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Understanding the Practical and Psychological Barriers to Clinical Trial Diversity and Accessibility

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Purpose: It is crucial to have diverse trial populations to assess the effectiveness of treatments in different patient groups. The purpose of this analysis was to investigate the motivations and barriers to clinical trial participation of potential patients and provide possible solutions to removing these barriers.

Patients and Methods: Participants across nine countries, with a variety of ethnic and gender identities, sexual orientations, and socioeconomic backgrounds were included. Potential participants were alerted to the survey via an awareness campaign which included a link to a landing page providing additional information, and the opportunity to sign consent and complete a survey. Survey questions were written to explore how culture, identity, and background influence participant attitudes toward clinical trials. Input into question format was sought from a cross-functional, international team.

Results: A total of 3858 participants "true completers" completed all questions in the survey. Of the "true completers" 72.5% of participants said that they would be willing to participate in a clinical trial, but only 23.9% of participants had done so before. The most common barrier to participation was fear of side effects (42.1%) followed by lack of knowledge of clinical trials (23.1%). Financial barriers were also identified, including "potential travel costs" (27.8%) and "a lack of financial compensation apart from travel costs" (24.4%). Survey respondents from minority groups showed a high willingness to participate, with 69.9% of participants who identified as women, 72.7% of LGBTQ+ participants and 96.1% of Black participants expressing an interest in participating in a clinical trial.

Conclusion: This survey suggested that insufficient trial enrollment is due to the presence of barriers, rather than an absence of motivation to participate, and should be used to inform new strategies for increasing the diversity of patient populations in clinical trials and making trial participation more widely accessible.

Keywords: survey, motivations, socioeconomic, LGBTQ+, gender, race

Introduction

Patient recruitment is a vital part of the success of a clinical trial; however, it can prove difficult and time consuming, particularly in minority populations.[1] Previous research has shown that socioeconomic status, cost of participation, insurance status, time and resource constraints, trust in the medical community, lack of comfort with the clinical trial process, and lack of awareness about clinical trials all impact the participation of minority groups in clinical trials.[1–4] An analysis of Phase 3 cancer clinical trials conducted between 2001 and 2010 found that 83% of participants were white, illustrating the underrepresentation of minority groups in trial populations.[5] As many treatments have varying side effects and levels of efficacy among different patient populations, it is crucial that clinical trial populations are representative of all patient populations, to identify how the effects of treatments vary before they are approved and prescribed.[2]

Here, we report the results from a large patient-centered survey which assessed clinical trial diversity, investigated the motivations and barriers to clinical trial participation of potential patients, and provided possible solutions to removing

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these barriers. To the best of the authors knowledge, this is the first survey to validate this information on a global scale and the largest of this nature conducted to date.

Materials and Methods

Survey Questions

Baseline characteristics of participants completing the survey included (but were not limited to) age, country of residence and nationality, education level, family structure, medical indication and condition severity, insurance coverage, racial/ethnic and gender identities, socioeconomic backgrounds, and sexual orientation.

The survey was conducted via ClinLife® (Clariness), a platform where patients have opted-in to receive information about clinical trials. An awareness campaign was used to further advertise the survey. Interested participants that clicked the link were taken to a landing page to learn more, sign consent, and complete the electronic survey. Social media (eg, Facebook, Instagram, Twitter), paid advertisements via native ad providers (eg, Google Ads), ClinLife® banner ads, and email advertising were also used to advertise the survey.

Survey questions were written to explore how culture, identity, and background influence participant attitudes toward clinical trials. The survey included 45 questions with a variety of numerical input, single choice, and multiple-choice questions. Additional details can be found in the Supplemental Materials. The survey was designed to assess a diverse range of characteristics, including but not limited to those listed here, to gain insight into both the practical and psychological barriers to participation in varied patient populations across the globe. The questions were reviewed by a cross-functional, international team to ensure cultural appropriateness. Respondents that answered all questions in the survey were considered "true completers". The survey was originally planned to be conducted in the United States, Mexico, United Kingdom, Poland, Germany, and South Korea; however, to ensure adequate representation from Asia, China, Malaysia, and Singapore were later added.

