White Paper

How Clinical Trial Design Impacts Enrollment of Diverse Populations

Does motivation to enroll in a study vary by race and ethnicity?

DENISE MESSER, MA, Director, Design Analytics, IQVIA Applied Data Science Center

Table of contents

Introduction

With the increased focus by regulators and the broader research community on ensuring historically under-represented racial and ethnic groups are included in clinical trials, IQVIA explored whether and how race and ethnicity influences motivation to enroll and stay within a study. This paper discusses our findings and how this data can be used to help sponsors calculate the impact of specific trial design elements on different race and ethnic groups.

IQVIA conducted a survey involving participants from different race and ethnicities, covering 42 questions regarding design elements in a clinical trial that may affect willingness to participate. The findings collected through an online survey capture qualitative data that has been quantified to apply to future protocols and patient burden assessments.

The survey measured the overall willingness to participate in a study, which protocol design elements affect interest in participation, by how much, and if these results differ by race and ethnicity.

Survey respondents were first asked how willing they would be to ever consider participating in a clinical trial: extremely willing, very willing, moderately willing, slightly willing or not at all willing. Respondents who answered "not at all willing" were screened out of the survey, and the remainder were presented 42 questions to assess how clinical trial protocol design elements would affect their willingness to participate in a clinical trial. For each design element, the respondents answered whether they would be extremely willing, very willing, moderately willing, slightly willing, or not at all willing.

The difference between their initial willingness and their willingness if the described design element was present in the trial was calculated as a change in willingness, allowing for quantification of the impact of each design element.

KEY FINDINGS

- Interest in participating in a clinical trial was highest for Hispanic and Black/African American respondents, followed by White and Asian
- Trial design had a greater impact on Hispanic interest than it did for other groups
- There were aspects of trial design that were only of concern to Hispanic or Asian respondents
- Black/African American respondents' willingness was less affected by trial design

Survey Results

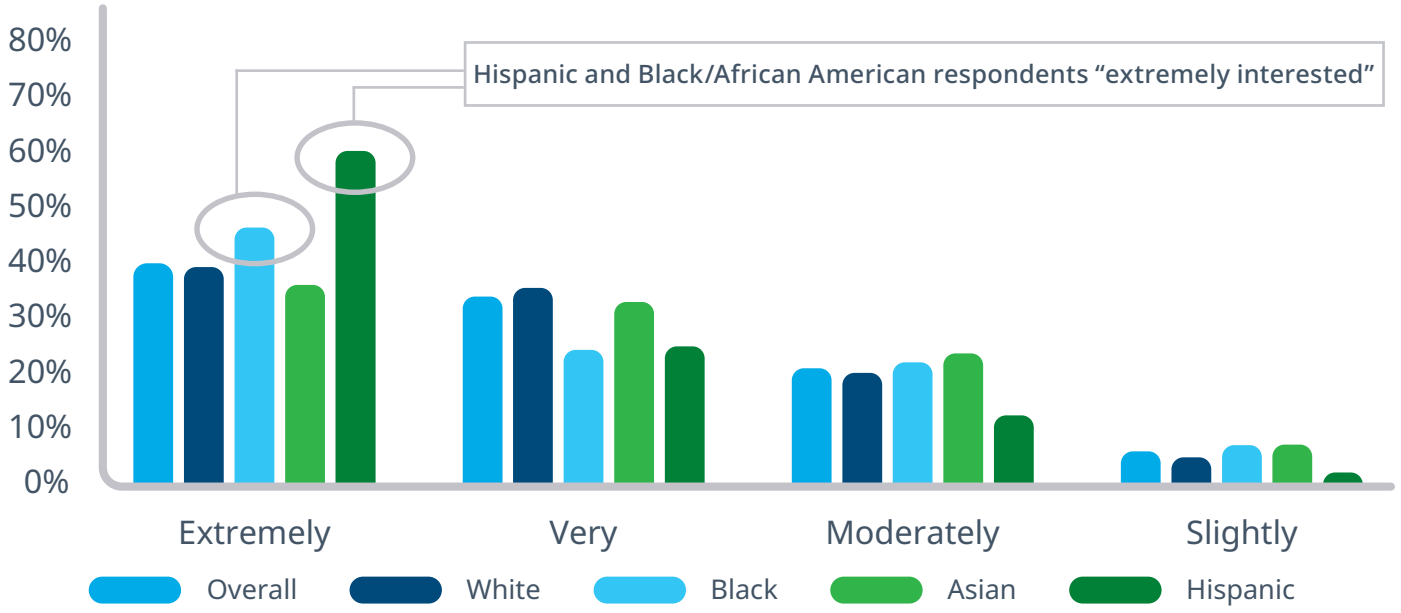
The results of the survey indicate that although Hispanic respondents were most willing to participate in a study, trial design had a greater impact on their interest than it did for other groups. On the other hand, Black/African American respondents were more willing than other races to participate, but their willingness was less affected by trial design.

