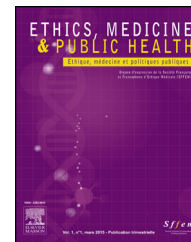




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STUDIES

Clinical trials participation among African Americans and the ethics of trust: Leadership perspectives



Participation des Afro-Américains aux essais cliniques et l'éthique de la confiance : perspectives de leadership

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Summary

Background. – Assuring health equity throughout the US continues to challenge the public and private research enterprise. Even with some progress, racial and ethnic health disparities continue, particularly among African Americans. Health equity for African Americans is improbable unless participation in clinical trials is measurably increased.

Method. – To inform efforts to enhance participation, interviews were conducted with three African American leadership groups from across the country to document their perceptions of why the research community is unable to engage African Americans effectively in clinical trials. The results of thirty-five interviews, conducted from three leadership groups, were analyzed and are reported in this article. The leadership groups include health/education, faith, and civic society.

Ethical considerations. – This research was conducted based upon the ethical protocols of the National Center for Bioethics in Research and Health Care, research ethics, and confidentiality.

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Results. – Findings indicate that trustworthiness must precede trust; both are essential in enhancing African American participation in research, especially in less understood clinical trials.

Conclusion. – Respondents agreed that the research community must demonstrate trustworthiness before trust can be established. They also indicated the importance of increasing the number of African American researchers in leadership roles. Also, suggestions were made regarding the need to develop short and long-term positive relationships between the research community and the African American population, at various levels, if increases in participation in clinical trials are expected. With the likely development of new clinical research and the attention to increasing excess deaths among African Americans, there must be representative numbers of African Americans and other underserved populations in leadership roles if health disparities are to be eliminated and health equity is to be achieved.

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MOTS CLÉS

Afro-Américains ;
Bioéthique ;
Essais cliniques ;
Éthique ;
santé publique ;
Confiance ;
Fiabilité

Résumé

Contexte. – Assurer l'équité en matière de santé aux États-Unis continue de défier les entreprises de recherche publiques et privées. Même avec quelques progrès, les disparités raciales et ethniques en matière de santé persistent, en particulier parmi les Afro-Américains. L'équité en matière de santé pour les Afro-Américains est improbable à moins que leur participation aux essais cliniques ne soit accrue.

Méthode. – Pour éclairer les efforts visant à renforcer la participation aux essais cliniques, des entretiens ont été menés avec trois groupes de dirigeants afro-américains à travers le pays afin de documenter leurs perceptions concernant les raisons pour lesquelles la communauté des chercheurs est incapable d'encourager efficacement la participation des Afro-Américains aux essais cliniques. Les résultats de trente-cinq entretiens, menés auprès des trois groupes de dirigeants, ont été analysés et détaillés dans cet article. Les groupes en questions incluent des dirigeants dans le domaine de la santé/éducation, la foi et la société civile.

Considérations éthiques. – Cette recherche a été menée selon les protocoles éthiques du Centre national de bioéthique pour la recherche et les soins de santé, l'éthique de la recherche et la confidentialité.

Résultats. – Les résultats indiquent que la fiabilité doit précéder la confiance. Les deux sont essentiels pour renforcer la participation des Afro-Américains à la recherche, en particulier dans le cadre d'essais cliniques moins bien compris.

Conclusion. – Les répondants ont convenu que le milieu de la recherche se doit de faire preuve de confiance avant de pouvoir établir la confiance avec la population afro-américaine. Ils ont également souligné l'importance d'augmenter le nombre de chercheurs afro-américains jouant un rôle de premier plan. Des suggestions ont également été faites concernant la nécessité de développer des relations positives à court et à long termes entre la communauté des chercheurs et la population afro-américaine, à différents niveaux, si l'on s'attend à une augmentation en ce qui concerne leur participation aux essais cliniques. Avec le développement attendu de nouvelles recherches cliniques et l'attention portée au nombre croissant de décès parmi les Afro-Américains, il est nécessaire d'avoir un nombre représentatif d'Afro-Américains et de membres d'autres populations mal desservies au premier plan afin d'éliminer les disparités et atteindre l'équité en matière de santé.

