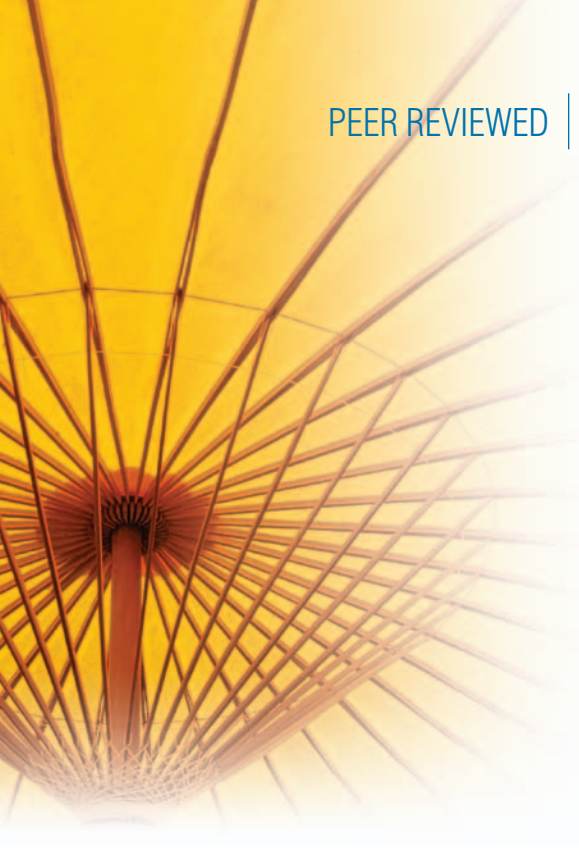

Seeing Things Differently

Cultural Competence and Minority Inclusion in Clinical Trials HS

Clinical data on communities of color are scarce, reflecting low participation rates in clinical trials while predicting continued gaps in evidence regarding safety and efficacy of new therapies.

In the United States, minorities are overrepresented in morbidity and mortality statistics, yet underrepresented in clinical studies.[1] Minorities are the fastest growing populations in the country; the U.S. Census Bureau estimates that by 2050, minorities will in fact be the majority at approximately 51% of the population.[1] However, clinical data on communities of color are scarce, reflecting low participation rates in clinical trials while predicting continued gaps in evidence regarding safety and efficacy of new therapies and uncertainty about meeting the expanding needs of emerging markets.[2]

Abundant scientific evidence supports the urgent need for new sensitivity initiatives to bridge attitudinal and logistical barriers to access, many of which find their origins in the medical system and cause underuse of services that leads to poor outcomes.[3]

The Science of Inclusion

Pharmacogenetic research in recent decades has uncovered significant differences among racial and ethnic groups in terms of metabolism, clinical effectiveness, side-effect profiles, and toxicity of drug treatments.[2] In peer-reviewed journals, nearly 30 therapies were found to have differences in safety or efficacy among various racial or ethnic groups,[4] suggesting that genetic polymorphisms differ in frequency on the basis of ethnicity and ancestry.[5] For example, African Americans respond less well than Whites to beta-blockers, ACE inhibitors, and other primary agents now used to treat heart-related conditions.[6] Differing dose guidelines have been established to reflect the role of ethnicity in drug response for Blacks, Asians, and Whites taking warfarin and a few other medications[7] (see Table 1).

Because less is clear about drug responses of other ethnic groups, additional research and development are necessary to understand and apply potential metabolic differences and to allow personalized therapy recommendations based on ethnic or racial origin.[9] Evaluating new pharmacological compounds in minorities is likely to reveal drug actions and side effects specific to these groups, and holds the promise of new therapies with specific advantage to these populations.

Scientific data demonstrate genetic differences in the expression of drug-metabolizing enzymes, but few studies have featured minorities in statistically significant numbers, or with sufficiently sensitive measures, making race- or ethnicity-associated differences in pharmacokinetics and pharmacodynamics less well understood.[7] To capture significant differences that may exist and ensure the efficacy of promising new treatments in the real

HS Home Study article

LEARNING OBJECTIVE

After reading this article, participants should be able to recognize central concepts of diversity in clinical trials, and to proactively apply this information toward a point of view that values and implements cultural competence.