CLINICAL TRIAL PARTICIPATION

Interest in participating in a clinical trial was highest for Hispanic and Black/African American respondents, followed by White and Asian respondents. While 73% of respondents overall indicated a willingness to participate in a clinical trial, Hispanics showed the most interest, at 85%. When we look at just those who are extremely interested, 60% of Hispanic respondents and 46% of Black/African American respondents said they were extremely willing to consider participating in a clinical trial, compared to less than 40% of White or Asian respondents (see Figure 1).

Figure 1. Willingness to participate in clinical trials

Interest by Race and Ethnicity



HOW TRIAL DESIGN AFFECTS WILLINGNESS

Impact of Design Elements

For most groups, responses to 26 of the 42 questions indicated a design element that would negatively impact willingness to participate to some extent. This was similar for White and Black/African American respondents; however, for Asian respondents, responses to 31 questions indicated negative impact. For Hispanic respondents, responses to 39 of the 42 questions indicated design elements that would negatively affect willingness to participate in a trial (see Table 1).

This indicates that, while every trial design element that affected willingness for the average participant also affected willingness for the average White, Black/African American, Asian or Hispanic participant, there were trial design elements that were only of concern to Asian or Hispanic respondents.

Table 1: Number of survey questions with negative, neutral, or positive change in willingness (out of n=42)

AVERAGE DIFFERENCE IN WILLINGNESS	OVERALL	WHITE	BLACK/ AFRICAN AMERICAN	ASIAN	HISPANIC
# Negative	26	26	26	31	39
# Neutral / None	15	15	15	10	3
# Positive	1	1	1	1	0

Degree of Impact

Even more interesting, the amount by which willingness was affected also differed by race and ethnicity (See Table 2). Statistical analyses for each response compared the overall average change in willingness to the average change in willingness for each race and ethnicity. Significance level of 0.05 was used, such that we can say that when considering a difference as significant from the overall we are 95% confident there is an actual difference between the two observations as opposed to just differences due to random variations.

- White respondents had fewest design elements with significant difference (7), and for those elements, their difference had more effect on willingness to participate if those elements were included in a clinical trial (all 7 higher than the overall average difference)
- Asian respondents had slightly more elements (10) with significant difference, and where they differed also had more effect on willingness (9 of 10 higher than the overall average difference)
- In contrast, although Black/African American respondents had more elements with significant differences than did White or Asian respondents (14), almost exclusively, while still negatively affecting interest, their willingness to participate would be slightly less affected (13 of 14 where the average difference was lower than the overall average difference)
- Hispanic respondents had the most elements with significant difference (26), and although for a few indicated less impact on willingness, usually they were more concerned than the average respondent or any of the racial groups (19 of 26 responses were higher than the overall average difference)

Table 2: Number of survey questions where race or ethnicity's difference from the overall average difference was statistically significant (out of n=42)

STATISTICALLY SIGNIFICANT DIFFERENCE FROM OVERALL	WHITE	BLACK/ AFRICAN AMERICAN	ASIAN	HISPANIC
# More effect on willingness	7	1	9	19
# Not statistically different	35	28	32	16
# Less effect on willingness	0	13	1	7

Design Elements of Note

The most surprising result was that where there were statistically significant differences by race and ethnicity in the amount these concerning elements affected willingness to participate, many of them affected the willingness of Black/African American respondents less than they affected the other race or ethnic groups.