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Introduction

Health is "the physical, social, psychological and spiritual well-being of the individual and group in their physical and social environment" [1]. Optimal Health is the best possible emotional, intellectual, physical, spiritual and socio-economic aliveness that we can attain [2]. A vision beyond

health to Optimal Health is a paradigm shift, for all peoples, especially African Americans who have experienced a disproportionate burden of morbidity and mortality [3,4]. If the goal is eliminating health disparities and achieving racial and ethnic health equity, another paradigm shift is needed. The shift does not minimize the importance of human and financial resources needed to eliminate health disparities.

However, achieving racial and ethnic health equity encourages a focus on research, specifically targeting current African American health status as a baseline, rather than comparing them to other groups. Comparing racial and ethnic groups has identified disparities, but these comparisons have done little to reduce them. New thinking about persistent health challenges may result in new strategies that include considering health equity and Optimal Health.

Current conversations about health continue to be both protracted and intractable in the United States and beyond. Except for selected Asian American ethnic subgroups, people of color in general, and African Americans in particular, lead in most categories of health inequalities [5]. Seldom, if ever, are positive and/or *just* health and health care outcomes reported in reference to racial and ethnic minority groups (people of color). To address this problem, research must include people of color in leadership roles, as well as participants in scientific research. By involving more people of color in the research enterprise, improvements in health and health care related to minority health are possible.

This article discusses the recent literature on the need to include African Americans in health research, specifically clinical trials (CTs). Further, we discuss salient research findings from a collaboration between Eli Lilly and Company (ELC) and the National Center for Bioethics in Research and Health Care at Tuskegee University (NBC). The collaboration included a multi-phase research effort to address the long-standing challenge of enhancing participation of African Americans in CT research. This collaboration was consistent with the Federal Drug Administration-Section 907: Inclusion of Demographic Subgroups in Clinical Trials, published in the Federal Registry for public review. The Action Plan (Section 907) thoughtfully considers public feedback, congressional requirements, and the initial report findings. The plan presents 27 action items that focused on three priorities:

- quality: to improve the completeness and quality of demographic subgroup data;
- participation: to identify barriers to subgroup enrollment in clinical trials and employ strategies to encourage greater participation;
- transparency: to improve the public availability of demographic subgroup data [6].

One strategy to address these priorities, and a major focus and primary interest of both ELC and NBC, was to discern the ethical problems related to historic and current challenges borne out of the lived experiences of African Americans related to clinical research and health care delivery. To explore the erroneous assumptions regarding the lack of African American participation by researchers and others, this project included a multi-phase research design to determine how to enhance African American participation in human subjects research [7]. The overall project included several components: Assessment, Advocacy, Coordination, and Evaluation. The Assessment Phase included individual interviews to elicit the perceptions of designated leadership groups about human subjects research participation. A specific focus of these interviews was to document the challenges and opportunities related to the issues of trustworthiness and trust. The study aimed to document other obstacles to participation in research, which might be

crucial to the appropriate biomedical and behavioral tailoring of pharmaceutical developments to better serve populations long excluded from CTs. The collaboration of ELC and NBC had the goal of eliminating health and health care disparities that were influenced by the lack of trust between the research community and African Americans. Both institutions acknowledged the legacy of the unethical U.S. Public Health Service Syphilis Study at Tuskegee [8–10].

