

Commentary

Racial under-representation in clinical trials: Consequence, myth, and proposition

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Abstract:

The historical under-representation of Blacks in clinical trials is well-documented. The ethical ramifications of racial under-representation in clinical trials are exacerbated by the epidemiologic and clinical consequences. For example, persistent under-representation undermines generalizability and challenges inferences regarding treatment safety and efficacy for minority races. The potential for such consequences warrants greater racial diversity in clinical trials. However, investigators have assumed that recruiting Blacks for clinical trials is hampered by unwillingness to participate. Recent reports indicate that the perception of unwillingness may be unjustified. An often overlooked aspect is that conventional recruitment strategies may be ineffective for recruiting racial minorities. Public health professionals from all disciplines have the collective capacity to improve racial diversity in clinical trials primarily because of access to minority communities. Public health professionals could facilitate an effort to encourage collaboration between trial centers and community health clinics in predominantly minority settings.

The historical under-representation of Blacks in clinical trials is well-documented.[1-10] Concerns of racial (and gender) under-representation led to the development of the National Institutes of Health (NIH) Revitalization Act of 1993 that incorporated guidelines on the inclusion of racial minorities as participants in clinical research.[11] The guidelines were intended to create awareness of minority under-representation and promote diverse participation. The NIH's recognition and action regarding disparate racial representation is ethically and scientifically mindful. Currently, NIH-funded trials are ~2.4 times more likely (55.8% vs. 23.7%, $p < 0.001$) than non-NIH funded trials to report racial characteristics.[4] The emphasis on greater accountability resulted in improved racial diversity, but the improvement is inadequate. Although statistical

significance may have been achieved because the study utilized a large sample size, NIH-funded trials are only somewhat more likely than non NIH-funded trials to include racial minorities (13.5% vs. 12.5%, $p < 0.001$).[4]

The ethical ramifications of racial under-representation in clinical trials are exacerbated by the epidemiologic and clinical consequences. Persistent under-representation undermines generalizability and challenges inferences regarding treatment safety and efficacy for minority races.[1-3,5,7,10,12] For example, recent evidence indicated that statin use prior to ischemic stroke incidence may be beneficial for preventing poor stroke outcomes among Whites, but statin pretreatment may be detrimental for Blacks.[13] The overall estimate suggested lower odds of poor outcomes among statin pretreated patients (OR=0.74,

95% CI 0.53, 1.02), but the race-specific estimates were markedly different on a multiplicative scale (Whites: OR=0.61, 95% CI 0.42, 0.86; Blacks: OR=1.82, 95% CI 0.98, 3.39).[13] Interestingly, the overall estimate in the investigation by Reeves et al. corroborated results from the landmark Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial.[14] However, the SPARCL investigators did not report racial characteristics of the study population or race-specific effect estimates. Stratified analyses would be justifiably avoided if Blacks were under-represented in the trial because sparse data yield unstable effect estimates, but the potential for differential treatment response between races reiterates the necessity for incorporating a sufficient number of minorities in clinical trials. Sufficient racial representation may allow for improved evaluation of race-specific effects.

The scientific community's justification for insufficient racial representation is, perhaps, the greatest concern. Investigators have assumed that recruiting Blacks for clinical trials is hampered by unwillingness to participate.[1,15] The Black community's mistrust resulting from unethical events in medical history is most often cited as the underlying reason for unwillingness to participate in current research.[1,15] However, recent reports, including a systematic review, indicate that the perception of unwillingness may be unjustified.[1,2,16] The sample of clinical trials identified by Wendler et al. yielded greater consent rates for Blacks than Non-Hispanic Whites (45.3% vs. 41.8%).[1] Blacks also demonstrated higher consent rates than Non-Hispanic Whites for surgical interventions (65.8% vs. 47.8%).[1] A separate investigation reported that willingness to participate in HIV vaccine trials was not associated with race despite a higher prevalence of general mistrust among racial minorities.[16] The emerging evidence indicates an unsettling disconnect between the perceptions of the scientific community and the reality regarding the willingness of Blacks to participate in clinical trials. Furthermore, the reports raise concerns that current approaches to minority recruitment for clinical research may be ineffective.[1,16]

Public health professionals from all disciplines have the collective capacity to improve racial diversity in clinical trials primarily because of access to minority communities. For example, public health professionals could facilitate an effort to encourage collaboration

between trial centers and community health clinics in predominantly minority settings. Community health clinics may be a valuable resource for recruiting racial minorities because of familiarity with the population. Efforts to inform community clinics of upcoming clinical trials and sustain access to information for providers and potential participants may gradually improve minority recruitment. Furthermore, mistrust may be reduced by involving community clinics. Minority populations may be more receptive to information and education regarding clinical trials from trusted providers rather than trial centers without pre-existing involvement in the community.[17,18] Community providers may also be more capable of providing pertinent information in a culturally sensitive manner.[17,18]

A comprehensive strategy based on some of the principles outlined herein was successful in recruiting and enrolling racial minorities for the Women's Health Initiative (WHI) trial and may serve as a practical model.[18] For example, non-minority women were more effectively recruited by mass mailings and presentations at community-based events, whereas minority women were more effectively recruited using referral programs and presentations at churches supplemented with mass mailings.[18] Black women who received the trial information had the lowest refusal rates compared to other races,[18] a phenomenon expanded to include all Blacks by Wendler et al.[1] Therefore, a critical issue may be simply ensuring that Blacks and other racial minorities receive the appropriate information.[18] Ultimately, mounting evidence indicates that conventional recruitment strategies may be limited by a lack of generalizability to other races, similar to the results from some clinical trials.

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