DISCLOSURES

Allison Kalloo, MPH: Nothing to disclose.

Table 1 Examples of Drug Efficacy Variations According to Race*

Brand name (generic)	Variation in Efficacy
Aricept® (donepezil)	Shown to be more effective in Black patients than others with Alzheimer's disease
BiDil® (isosorbide dinitrate and hydralazine hydrochloride)	First drug approved for marketing to a specific ethnic group; used in addition to routine heart medicines to treat heart failure in Black patients
Coumadin® (warfarin)	Different dosing requirements noted for Blacks, Whites, and Asians
Crestor® (rosuvastatin)	Demonstrates cholesterol-lowering efficacy in Blacks, Hispanics, and South Asians; Asians require a lower dose while Blacks need a higher dose

*Source: Yesuda et al[7] and excerpted from *A Question of Color* by D. Anderson Company, 2010.[8]

world, study participants must reflect population diversity—giving cultural competence a critical role in clinical trials. Higher mortality and morbidity among communities of color underscore the relevance of personalized medicine and suggest an onus on drug sponsors to factor in ethnicity during study and recruitment design.

Social Savvy in a Clinical Context

The root causes of disproportionate disease burden in the United States are complex, but often entrenched in historic and persistent systemic inequities.[10] Access to cutting-edge advances and state-of-the art care discovered in clinical trials is not routinely available to communities of color, which results in therapies that often fail to meet the needs of diverse populations and contributes to ongoing health disparities.[1] Black men in Washington, D.C., have shorter lifespans than men in India or Caucasian men in their own hometown;[11] the causes are almost entirely social, according to a 2008 report from the World Health Organization.[12] Racial dynamics can vary across the globe, but social determinants of disease are universal and irrefutable, particularly in disease areas with substantial ethnic inequalities.[13]

Indigenous subpopulations in many countries with a legacy of colonization and longstanding discriminatory practices share a distrust of government agencies.[14] These societies have tended to retain power imbalances that affect current access to care, with persistent psychosocial stressors that contribute to health disparities.[14]

In the U.S., a complex historical milieu and power imbalance between cultural groups play a part in health disparities and clinical trial participation disparities alike.[15] By contrast, U.S. power players in scientific discovery—those making hiring decisions, designing protocols, both awarding and winning grants, running drug corporations, and recruiting patients—are largely not minorities.[16] To put it into context, Black doctors comprise less than 4% of U.S. physicians,[17] and of these approximately 30,000 Black physicians, less than 1% are active in clinical research.[18] This power disparity forces a dominant group point of reference, exacerbates vulnerabilities, and perpetuates other disparities.[15] This disconnect, if unchecked, will continue to block access to the process and to engender distrust, suspicion, misinformation, and antipathy about clinical research.

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Addressing residual sociopolitical tensions, improving intercultural communication, enhancing transparency, and evoking a sense of safety in clinical settings have profound potential for practical outcomes. Expert findings support cultural competence as a viable move in the right direction, compelling federal policy makers to focus on it at official levels to stem the tide of disproportionate disease burden.[12]

David Satcher, MD, former U.S. Surgeon General, has found that targeting the social determinants of health is a cost-effective measure for closing gaps and improving health for all.[19] Communication between providers and patients affects the appropriateness and quality of health services provided.[10] Likewise, the pharmaceutical industry would want to incorporate cultural insights early enough along the study timeline to elicit useful data that will design more inclusive protocols, prevent serious adverse events and costly drug recalls, and ultimately bring quality medical advances to emerging markets. Cultural competence is that social savvy.