The main objective of the research was to inform the development of evidence-based strategies that would build relationships between African American leadership groups, their constituencies, and the research community. To accomplish this objective, in-depth interviews with a national convenience sample of leading policy, education, health, faith, and civic society members of the African-American community were conducted. These categories were selected because they represented leadership groups that historically have provided guidance through major social justice challenges [11,12]. These leadership groups continue to advocate on behalf of African American and other vulnerable populations on all aspects of health and well-being. They serve as more than stakeholders because they have been, and continue to be, sustaining pillars for the African-American community. These pillars have survived periods of social injustice including, but not limited to, segregation, the Jim Crow era, desegregation, integration, the Civil Rights Movement, Black Power Movement, etc. [13]. These individuals and organizations continue to be the major decision-makers in the African American population. The respect they command, both in and outside of the African American community, assures a venue to translate trustworthiness into trust.

The interviews addressed three major research questions:

- why do African Americans not trust research conducted by the scientific community?
- what is needed to eliminate the barriers to participation in research, while enhancing the trustworthiness among the scientific community?
- what recourse would be available when bioethics and public health ethics violations occur?

It is important to note that a pedestrian definition of trust is insufficient to cover the various nuances associated with this research effort. Thus, we begin by teasing out these nuances and settle on a definition of trust that is more guiding and compensatory. Space would not permit an exhaustive explication of trust (and its trustworthy dialogic), but a general accounting of trust as entailed in this research, as well as trust particularized to the African American community, is helpful.

First, on a truncated general account, (one that clearly says little about the epistemology of trust but maximizes trustworthiness as a condition that would allow trust to flourish) Carolyn McLeod offers several views on what makes trust warranted (note the import of trustworthiness). She suggests, “trust” is warranted, that is:

- well-grounded, only if the trustee is trustworthy, which makes the nature of trustworthiness important in determining when trust is warranted;

- justified, sometimes when the trustee is not in fact trustworthy, which suggests that the epistemology of trust is relevant;
- plausible, only when it is possible for one to develop trust, given one's circumstances and the sort of mental attitude that one can will oneself to have without any evidence of a person's trustworthiness [14].

What is entailed in each of the above points is that trustworthiness is a *sufficient* condition for trust to flourish. However, if there is historical evidence in support of distrust, our research indicates that trustworthiness is a *necessary* condition for trust. Given that the one trusting is choosing to make herself vulnerable to the trustee, and furthermore, given that there are no guarantees that the trustee will keep her promise, the wisdom burden is on the one trusting to self-protect.

Second, our research goes beyond trust generally to a particularization of trust that speaks to justification (this is derived from above). Even though our research has shown that there is a justification for distrust, two thoughts should remain in the forefront:

- "one can will" oneself to trust—but this should be measured by the number of options available. The fewer options a person or group possess, the greater the need to trust "without any evidence of a person's trustworthiness";
- "racial/ethnic minorities (people of color) should not be considered inherently mistrustful, even if the mistrust can be justified by historical injustices and disparities in available, assessable, acceptable, and quality healthcare. Such characterizations may create provider bias that, in turn, create major barriers for referral and compliance in clinical trials" [15].

African Americans are suspicious—and they have a right to be [16]. One can argue that they should prioritize their suspicion and distrust of certain systems to give themselves a better chance for quality health and healthcare. On the other hand, one can argue that those who desire to be trusted should invest in their own trustworthiness by developing an attitude and a culture of empathy, compassion and care. It is very difficult for a person not to trust someone who proves his trustworthiness.

In *Trust and Trustworthiness*, Russell Hardin writes of the synergy between the two terms [17]. However, he notes that discussions of trust rarely mention trustworthiness though it is often implied. L. Hertzberg writes, "Trust is always for something we can rightfully demand from others: misplaced trust, accordingly, is not a shortcoming on the part of the trustful person, but of the person in whom the trust was placed" [18]. This idea shifts the blame of a lack of trust, that is often placed on the African American community, to a lack of trustworthiness on the research community [19]. And it provides a basis for the development of an argument that fixes trustworthiness as a feature of care—i.e., a preoccupation with doing right to persons who have made themselves vulnerable.

