Perspective:
COVID-19

Impact of COVID-19 on Clinical Research and Inclusion of Diverse Populations

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The randomized clinical trial (RCT) has long been recognized as the 'gold standard' for developing evidence for clinical treatments and vaccines; however, the successful implementation and translation of these findings is predicated upon external validity. The generalization of RCT findings are jeopardized by the lack of participation of at-risk groups such as African Americans, with long-recognized disproportional representation. Distinct factors that deter participation in RCTs include distrust, access, recruitment strategies, perceptions of research, and socio-economic factors. While strategies have been implemented to improve external validity with greater participation among all segments of the population in RCTs, the coronavirus disease 2019 (COVID-19) pandemic may exacerbate disparities in RCT participation with the potential impact of delaying treatment development and vaccine interventions that are applicable and generalizable. Thus, it is essential to include diverse populations in such strategies and RCTs. This Perspective aims to direct attention to the additional harm from the pandemic as well as a refocus on the unresolved lack of inclusion of diverse populations in conducting RCTs. *Ethn Dis*. 2020;30(3):429-432; doi:10.18865/ed.30.3.429

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Introduction

During this critical time of the coronavirus disease 2019 (COVID-19) pandemic, media reports and communications referencing on randomized clinical trial (RCT) evidence and the efficacy of treatments and vaccines have emerged at an unparalleled rate. An important consideration for RCTs is the external validity and generalizability of the results to all segments of the population, in particular, high-risk populations such as African Americans, Hispanics, Asian Americans, Native Americans, Alaska Natives, and Pacific Islanders.[1] Historically, many of these individuals have been underrepresented in clinical studies, which complicates the generalizability of RCTs results.[2] Numerous factors contribute to the poor participation in RCTs, including the lack of trust in the clinical research process.[3] Regardless of the reasons for the disparities in clinical and translational research, the disproportionate low accruement of minority groups jeopardizes the interpretation of RCT results and significantly delays the implementation of high-impact interventions for these at-risk populations.[4] The parameters associated with the lack of RCT participation have been well-assessed with specific interventions designed to increase recruitment.[5] While these strategies and programs have sometimes been effective in RCT accruement, the disproportionate representation continues to challenge the external validity of many RCTs.

COVID-19 appears to be an excess burden for underrepresented minority groups due to higher rates of infection, hospitalizations, and mortality.[6] These disparities are further complicated by higher rates of co-morbidities and socio-economic factors that impact COVID-19 infection and outcomes. Conditions including diabetes, hypertension, kidney disease, cardiovascular disease and cerebrovascular disease contribute to COVID-19 outcomes and are also associated with a higher prevalence among these minority segments of the population. While accelerated plans for COVID-19 treatments and vaccines are being promoted, such interventions will be dependent on expediting proper RCTs.[7] It is imperative that these RCTs include representation and participation

of all groups. The pandemic may worsen the ability to ensure inclusion of diverse populations due to the nature of the infection unless specific strategies are implemented.

The reasons underlying the lack of participation in RCTs by minority groups and the initiatives for addressing this disparity are relevant to the COVID-19 pandemic and include factors in systems and individuals.

Systems

Perception and understanding of the RCTs and results can affect participation. Specifically, many RCTs that include inadequate representation of minority groups such as African Americans are reported as 'strong conclusive evidence' resulting in the perception that the participation of all at-risk groups is not that essential.

The COVID-19 RCTs may also be faced with this perception resulting in a further distrust of the clinical and translational study dynamics. In turn, this is an opportunity for clinical researchers to emphasize minority and diverse RCT participation with focused strategies for accruement and retention. Such communication of the critical importance of inclusion for both the researchers and the population can be used to address negative perceptions of RCTs and building trust. Further, the pandemic provides an education opportunity to distinguish the proper 'physical distancing' from 'social distancing,' where social interactions are especially important for minorities.