This study was conducted in accordance with the principles of the Declaration of Helsinki. Institutional review board approval was not required as there was no intervention or human research conducted as part of this study. Written informed consent was provided by the participants. Additional details can be found in the Supplemental Materials.

Statistical Analysis

No formal statistical analysis was planned or performed.

Results

Participant Characteristics

Of the 6382 participants across nine countries, 3858 (60.5%) were classified as "true completers" as they answered all survey questions. Only data from "true completers" are presented here. The majority of participants were female (69.8%) and most identified as heterosexual (81.9%; Table 1). The majority of "true completers" (72.5% of participants) said that they would be willing to participate in a clinical trial, but only 23.9% of participants had previously done so. When assessed by historically under-represented participant subgroups, 69.9% of women, 72.7% of LGBTQ+ (defined as asexual, bisexual/pansexual, homosexual/gay/lesbian, or Queer), and 96.1% of Black participants indicated a high willingness to participate in clinical trials. No differences in other under-represented patient populations were noted.

Barriers to Participation in Clinical Trials

When asked "which three of the following reasons would be most likely to prevent you from participating in a clinical trial?", the most common answer was "I am afraid of side effects' (42.1%), followed by "I feel I know too little about clinical trials" (23.1%), and "I fear I will get the placebo" (14.6%; Figure 1), which were all considered psychological barriers.

The most common practical barriers cited by participants were "the time commitment is likely not compatible with my daily life" (29.2%), "the potential travel costs" (27.8%), and "lack of financial compensation apart from travel costs" (24.4%).

Table 1 Demographics of Analysis Participants

	Participant Response	
	True Completers N (%)	**Overall N (%)**
Country of Residence		
Germany	820 (21.3)	1255 (19.7)
United States	865 (22.4)	956 (15.0)
Poland	631 (16.4)	1219 (19.1)
United Kingdom	576 (14.9)	919 (14.4)
Mexico	455 (11.8)	701 (11.0)
Korea	238 (6.2)	416 (6.5)
Malaysia	170 (4.4)	342 (5.4)
Singapore	60 (1.6)	88 (1.4)
China	2 (0.1)	2 (0.0)
Other	41 (1.1)	61 (1.0)
No response	N/A	423 (6.6)
Ethnicity		
White	2023 (52.4)	2682 (42.0)
Hispanic or Latin American	432 (11.2)	625 (9.8)
East Asian or South-East Asian	408 (10.6)	675 (10.6)
Prefer not to say	226 (5.9)	484 (7.6)
Mixed heritage	112 (2.9)	161 (2.5)
Black	102 (2.6)	115 (1.8)
South Asian	13 (0.3)	20 (0.3)
Native American or Alaska Native	13 (0.3)	17 (0.3)
Middle Eastern or North African	7 (0.2)	12 (0.2)
South African	4 (0.1)	8 (0.1)
Polynesian/Pacific Islander	3 (0.1)	4 (0.1)
Other	515 (13.4)	864 (13.5)
No response	N/A	715 (11.2)
Sex		
Female	2691 (69.8)	3965 (62.1)
Male	1142 (29.6)	1589 (24.9)
Prefer not to say	16 (0.4)	43 (0.7)
Intersex	9 (0.2)	14 (0.2)
No response	N/A	771 (12.1)
Sexual Orientation		
Heterosexual/Straight	3161 (81.9)	4356 (68.3)
Bisexual/Pansexual	225 (5.8)	311 (4.9)
Homosexual/Gay/Lesbian	143 (3.7)	181 (2.8)
Prefer not to say	110 (2.9)	185 (2.9)
Asexual	101 (2.6)	145 (2.3)
Queer	44 (1.1)	64 (1.0)
Other	74 (1.9)	113 (1.8)
No response	N/A	1027 (16.1)

Abbreviation: N/A, not applicable.