Consequently, in this article we clarify the structure of trust and trustworthiness, and show how these specific dispositions are not merely attitudes and beliefs. Rather, we show how they represent feelings and emotions. These feelings and emotions constitute foundations for normative

moral claims and judgments from both moral rationalism and moral sentimentalism. From the onset, it is not hard to discern how trust and trusting would make normative ethical sense from a Kantian (Immanuel Kant, 1724–1804), rule-based, obligatory, and deontological perspective. Trust, as a rational concept, makes perfect societal sense. Any calm, rational person, of average intelligence should not only see trust as a rational virtue, but they should see trust as an admirable disposition and the lack of trust (as opposed to a justifiable mistrust or distrust—both of which may be prudential) as perhaps having a deficiency of some sort. Trust is organic; mistrust or distrust is prudential on a rationalist account. But a sentimentalist account seems to be veridical as well.

To be sure, everything we have said about trustworthiness thus far has tremendous value in cognitivism, and certainly this is easy to see. Cognitivism asserts that ethical sentences have truth value (they are either true or false) and are, therefore, propositional (rationally and sentimentally). A trustworthy person is acting morally when she keeps her promises, is reliable, or she acts in such a way as to not compromise the vulnerability of the trusting agent. Regardless of the metaethical canopy (moral realism, moral relativism—or anti-realism), such that one can speak propositionally, sentences can be constructed in defense of trustworthiness (e.g. a doctor may say to a patient, "I am committed to maintaining the integrity of the informed consent document." If she maintains the integrity of the document, her proposition is said to be true, therefore, in this instance, and with respect to this patient, the doctor is acting in a trustworthy fashion. She is acting morally. She is acting untrustworthily, otherwise, and therefore she is acting immorally). Trust, however, is something different and ought to be the subordinate of (and even contingent upon) trustworthiness. Trust is not a moral attitude, it is an instinctive one, genetically based and socially developed.

Infants exhibit and express trust among their first instinctive actions. They are not acting cognitively, thus morally. They are acting instinctively. One can even say that they are acting phenomenologically. It is certainly true that trust (can and likely) is a disposition that has evolved in a kind of Social Darwinian way, but this evolution doesn't mitigate a phenomenology to trust. Other terms may be applicable (e.g., faith, confidence in, reliance, or dependence), but additional terms are simply synonymous with the phenomenology of trust. Indeed, the infant's trust of parent, particularly if the mother is breast-feeding, is an inductive-base survival instinct—it is less of a proposition to trust and more of a non-cognitivist action that can be interpreted as trust. But phenomenologically, it is the most basic trust of instinctive, sentient creatures, of which the human infant is one. The infant could never survive without a disposition to trust. From the beginning of life, trusting is necessary, natural and universal. As the infant continues to trust, and as the parent continues to *care* for the infant with consistency, they represent themselves as being trustworthy, i.e., reliable and competent to the point that trusting is less of a cognitive choice [20]. Reliable and competent parents, i.e., trustworthy parents, earn the trust of their children, which has far-reaching implications for both parent and child. First, the infant instinctively and justifiably allows itself to be vulnerable to the parent or their designee because past trusts

were met efficaciously. Second, because trustworthiness is established and demonstrated with consistency, the child is then justified in extending the parent's competence from feeding to other care-competencies, like changing their diaper, protecting them from darkness or loud noises, etc. Trustworthiness, then, is contingent upon the trustee's cognitively inculcating certain values and principles that would increase the dialogue between the trusting agent and the trustee. In short, trusting is organic and non-moral (a thief ought to be able to trust his comrade, or co-conspirators in an evil plot trusts each other). Trustworthiness, on the other hand, is virtue based. Character is essential to being trustworthy.