Through a Different Lens

The rapid changes in the cultural makeup of the U.S. will necessitate adjustments in the way research is conducted, with

these demographic shifts increasingly requiring researchers to better understand cultural differences and how they potentially affect research study design, analysis, and interpretation, as well as how to ensure that their research is applicable and adapted to diverse populations' needs.[20]

The changing demographics and economics of a growing multicultural world—and the longstanding disparities in the health status of people from diverse ethnic and cultural backgrounds—now challenge healthcare providers to consider cultural competence as a priority.[10]

Stereotyping, institutional racism, and dominant-group privilege continue to play significant roles in patient-provider dynamics and exacerbate health disparities.[21] Smedley and colleagues determined that health professionals must be cognizant of the marked effect of racism on health status, behavior, and healthcare interactions.[10]

Appreciating the nuances of these power dynamics can prevent blind spots and create more sensitivity, responsiveness, and access. Resolving underrepresentation in clinical trials is so vital to the wholesale success of scientific discovery that its very integrity hangs in the balance, with participation inequities presenting a major glitch in an otherwise modern healthcare system.

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Systematically woven into study components and interactions, applied cultural competence is potentially transformational for the industry. However, simply inserting brown faces and ethnic catchphrases into vanilla materials is insufficient. To ensure a better vantage point regardless of setting or funding source, investigators should covet the deeper insights possible regarding sensibilities, perception of the medical establishment, family values, and the ways different cultural groups tend to receive and process information.

Proactive sensitivity measures, applied consistently, stand to save study resources by allowing better planning, budget allocation, recruitment efficacy, and applied logic, and even averting regulatory snafus. In this regard, cultural competence provides the traction and prism often lacking in patient recruitment.

Transforming the Culture of an Industry

Twenty years following the National Institutes of Health (NIH) Revitalization Act of 1993 mandating minority participation in federally funded studies, anemic compliance still frustrates strategies to overcome impediments to inclusion.[22,23] A review of literature from 1989 to 2000 found that only two out of 253 clinical trials even reported their results by race or ethnicity, regardless of funding source.[24] Studies continue to find that few minorities are being invited to participate in clinical trials, even when the diseases under study predominantly affect them.[25]

In the aftermath of the Tuskegee syphilis fiasco, and despite the recollection of it by some African Americans,[26] willingness to participate is not the barrier it had been in previous times.[27] In fact, recent studies found minorities as willing as Caucasians,[1] suggesting that minority involvement in clinical research is more closely linked to access than attitudes. Having never been asked to participate in research is a prime barrier to access; witness, for example, the lack of participation of HIV-infected African Americans in treatment trials despite gross disparities in and desperation stemming from that diagnosis.[20]

A review of consent rates for clinical research by race or ethnicity underscores access as the most important determinant of minority participation.[28] Researchers at the NIH and Yale School of Medicine found that minorities participate in clinical trials at the same rates as Whites when they meet study criteria and are informed about the opportunity to enroll. They found big differences, however, regarding who was asked to participate, debunking the myth that minorities are less willing to participate.[29]

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Meanwhile, sweeping efforts such as the Clinical Trials Transformation Initiative[30] imply industry-wide changes that identify and direct pragmatic, yet innovative, inclusion practices that will bolster the quality and efficiencies of research overall.

Successful diversity in trials is associated with the value investigators place on inclusion of minority participants in their research,[31] when cultural obstacles are not viewed as *faits accomplis,* and intrinsic fears of failure are overcome. Communication skills and tactics matter; access relies on increasing industry sensitivity, acknowledging prior medical atrocities, reviewing patient protection practices, and articulating appropriately the importance of minority participation.[32]

Among African American women, culturally appropriate methods rather than generic, "one-size-fits-all" recruitment was more likely to improve recruitment success rates.[33] Success in recruiting African American males for research on prostate cancer prevention was attributed to race-concordant recruitment materials informed by the target population.[34]

Overall, improving inclusion is predicated on industry reform in attitude, priorities, and practices.