The availability of clinical research is a major systems consideration; often, RCTs are associated with academic medical centers where minority groups may have less access. This is further complicated by the low number of underrepresented minority RCT clinical investigators. Still, this lack of involvement in RCTs serves as an opportunity to identify study sites that are easily accessible to all groups, such as regional medical centers. Further, COVID-19 clinical trial initiatives represent an opportunity for the development of continuing medical education and distance learning tools that could potentially aid in the acquisition of clinical research competencies among the community-based health care workforce.

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Contributing to the system category of barriers to participation in RCTs is the lack of community engagement. Such communication and involvement are essential to RCT success. In one sense, the COVID-19 pandemic is a barrier to community engagement with the associated "social distancing" and limited interactions. However, this is an opportunity for innovative strategies that enhance community engagement while respecting the restricted social interactions.

Individual

An equally important consideration of barriers to RCT participation are factors in the individual category that include: 1) awareness of clinical trials; 2) perception of the RCT infrastructure; 3) attitude and experience; 4) perception of patient's ethnicity; 5) eligibility; 6) trust; and 7) access.

The simple lack of awareness of RCTs on the individual level remains a major barrier for RCT participation. In this case, COVID-19 might be a mechanism to enhance the knowledge and awareness of RCTs. Specifically, when communicating COVID-19 clinical study plans, announcements might indicate RCT participation as socially responsible in addition to highlighting the important role that RCT participation by minority groups plays in the scientific enhancement and external validity of RCTs. As such, this pandemic provides an opportunity to engage the community and build trust.

The perception by the individuals of the RCT structure and administering institution is certainly a factor in participation. Previous experienc-

es, as well as hearsay, impact participation in RCTs. These interactions and stories have become major content for social media and the 'rumor mill' in conjunction with the pandemic. Again, these issues represent an important opportunity for RCT leaders to describe the interventions to address negative experiences from the past and provide assurances for positive participation for the future.

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Inclusion and exclusion criteria are critical components of the RCT process; yet, these screening factors can disproportionately impact the ability of underrepresented minorities to participate in RCTs. Moreover, various COVID-19 trials include co-morbid conditions more prevalent among under-represented minority groups, hence, rendering them ineligible to participate. RCT investigators could, as appropriate, modify the inclusion and external criteria to enhance participation.

Mistrust has long been recognized by RCT investigators as a factor that limits RCT participation and it is a major detriment to RCT external validity. Given the increased risks for COVID-19 infection, hospitalization and mortality rates among minority groups, it is equally probable that the 'lack of trust' attitude might be sustained. Thus, RCT leaders should develop focused strategies to build and sustain trust. These strategies may include acknowledging historical accounts of unethical treatment, recognizing personal bias and systemic inequalities that exist within the health care system and making a commitment to address barriers through effective policies and procedures that limit unfair treatment.

Access to RCTs is another factor impacting participation and is affected by many social determinants and socioeconomic factors including transportation, study visit time of day, time constraints, and the ability to take time off from jobs. Moreover, due to the lack of transportation, especially with COVID restrictions that have many public transportation systems being diverted or shut down, many individuals may be even more limited by options in transportation. Thus, COVID-19 continues to present an issue in participation by minority groups in RCTs. These challenges represent an opportunity to design innovative RCT access strategies such as telehealth and telecommunications, which by necessity have been enhanced with the COVID-19 pandemic.

Conclusion

The participation of all segments of the population including underrepresented minorities in RCTs is essential for external validity and translatability of evidence acquired from COVID-19 RCTs. While the COVID-19 pandemic both impacts and highlights disparities in clinical trial participation, it can also be considered an opportunity to address and improve this major clinical research issue.

Conflict of Interest

No conflicts of interest to report.

Author Contributions

Research concept and design: Lackland, Voeks; Data analysis and interpretation: Lackland, Sims-Robinson, Buie; Manuscript draft: Lackland, Sims-Robinson, Buie, Voeks; Statistical expertise: Voeks; Administrative: Lackland, Sims-Robinson, Buie; Supervision: Lackland

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