Time Commitment and Motivation

The inability to commit the time to participate in a clinical trial was cited as a barrier by 29.2% of participants, due to either willingness or ability. An altruistic motivation was cited by 39.5% of survey respondents overall, and even by 19.1% of people who did not want to participate in trials. Even for those who cite time commitment as a barrier, participation in a clinical trial may satisfy an altruistic desire to contribute to society or the advancement of science.

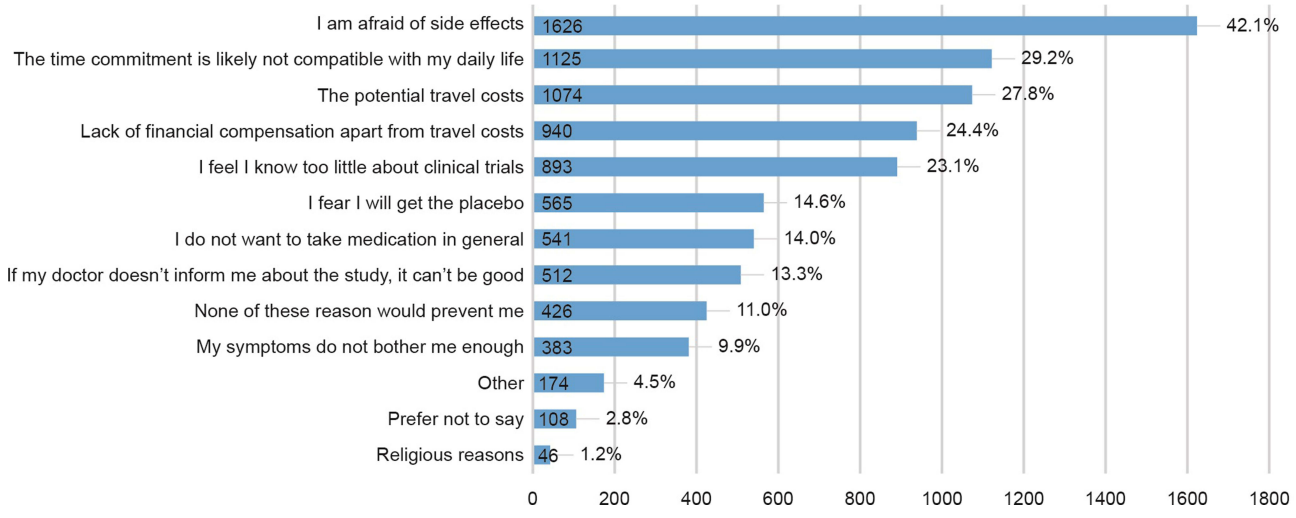

Figure 1 Barriers to Participation.
Note: up to 3 answers were allowed per respondent.

Financial Cost of Participation

Financial security was self-reported in the questionnaire. Of the "true completers", 33.1% said that they "do not feel at all financially secure", 24.1% feel "somewhat financially secure", and 28.6% feel "very financially secure".

Of the three most cited practical barriers to participation, two distinct but closely related financial barriers were "potential travel costs" (27.8%) and "a lack of financial compensation apart from travel costs" (24.4%). A lack of financial compensation apart from travel costs might include lost wages, or the cost of child/dependent care. The direct cost of travel to a study site might be train and bus tickets, or the cost of fuel for a car. Travel costs were cited as a barrier more frequently by participants with lower levels of financial security (Figure 2).

"A lack of financial compensation apart from travel costs" was cited as a barrier for 34.7% of bisexual/pansexual participants, and 44.6% of homosexual participants, whereas 28.0% of heterosexual participants cited it as a barrier. Only 17.2% of asexual participants and 23.1% of participants who identified as Queer cited a lack of financial compensation as a barrier. This indicates that the interaction of LGBTQ+ identities and financial privilege is a complex one, rather than marginalization leading directly to less financial privilege. In terms of race, 61.8% of Black participants cited a lack of financial compensation as a barrier compared with 28.9% of White participants.