The Impact of Cultural Competence

Study homogeneity poses both ethical and practical threats to scientific integrity. Status quo patient recruitment tends to overlook or ignore participation barriers, which compromises the equity of medical progress, perpetuates health disparities, and leaves the most vulnerable behind. The National Cancer Institute puts it this way: "If trials do not include minorities, then there is a question of whether or not the results of the studies are relevant to everyone across the board."[35]

Cultural competence can be defined as a set of behaviors, attitudes, and policies that promotes ethical, effective interactions between people of different cultures, backgrounds, and relative power. Power imbalances necessitate cognizance of those social issues affecting minority participation.

Authentic cultural competence in clinical settings implies:

- Understanding and acknowledging white privilege,[36] historical inequities, and past abuses;
- Respecting disparate cultural values and priorities;
- Educating staff on confounding social, economic, and political variables in health, healthcare, and clinical research;
- Pursuing opportunities to share power, collaborate, and facilitate safe and open dialogue with communities of color;
- Accepting change as essential (on personal, professional, and institutional levels); and
- Adapting attitudes and sites to be receptive to the unique needs of others.

Cultural competence can be crucial to successfully recruiting and retaining diverse individuals.[37] As a cogent soft skill that can deliver stronger data by taking into account differences in language, communication nuances, and cultural beliefs,[38] cultural competence has implications in hypothesis development, protocol design, outreach and marketing strategies, consent activities, data collection, analyzing and interpreting research findings, drawing conclusions, and presenting results.[16] The resulting broader perspective ultimately distributes both the fruits and burdens of clinical research more equitably.[16]

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Steps toward realizing effective strategies for minority inclusion and cultural competence in clinical trials should involve the following actions:

1. Recognize the dire need, then act on it by training researchers and patient-facing personnel in cultural awareness, sensitivity, and responsiveness.
2. Define populations to be included, depicting diversity within them as well (i.e., varied lifestyles, occupations, skin tones, hair styles/textures).
3. Solicit the support and talent of ethnic minority professionals and local organizations to develop outreach and marketing methods from insider perspective.
4. Plan focus groups and community discussions for specific, first-person feedback about potential barriers.
5. Recruit from new inner-city and rural sites with high ethnic minority populations.
6. Optimize study eligibility, casting inclusion and exclusion criteria more broadly with robust protocol design that accepts more comorbidities.
7. Reduce complexity and length of consent forms; design consent procedures and interface with diversity in mind; outsource to communication experts.
8. Implement tailored, creative marketing recruitment strategies informed by earlier community interface, including mass and social media tactics that reflect high minority consumer patterns.

Banking on mainstream messages, stock tactics, and business as usual to motivate special populations to participate is untenable and will continue to come up short. Alternatively, a tailored and sensitive approach can result in a solid blueprint for inclusion that will resonate with communities of color. Then, cultural competence becomes a practical application that holds widespread potential for robust study diversity and data integrity, discerning important differences and allowing researchers to round out missing facts and fill in blanks that ensure evidence-based conclusions.

Conclusion

Current census projections and ample science substantiate the need to boost minority participation in clinical trials. Rather than minorities lacking a willingness to participate in studies, the real glitches are an absence of culturally appropriate methods and insufficient effort on the part of investigators to motivate and enroll them. The industry's wholesale attitude and efforts concerning inclusion will shape minorities' attitudes toward participating. Undoubtedly, communities of color will participate in clinical research when invited and barriers to their participation are systematically removed.

The challenge to industry is explicit and twofold: First, liberation from the homogeneous status quo of patient recruitment, then entrusting innovation with crafting culturally relevant strategies that motivate a sense of vested interest and take up residence in the realm of sensibilities and social justice. Lest we prolong defaulting on this collective obligation, honing our acuity for better data through meaningful interactions with special populations demands forethought, proactive intent, deliberate study design,

supportive infrastructure, a bit of creativity, and a shared sense of urgency.

Cultural competence becomes a practical application that holds widespread potential for robust study diversity and data integrity.

Exclusion—whether by neglect or design—leaves holes in our science and makes "discovery" little more than a cliché. Limited data are simply not an option.

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