Would anyone trust their doctor or attorney if he or she is of questionable character? Would any child trust a parent whose character has been demonstrably unreliable? Alternatively, would African Americans or any cautious group trust clinical trials researchers? Certainly not—and the historical evidence bears this out. Trust is a great principle for the provision of (utilitarian) happiness because a society is better off having most of its citizens trusting than distrusting—becoming vulnerable knowing that most people value trusting relationships is better than never becoming vulnerable, never trusting, never flourishing. Trusting, on a rule-utilitarian account is a good disposition to have, but if there is a demonstrable lack of trustworthiness in the character of those demanding trust, there can be no societal, viz, no flourishing in clinical trials. Until the last two decades, trustworthiness was historically—and unfortunately—left out of the structure of trust. Trust is dialogical with trustworthiness. There is no valid or meaningful trust if it functions, independently. Mono-logical trust has no value; it is itself vulnerable to gullibility if it is not made to be dialogical. On our account of trust (discursive trust, i.e., trust that is tied to trustworthiness), cognitive-trust and its counterpart (character-based) virtue-trustworthiness are valid and necessary for the participation of African Americans in clinical trials. This kind of dependent cognitive-trust/virtue-trustworthiness is advantageous to our present concern.

Background

Report of the Secretary's Task Force on black and minority health

In 1985, the US Department of Health and Human Services released the, *Report of the Secretary's Task Force on Black & Minority Health*, also known as the Heckler Report [21]. This pivotal report is the first time in U. S. history that the federal government acknowledged that morbidity and mortality could be chronicled by race and ethnicity [22]. More than thirty years later, African Americans still suffer from similar, and in some instances, worse health gaps and disease prevalence as presented in the report [23]. The US Department of Health and Human Services' Office of Minority Health was established as an outcome of the 1985 finding [24].

Clinical Trials participation rates

According to Institute of Medicine, researchers failed to recruit an adequate number of subjects for clinical research 27% of the time, and 90% of clinical trials worldwide failed to enroll subjects within the allotted time [25]. Overall, the rate of participation in clinical trials is poor among certain groups and declining; however, it is poorest among African Americans. Little has been done to address or overcome recruitment obstacles for the general population.

African American participation rates

The recruitment and inclusion of the general population in clinical trials is difficult and in comparison, so is the rate of African American participation. In 2013, a report was drafted as a requirement by The Food and Drug Administration Safety and Innovation Act [26]. The FDASIA documented data on the participation of demographic subgroups (sex, age, race, and ethnicity) in clinical trials focused on new drugs and biological devices. African American participation in many of the studies was not representative of the US population or disease prevalence; specifically, for type 2 diabetes mellitus (T2DM). African American representation in clinical studies was less than 5%; however, African Americans make up approximately 13.3% of the U.S population and have a higher prevalence of T2DM. The continual lack of participation of African Americans, disproportionately affected by many diseases, will only perpetuate the current health gaps.

Why African Americans do not participate?

Retention, protection and reward

The literature related to African American participation in clinical trials is significant, with numerous explanations [27], but minority recruitment into clinical trials continues to be a challenge [28]. Woods et al. reported that some of these challenges include transportation, work-related and family responsibilities, fear or suspicion of researchers and the institutions that promote clinical trials, and cultural factors that ultimately influence trust and trustworthiness [29].

The United States Public Health Service Syphilis Study at Tuskegee

The United States Public Health Service (USPHS) Syphilis Study at Tuskegee is often used as a touchstone for many African Americans' understanding of clinical research [30,31]. From 1932 to 1972, approximately 623 African American men located in Macon County, Alabama participated in a study to document the natural progression of syphilis in the Black population. The USPHS scientists/physicians engaged in an unethical investigation to document the adverse effects of the syphilis virus on the organs in the human system. Originally, the title of the study was the "Tuskegee Study of Untreated Syphilis in the Negro Male in Macon County Alabama" [32]. The participants were told they were being treated for "bad blood," a local term used to describe fatigue, anemia, and malaria,

among other maladies. In exchange for participation, the men were offered meals, free health treatments (not for syphilis), and ensured burial stipends after their deaths [32]. Initially there was no proven treatment for the disease. However, after penicillin was determined a cure for syphilis in 1947, treatment was still withheld from the men. In fact, a unique “surveillance system” was designed to track the men wherever they went in the U.S. to assure that they would not receive treatment anywhere for the disease. By this time, many of the men had died and some of their wives and children had been infected [33]. The establishment of Institutional Review Board regulations to approve all human subjects research was a direct result of the USPHS Syphilis Study at Tuskegee.

