory responsibilities for their departments; more likely to either be or report to "upper management" and shareholders; and more likely to have had long experience with the challenges of incorporating new practices. It would further stand to reason that direct, long-standing experience with the difficulties and risks of implementing new practices could negatively influence how critical such changes were felt to be. Consequentially from the perspective of implementing DEI-oriented programs, individuals who have spent more time in their roles are more likely than junior staff to make decisions regarding clinical trial execution, and thus their beliefs about what is (and is not) critical carry more weight. Skepticism from such individuals about the importance of diversity is unfortunate because it is exactly these more senior individuals on whom successful implementation of DEI-related programs would rely. When asked to describe the key enablers of variability and flexibility in clinical trial execution in support of DEI, one respondent insightfully responded: "experienced clinical scientists, supported by leadership, to drive clinical operations to execute the plans."

Another useful finding from this analysis was the relationship between how important participants believe participant diversity to be, and why they believe it to be important. Not surprisingly, respondents who saw the pursuit of diversity as a scientific or ethical imperative were more passionate about its importance than were those who valued diversity for other reasons. Every aspect of diversity studied here is arguably important from a scientific perspective, as well as from an ethical perspective. As reflected by one respondent: "Appropriate representation of ethnic groups and sex are critical to the scientific validity of research findings, and their absence can lead to false conclusions. Representation of patients across the spectrum of disease is crucial to ensure deep understanding of new drug therapies. While, initially, the push for diversity may be driven by the ethics of inclusion, ultimately, it

benefits drug developers by...ensuring the medicines being tested work as expected in different ethnicities and at different points along the disease pathway." Nevertheless, significant fractions of the respondents saw the pursuit of diversity, at least of some types, not to be driven by these values.

Understanding the patterns unveiled in this study's analyses can inform policies and programs designed to effectively encourage personnel to make diversity-oriented decisions. If people motivated by scientific and ethical considerations are more likely than others to make decisions that prioritise diversity, then perhaps education surrounding the scientific and ethical rationales for diversity, and selection of leaders who understand and embrace these rationale will lead to more diversity-oriented decisions. Further, as senior staff will always play key roles in determining how clinical research is executed and will make such decisions based on their own beliefs and experiences, it is important to augment the findings of this study, which included only a minority of respondents in this category, by expanding participation of such individuals in the dialogue to more fully understand their perspectives. Another limitation of this study is that participants were not asked to report personal demographic data including their own genders, races, and ethnicities. Diversity of research staff is known to be highly associated with diversity of trial participants,[12] and conceivably, respondents who had spent less time in their roles and at their companies may themselves have been more diverse. Additional studies and analyses such as the ones performed herein promise to more fully elucidate the reasons for continued failures to achieve DEI goals in clinical research, and thus will serve to support the design of DEI-promoting policies and programs.

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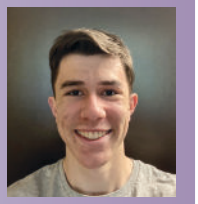

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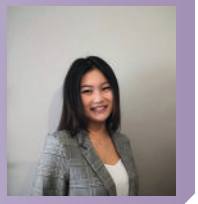

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