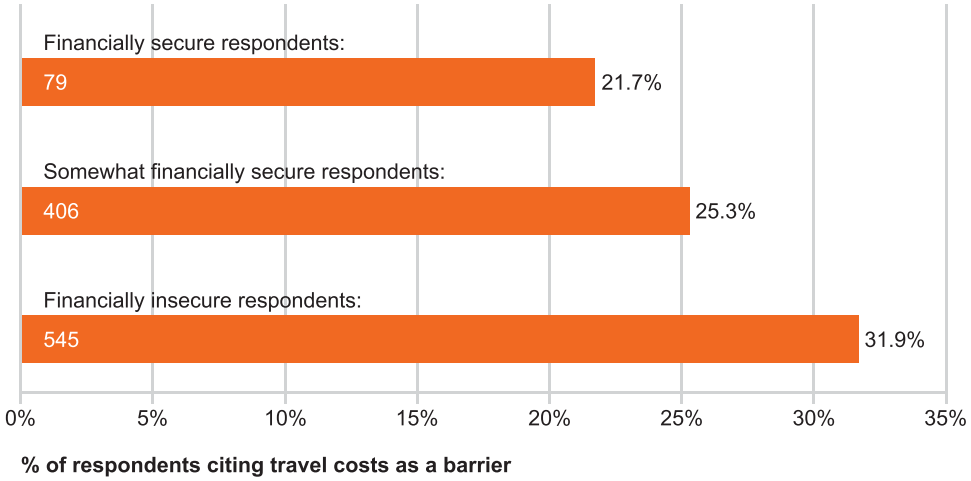

Figure 2 Impact of Travel Costs on Survey Participants Increased with Increasing Financial Insecurity.
Note: Participants self-identified their level of financial security in answer to the question "Which of the following best describes your feeling of financial security?".

Psychological and Knowledge Barriers

Past experiences with clinical trials seemed overwhelmingly positive, with 91.3% of previous clinical trial participants saying they would be willing to participate again. The greatest barrier to trial participation regardless of participant characteristic was a fear of side effects (42.1% of "true completers"). For those that had previously participated in a clinical trial only 28.0% said they feared side effects compared to 46.9% of those who had not participated in a clinical trial previously. Lack of clinical trial knowledge was cited as a barrier by 23.1% of all participants. Among those who were unwilling to participate in clinical trials, 31.4% cited a lack of knowledge as a barrier, and 32.3% said they did not have a good understanding of clinical trials. In addition, 14.6% of survey participants cited a fear of receiving placebo as a barrier to trial participation. Conversely, "learning about my condition or the treatment" was the top motivation (42.4%) to participate in a clinical trial.

Discussion

These results provide a greater understanding of barriers to clinical trial participation and how they vary by factors such as gender identity, medical history, race/ethnicity, and healthcare systems. Barriers and motivations commonly cited by people in the US were validated on a global level. Individual differences are not discussed because although there were some instances in which responses varied by country, globally, the findings were predominantly consistent.

Whilst the barriers to clinical trial participation are well documented, as noted by both patients and healthcare professionals,[3,6,7] the challenges posed by this complex interplay of demographic factors call for correspondingly complex and diverse solutions. Such solutions aim to increase trial enrollment rates and trial diversity on a global scale.

A lack of sufficient time to participate in a clinical trial was more likely to be a barrier for participants from financially insecure backgrounds demonstrating that a time commitment is linked to financial barriers. The time spent by a person traveling to the study center, completing required assessments, receiving the treatment, and traveling back is likely to result in time taken out of their paid employment, housework, childcare, or the care of family members.