Mays discusses the accepted notion that the lack of success in addressing health disparities in the African American community is attributed to skepticism towards research because of the Tuskegee Study of Untreated Syphilis in The Negro Male [28]. This belief is held despite studies that conclude that, while many African Americans may have little knowledge about the specific events associated with the Syphilis Study, there remains a “site of memory” that serves as a barrier among African Americans and other vulnerable populations about participating in human subjects’ research [32]. While willingness to participate may not necessarily be directly linked to the study in Tuskegee, there is a hesitation by many people because of myths that are associated with it. Myths influence perceptions whether they are true or false [31]. These myths perpetuate the legacy of the USPHS Syphilis Study as being the major cause of mistrust [33]. However, current bioethics and public health ethics violations continue to foster distrust in human subject research, including clinical trials.

African Americans’ willingness to participate in clinical trials

Few studies contradict the previously stated barriers to African American participation in clinical trials. Research reiterates the various themes surrounding this matter by constructing similar conclusions in varying populations [34]. Few data that link an individual’s willingness to participate in biomedical research and awareness of the study at Tuskegee. Instead, Katz and Warren suggest many other factors such as racial discrimination, health quality, and/or access to health care [31]. These current experiences result in African Americans cautious approach to research. The Tuskegee Legacy Project (TLP) Study (1992–1999; 2001–2009), addressed barriers related to the recruitment and retention of Blacks and other minorities in biomedical research studies [34].

Gaps in the literature

While many studies examined the attitude of the subjects recruited into clinical trials, or those who chose not to participate, very few studies have focused on the perspective of clinical researchers and barriers presented in the recruitment process. Few studies consider the perspectives of trustworthiness and trust and how these two themes are interpreted and perceived by those African Americans who belong to key groups that have influenced other African Americans throughout history, such as: (a) health and

educational professions, (b) faith-based leadership and (c) civic society.

Further, the current literature surrounding African Americans and clinical trial participation is limited in utility because few solutions have proposed and little has been done to rectify the lack of perceived trustworthiness of the research community.

Study methodology

The research team assembled by the NBC included a health service research scientist/principal investigator, statistician/computer analyst, medical anthropologist, and project director. The team met quarterly to discuss the implementation of the research. We conducted thirty-five interviews among three gatekeeper leadership groups over a 12-month period. We completed a review of the literature, which identified salient topics in the recent biomedical, behavioral, public health, and bioethics literature related to clinical trials, particularly those associated with African Americans and highlighting clinical trials.

Sample

The three groups (and other key selected individuals, who did not fit into these categories, for example, Opinion Leaders) comprised the convenience sample. Individuals were identified based upon their economic, strategic, intellectual, and political positions.

Health care professionals have large patient populations that they influence in a variety of ways. They also have a large impact beyond their patient populations to include health profession students, economic peers in other professions, and members of other economic groups. Campbell explains, the physician is seen as trustworthy, as someone whose views can be respected and depended upon [35]. Within the African American community, the role of physicians as representing authority is even more salient.

The faith community leadership has historical influence, not only with their specific congregations but also by reaching large sectors of the African American community because of the strong religious orientation of these communities. The PEW Research Center reports that 83% of Black people in the U.S have an absolute belief in God. Their White, Asian, Latino counterpart’s record, 61%, 44%, 59%, respectively [26]. The challenge for this research project was in scheduling interviews with faith leadership outside of the theological education sector.

