

EDITORIAL

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Distrust and minority trial participation: more than meets the eye

Raegan W Durant¹

Racial and ethnic minorities continue to be under-represented in clinical trials [1,2]. Compared with whites, these minority groups frequently suffer disproportionately with poorer outcomes from many diseases [3]. However, clinical trials focused on those same conditions often lack minority representation commensurate with the disease burden in these often overlooked populations [1,2]. The under-representation of minority populations in clinical trials has both methodological and ethical implications [4]. Inadequate enrollment of racial and ethnic minorities threatens the generalizability of study results to these under-represented populations [4]. Consequently, the limited inclusion of racial and ethnic minorities in clinical trial populations may hinder efforts to develop novel solutions that address racial differences in disease outcomes [4]. Beyond these methodological considerations, low minority representation in study populations also diminishes the opportunities for traditionally underserved minority groups to share equally in the benefits and risks of trial participation [4]. These potential implications of inadequate representation underscore the need to address the persistent racial and ethnic disparity in trial enrollment.

In order to elucidate ways to increase minority participation, investigators have explored a number of potential minority recruitment barriers, including a lack of awareness of clinical trials, unmet transportation needs, conflict with dependent care responsibilities and stringent trial inclusion and exclusion criteria [5–7]. However, distrust among racial and ethnic minorities is the most often cited barrier to enrollment in these subpopulations [8–13]. Similarly, investigators have also demonstrated that a lower level of trust among African-Americans is associated with decreased willingness to participate in clinical trials [9,14]. Distrust may be borne of a broad perspective and collective life experiences. However, specific distrust in physicians is frequently the primary focus of examinations of barriers to minority recruitment into clinical trials [15,16]. The physician–patient relationship is a common context for exploration of trust in the medical literature [13], in large part because individual physicians often serve as the face of the healthcare system and frequently play a major role in referring patients to clinical trials. Therefore, the assessment of trust in these common and very tangible patient–physician relationships has become an outsized surrogate for distrust of other individuals and entities in clinical settings. However, such a narrow focus ignores the possibility that potential research participants may be influenced by broader experiences and perceptions related to clinical institutions and entire healthcare systems [8,10,17–20]. If such a broader outlook is characterized by distrust, negative perceptions of healthcare at the institutional and system level could be additional hindrances to minority research participation [10]. Furthermore, distrust is not rooted solely in clinical experiences or perceptions of clinical settings.

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¹University of Alabama at Birmingham School of Medicine, Birmingham Veterans Affairs Medical Center, AL, USA
E-mail: rdurant@dopm.uab.edu

Potential minority research participants may also form distinct opinions about medical researchers, research institutions and the research enterprise as a whole [8,10]. Although the clinical and research realms overlap significantly, individuals may develop unique perceptions of individual researchers and research institutions that differ from perceptions of parallel clinical personnel and clinical institutions. Therefore, investigators have begun to assess the distinct dimensions of distrust established in research and clinical contexts [10,17–21]. Although the dimensions of distrust are overlapping, unique factors may influence patients' perceptions and faith in clinical and research personnel, institutions and systems. Since multidimensional distrust may be a barrier to minority research participation, comprehensive approaches are needed to address all types of distrust in minority populations.

Despite utilizing multidimensional approaches to measure distrust among minorities [10,20], investigators have often used more focused approaches aimed at eliminating distrust in relatively narrow contexts. For example, multiple interventions have been designed to address interpersonal distrust by improving communication between patients and physicians [16]. Other observers have suggested increasing the diversity and cultural competency of investigators and other research staff as a means of better engaging minority groups [22]. Such interventions may effectively ameliorate interpersonal distrust between potential minority participants and physicians or research staff [8]. The resultant improvement in the quality of individual interactions with clinical and research staff may facilitate minority referral to and enrollment in specific clinical trials. Although each of these focused efforts may be instrumental in minimizing interpersonal distrust among racial and ethnic minorities, they are often implemented in isolation [23], limiting the ability to address the minority distrust at the institutional and system levels. Moreover, efforts aimed at improving interactions between potential minority participants and clinical or research personnel may also be trial-specific with limited generalizability to other clinical settings or studies. Therefore, single interventions focused on improving interactions with physicians or researchers may be inadequate to address multilevel distrust hindering minority research participation.

Increasingly, investigators should begin to pursue multidimensional approaches to address minority distrust. Rather than individual clinicians or researchers assuming the sole responsibility for eliminating minority distrust in their own personal interactions or specific studies, efforts to eliminate distrust and improve trial recruitment among minorities have to span entire institutions and communities. Building on trial- and

clinic-specific efforts, research and healthcare institutions must cultivate mutually beneficial partnerships with racial and ethnic minority communities. These partnerships should be aimed at empowering minority communities to define their own research priorities, based on their highest priority healthcare needs. The establishment of a community advisory board with representation from minority communities may be helpful both in reducing institutional distrust among minorities and providing them with a voice in setting the research agenda. Longitudinal partnerships through the engagement of minority populations may minimize some of the uncertainty and misgivings about research that frequently underlie distrust and impede minority trial participation. Broad-based educational programs aimed at increasing minority awareness of the role of clinical research in healthcare may also be an effective approach. These programs could potentially highlight the critical role of clinical research in the development of new healthcare technologies and therapies. In addition, programs could also help to define certain nuances of clinical trials, such as blinding and randomization, that otherwise may increase uncertainty related to trial participation and reinforce distrust among racial and ethnic minorities.

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Of course, the implementation of multifaceted efforts to engage minorities in research may require resources and time that are often in short supply when conducting clinical trials. While individual investigators or specific study budgets might have difficulty supporting these efforts, research and clinical institutions as well as research funding sources could provide the resources necessary to support long-term community engagement. Although longitudinal minority engagement efforts may not be specific to a particular trial, the long-term relationships with minority populations would potentially facilitate minority enrollment across multiple studies within an institution. The collaborative partnerships with racial and ethnic minority communities would serve as a precursor to more trial-specific recruitment approaches. Any resultant increase in minority research participation could potentially optimize the generalizability of all study results and achieve greater equity in exposure to the benefits and risks of research participation.

At the system-level, ethical policies guiding all human subjects research may serve to address distrust among minorities, but, like many laypeople, these groups may be largely unaware of these protections.

Targeted efforts to publicize the regulatory safeguards for human research subjects, especially in vulnerable populations [24], may also help to address minority distrust in the research enterprise. Educating potential participants about the multilayered regulation of human subjects research may help to eradicate a common fear of research abuse. In clinical contexts, uncertainty over system-level factors, such as insurance coverage of experimental therapies, may also deter minority participation in clinical trials [25]. Similar to the research context, uniform policies should be established so that patients can confidently manage any ancillary healthcare issues in the setting of a clinical trial.

Distrust is multidimensional and can hinder minority participation in clinical research at multiple levels. Accordingly, narrowly focused interventions utilized in isolation to improve a specific type of distrust among

minorities may be insufficient to overcome other types of distrust that go unaddressed. Therefore, clinical and research communities must develop and implement multifaceted and longitudinal approaches to address distrust among racial and ethnic minorities in order to improve minority participation in clinical research.

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