Financial reimbursement of direct trial costs alone may not overcome additional barriers faced by potential trial participants, including inability to get time off work, upfront cost of travel to the study site, and arranging care for dependent family members, as noted above. Minimizing the time commitment overall for a potential patient through the design of a clinical trial has the potential to address both financial and time barriers cited by respondents in this survey. Reduction of physical site visits, localized options for some clinical assessments, arranged travel, and providing clear communication of financial reimbursement arrangements to potential participants, could increase the participation of patients from financially insecure backgrounds. Participants from under-represented groups, such as the LGBTQ+ community or some racial/ethnic minorities, cited financial barriers to trial participation more highly, and are likely to find the indirect costs associated with clinical trial participation prohibitively high.

Where financial barriers are addressed, providing information to potential participants of the altruistic aspect of trial participation may be impactful and inform their decision to commit time to a trial. Additionally, working closely with a person to schedule on-site appointments that fit their work or family schedule and making some trial requirements accessible from home can increase willingness to participate. For example, if a clinical trial requires a person to have regular check-ins with healthcare professionals, these check-ins might be done remotely or with a local healthcare provider; or, the patient could be supported to self-administer the treatment at home.

The final barrier identified was driven by a person's expectation of what might happen to them and a lack of knowledge or information about what a clinical trial involved. Such fears can come from a history of bad experiences with doctors and healthcare systems, which disproportionately occurs in underrepresented communities. For instance, survey respondents identifying as non-binary reported greater dissatisfaction with their doctors than any other gender identity. Educational materials can empower potential trial participants to engage with healthcare professionals and ask the questions they have and understand the support available to them to participate.

In Phase 2 or Phase 3 studies, the investigational treatment has already been tested on dozens or even hundreds of people, helping the study researchers understand the treatment's side effects and refine their research methods. By supporting healthcare professionals in providing clinical trial information, potential patients can be better informed when discussing side effects by receiving accessible information that they can review with carers and family members at their own pace. Although a relatively small number of participants (14.6%) cited fear of

receiving the placebo instead of the real treatment as a barrier, this was still the third most-cited psychological barrier identified. A fear of receiving placebo could be addressed through conversations with potential participants to explain the role of a placebo and that by participating they would still be contributing to the development of a treatment that could eventually help them and other people with the same condition.

When analyzing the survey results, it was crucial to consider the analysis' potential limitations. First, the participants that responded may not be completely representative of the general population. The analysis included participants who are more likely to answer a survey and have already expressed an interest in clinical trials, for example, those with an existing illness, scientific curiosity, or healthcare experience. This explains some differences between our data and similar data from the general population – less than 5% of the general population have participated in a clinical trial versus 23.9% of the survey participants. However, this bias does not invalidate the findings of the survey. Therefore, the conclusions taken from these data are empirically grounded and relevant to the goal of boosting participation in clinical trials. Second, this survey was novel in exploring why potential patients would or would not participate in clinical trials, so it did not include formal statistical analyses. Rather than looking for statistical significance, the conclusions from this exploratory survey should form the basis of future hypothesis-driven confirmatory research. Additionally, answers to the survey questions could vary depending on the participants country of origin, culture, experiences of healthcare systems, age, ethnicity, and gender. Despite the inclusion of 9 countries to help capture an inclusive global perspective, global variations are vast and complex, and there are regions that are not represented such as South America, Africa, and the Middle East. Furthermore, the 9 included countries are a single country representation of the region and variation could be present across the region. To ensure adequate representation from Asia, China, Malaysia, and Singapore were added after study initiation and therefore the number of responses per country were lower than in Europe and North America.

Conclusion

In conclusion, the results of this survey identified that the lack of representative enrollment in clinical trials is a result of barriers, rather than an absence of motivation to participate across all groups. These barriers are common across countries and respondent characteristics but differences were noted as some groups cited some barriers more highly than others. It is therefore critical when considering your study design to consider a patient's time and finances, in addition to providing the right information, as for some underrepresented groups this will be more important than others. The insights from this exploratory survey should be used as a stepping stone to help form the basis of future hypothesis-driven confirmatory research, and to inform new strategies for increasing the diversity of populations in clinical trials and making trial participation more widely accessible.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

Amy Froment and Kristin L Parkhurst are employees of and stockholders in Regeneron Pharmaceuticals, Inc.

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