Civic groups and other social organizations continue to play important roles in providing leadership for the African American population. While many social organizations have primary social, rather than social-action roles, most of them include civic and social responsibility within their missions. The National Association for the Advancement of Colored People and the National Urban League remain the two strongest civic organizations serving the African American population. We interviewed representatives from both organizations and the leadership from 100 Black Men, Inc.

The sample included:

- the president and two past presidents of the National Medical Association;

- presidents/deans of the Black medical and dental schools;
- the president of the National Dental Association;
- the presidents and/or deans of four predominately, Black theological seminaries;
- leaders/presiding pastors of two major religious institutions;
- leaders of the NAACP and Urban League;
- 100 Black Men Inc.;
- selected opinion leaders.

The Director of the NBC (PI) conducted all interviews to assure consistency in the interview process. A firm was contracted to transcribe the audio and provide transcriptions to the research team.

Analysis

The transcripts from the interviews were entered into the Atlas-ti database and coded for analyses. Coding in qualitative research accommodates the exploratory nature of open-ended questions, and the complexity of textual responses obtained. Thus, the basic qualitative coding unit is a text segment, rather than a questionnaire response. Informed consent forms were discussed and signed by each interviewee and the Principle Investigator.

Findings

Generational differences [different audiences]

The interviews identified salient perspectives on the generational and sex differences of potential CT target populations. The most pervasive theme regarding age cohorts was the difference in methods and motivation for accessing information in general, and health information specifically. As one respondent stated:

“This generation can press a remote and they get immediate feedback. We live in a world of technology whereby generations may not see the need for research because they do not fully understand the paths people have tread to get where we are today. So, I think it is a generational gap, and we need to educate them on the importance.”

Social media, as used by the younger generation, was identified as key to how they seek information, rather than personal communication with trusted persons, e.g.:

“What is Facebook saying about it? What is social media saying about it? They’re even looking for ways to participate.”

In contrast to describing the “millennials,” the older generation was called the “silent generation” by interviewees:

“We know the silent generation, the older generation, they look at things differently. Their values and their attitudes are different, and the way they perceive information is different from the millennials.”

Differences were also noted regarding the issue of trust; the younger generation was mistrusting the “system” and not necessarily separating science from government. Their mistrust was not necessarily grounded in a historical perspective:

“When you look at the younger generation, they may not have the historical perspective of the mistreatment and the ethical conduct from years past of African Americans in experiments, but their mistrust would come more from the whole system of government. . .”

One of the medical leaders expressed hope that the younger generation would take more responsibility for community health, clearly a message about recruitment regarding participation and the importance of tailored medications:

“Well, I would like to think that there is a new generation of people coming out who would look at the health system in a new way and see their responsibility in it, not just as patients or potential patients, but their responsibility as a part of the community to make sure that it serves the needs of the community.”

The value of reaching the younger generation was also noted, highlighting their economic power and the importance of information and education.

Understanding of research and the importance of research

The leadership interviews were eloquent regarding concerns that the African American community does not fully understand what research entails, nor the importance and/or relevance of research to the health and well-being of their community. Critical was the idea that understanding the rationale for the development of population-specific drugs (epigenetics) and environmental/contextual effects/stressors such as poverty, racism, stress, and allostatic load were missing in most sectors. They saw this lack of understanding as one of the major obstacles to participation:

“I think that the lack of understanding has to be in the introduction and understanding of research and all of its dimensions. And I think that a good starting point must be in our academic institutions and letting that flow out and permeate the entire Black community.”

The quality of the relationship between people, groups and institutions

Many of the respondents spoke about a fundamental lack of any relationship between the health system and the African-American community, not only the issue of medical mistrust (to be discussed following), but even the basics of protection, care and caring, and services. While doctors were the focus of the responses, the implication that the system does not serve the Black community in many ways was salient. As one respondent stated:

"I think Black people need to be convinced that the healthcare system actually does care about them and their health, and not just their disease, but about them and their health. I think that sense of caring, the sense that this is truly a health care system for Black people is missing."