Respondents of each race and ethnicity also differed in which design elements they were most concerned about, particularly in the effect of visit schedules and noninvasive imaging procedures on willingness to participate.

Visit schedule: The length of required visits to the clinic was one of the design elements with the most impact on willingness to participate, and while this was true for each race and ethnicity, the average effect for Black/African American respondents was lower than for other groups, including among several suggested visit lengths and regarding a requirement for an overnight stay. Additionally, for each number of visits and frequency of visits that affected willingness overall, Black/African American respondents also showed less effect on willingness. Responses on visits was mixed for Hispanic respondents; although their willingness was less affected by overnight stay requirements and the highest visit frequency asked about, they showed the same concern as the overall at most visit numbers and frequencies, and were more concerned, i.e., had a small change in willingness, even at the lowest visit number and frequency, which did not affect willingness for others.

Noninvasive imaging procedures: Procedures such as computed tomography (CT scans), positron emission tomography (PET scans), and other types of noninvasive imaging did not affect willingness for most respondents, but Asian and Hispanic respondents were more likely to indicate that some of these would affect their willingness to participate.

Implications and next steps

The increased attention to improving trial design and operations to ensure adequate participation among racial and ethnic minorities is welcome. However, assuming a lack of willingness and the inherent added time and cost to recruit minorities could stymie overall progress. It is imperative to continue to confirm and champion interest in participating in clinical trials among these populations, as is presented in publications since 2003[1] through our own most recent contributions, including Renewed Interest in Clinical Research Helps Change the Conversation about Trial Participation[2].

Interest in clinical trial participation does not counteract the challenges of participating; however, making protocol design decisions without sufficient data or insights from diverse participant groups may lead to changes that have less positive effect than expected. IQVIA's patient burden scoring algorithm can help guide evidence-based design decisions. Delineating perception of burden differences by race and ethnicity in a data-driven way allows us to advise sponsors on changes that may — or may not — impact diversity and inclusion enrollment success. This data is an important component of our overall approach and recommendations to sponsors to meet their diversity and inclusion goals, including validating the study design plan against differences in preferences amongst the desired populations to help ensure the design does not inadvertently lower the chances of diversity and inclusion success from the start.

While this survey provides many insights and data points to better understand protocol burden, it is just one of many steps we are taking to improve and incorporate the perspectives of diverse populations in trial planning. The next step might be to determine willingness based on other population diversity factors that may drive differences and learn more about why perceptions differ by such demographics as race and ethnicity.

	2021 IQVIA PATIENT BURDEN SURVEY	2020 U.S. CENSUS	2015 – 2019 FDA CLINICAL TRIAL PARTICIPANTS
TOTAL	100% (n=1693)		
WHITE	71% (n=1198)	71%	78%
BLACK/AFRICAN AMERICAN	16% (n=267)	14%	16%
ASIAN	6% (n=97)	7%	2%
AMERICAN INDIAN/ ALASKAN NATIVE	3% (n=54)	3%	1%
HAWAIIAN/PACIFIC ISLANDER	0.5% (n=8)	0.5%	Not available
OTHER RACE	4% (n=69)		3%
HISPANIC	11% (n=184)	19%	11%

Addendum: Further details on IQVIA's patient burden methodology

IQVIA has been scoring trial designs for patient burden utilizing survey data since 2011, highlighting trial design elements that may be seen by participants as burdensome and/or affect their willingness to participate in a clinical trial.

In October 2017, after intensive external and internal literature research and IQVIA experience with patient recruitment and retention, we utilized IQVIA's opt-in database of individuals interested in clinical research to survey 1,000 U.S. respondents with 42 questions about how design elements in a clinical trial might affect their willingness to participate. Examples of design elements affecting willingness included visit schedule, chance of being randomized to a placebo arm, and procedures that might be conducted during a trial. Asking respondents their initial willingness to participate in any clinical trial and comparing their willingness if each design element was present enabled calculation of how much each element affected willingness to participate. Results in the 2017 survey were similar to the original 2011 element scoring with only a few elements no longer indicating an effect on willingness to participate, such as noninvasive imaging (although we know these procedures may contribute to site burden or protocol complexity).

In 2018, IQVIA developed the results from this quantification of effect on willingness to participate into a new algorithm for scoring patient burden while drafting clinical trial protocols; this survey methodology and algorithm was presented at the SCOPE (Summit for Clinical Ops Executives) conference in Orlando, Florida. Use of this algorithm since 2018 on over 700 trials that have received our Data Informed Protocol Assessment service has allowed IQVIA to benchmark how clinical trial burden scores differ by therapeutic area and by phase.

Because race and ethnicity of the respondents was not gathered during the 2017 survey, it was re-issued in August 2021, again utilizing IQVIA's patient community database. In this round, 1,693 U.S. respondents self-identified their race and ethnicity to complete the survey. As in 2017, respondents to the 2021 survey were adults of all ages and medical status.

First, the results of the 2021 survey were compared to the 2017 results, where with few exceptions, similar effects on willingness to participate were calculated, validating that the algorithm continues to capture which design elements are important to patients and how much they affect the decision to enroll and to continue participating.

The survey was open for six weeks while gradually closing race categories to gather responses roughly equivalent to U.S. population percentages[3] and/or the percentages by race and ethnicity among participants in recent clinical trials as reported by the FDA[4].

Ethnicity was collected separately from race. Those who identified as Hispanic also identified as one of the races: White, Black/African American, Asian, American Indian/ Alaskan native, Hawaiian/Pacific Islander or Other Race. Statistical analyses for each of 42 questions were conducted, comparing the overall average change in willingness versus the average change in willingness for each race (White, Black/African American, Asian) and by ethnicity for those who indicated they were Hispanic, with a significance level of 0.05.

The low prevalence of Hawaiian/Pacific Islander in the U.S. population, and subsequently also in their representation in the survey (n=8 respondents), was not enough to distinguish burden perceptions for this race. Similarly, although American Indian/Alaskan native participation in the survey was not too low to run a statistical comparison (n=54), no significant differences were found for these respondents, even where a calculated difference was the same as that of another race or ethnicity. Therefore, although data from each of these races are included in the overall scoring algorithm, their differences by race are not used in our diversity and inclusion analyses.

The patient burden algorithm is meant to drive conversations to focus on how protocol requirements might be seen from a participant's perspective and is only one means by which IQVIA surfaces the voice of the patient. These insights can be coupled with other services IQVIA offers to understand patient perception of protocol design, including social listening, patient focus groups, desktop research, and bespoke surveys of how patients feel about their diseases, treatment options, and/or the planned design of a given trial protocol.

References

1 Fisher, J and Kalbaugh, C. (2011). Challenging Assumptions About Minority Participation in US Clinical Research. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3222419/

2 IQVIA. (2022). Renewed Interest in Clinical Research Helps Change the Conversation about Trial Participation. Retrieved from: https://www.iqvia.com/library/white-papers/renewed-interest-in-clinical-research-helps-change-the-conversation-about-trial-participation

3 US Census Bureau. (2020). Census Table DP05: ACS Demographic and Housing Estimates. Retrieved from https://data.census.gov/cedsci/table?q=United%20States&g=0100000US&tid=ACSDP1Y2017.DP05&vintage=2017&layer=state&cid=DP05_0001E

4 US Department Health and Human Services. Food and Drug Administration. (2020, November). 2015-2019 Drug Trials Snapshots Summary Report. Retrieved from https://www.fda.gov/media/143592/download

About the author

DENISE MESSER, MA
Director, Design Analytics
IQVIA Applied Data Science Center

Denise Messer has over 25 years of experience in research and clinical trials, including expertise in clinical trial planning and design. She has spoken at conferences and been published in industry journals on topics including assessing and scoring trial patient burden, highlighting the voice of the patient in trial design, and assessing protocol complexity. At IQVIA, she helped develop the IQVIA Data-informed Protocol Assessment (DIPA), using data to highlight areas for protocol optimization before operationalization, including creation of a patient burden algorithm and protocol scoring benchmarks.

CONTACT US

iqvia.com