Also commented on were the obstacles presented by Pharma:

"Lack of knowledge of Pharma about the core values and cultural norms. I think dealing with our community from a point of intelligence is the way to go."

The overall conclusion of the respondents regarding relationships and CTs was, "If people see themselves as part of a system that cares, they are more likely to participate."

The implications of this recommendation go far beyond the focus of CT recruitment and participation and speak to the issue of health disparities and underserved/poorly served communities.

Medical mistrust

There is a significant literature exploring medical mistrust, which demonstrates an overall distrust by the African American community of research and the research community [16,36,37]. The leadership interviews confirmed findings in the literature regarding the importance of understanding issues of interpersonal trust within medical/health care relationships, and issues relating to the history and current experience of individuals and groups [34–36,38]. The importance of legitimate sources of information, which may vary by topic, was raised, as well as how legitimacy is assessed considering trust and other factors. Also emerging as important were discussions about the role of the physician in building trust and the need for more Black physicians, as well as their advocacy and education about the substance and availability of CTs. However, concern was expressed about the lack of knowledge of CTs even among physicians. As one respondent stated, "When health providers are not telling patients about clinical trials, maybe it's because they're not aware of them themselves." Others questioned practitioner's knowledge and awareness of CTs as a basis for a lack of advocacy.

Suggestions for addressing medical mistrust were forthcoming:

"I think that to overcome the distrust we have is to educate people on why research and the clinical trial process is important to creating medicine and therapies that work. I don't think a lot of people realize that the process through which medicine is created has a component of it that evaluates people and their medical profiles."

"I also think that we know intuitively that Black people have different, differential, unique health challenges. We don't trust that the mainstream pharmaceutical companies and the established medical profession will deal with that, but the education is that participating in the clinical trial process allows medicines and therapies to be built and designed with our challenges in mind."

One of the most insightful comments, which addresses essential issues underlying medical mistrust, was the following:

"The health professions have to be able to show that the greater purpose of medical research, medical practice, public health, are absolutely to maximize the health and well-being of all people; and research that is conducted is not designed to sacrifice any person or group, or group of persons for the sake of everybody else."

"...the health [professions] really have the greatest priority to be trustworthy. That doesn't mean they are trustworthy."

Oversight, protections, and consequences of violations

One of the major objectives of the study was to understand how the leadership viewed the issues of protections for participants and what consequences they believed existed and/or should exist. Discussions about private versus public sector research elicited the opinion that Pharma was motivated by "quest for profit and reputation", rather than a commitment to health. On the other hand, many of the interviews cautioned about the African American community's distrust of the "system" in general as well as the health care and research sectors. One of the areas of the interview focused upon the differences between the public and private sectors to better understand what issues of trust and trustworthiness might emerge, and as a segue into issues of protections and consequences.

Giving "teeth" to the protections was clearly a concern. The following views provide insight into the opinions and priorities expressed:

"Now, clearly, there has to be enough protection in the patient information that one understands the risk before going into it. And so, I think that that's the first level of assurances."

"To enhance the protocols in the clinical trials, the engagement really goes back to having an infrastructure that is sustainable and is long-standing that allows for the training of people, for the education of various patients that will come through there, and the support system is there."

"They were very big on IRB, institutional review boards, and these particular committees being composed of not just components of the people who are doing the research, but an ethical committee that encompasses several people. So, when you start to put those type of committees and those boards in place, it sorts of enhances the protection."

Regarding policy implications, one of the leaders suggested:

"I think individual institutions and organizations that are performing clinical trials have their own set of policies. But having universal policies that are available to the public provides understanding of how clinical trials

are conducted, how they're provided oversight, so things of yesteryear do not occur again."

Others stated:

"They're universal policies. There should be universal policies set on clinical trials and research, and those should be known at every level."

Key suggestions for elimination of barriers to recruitment

Throughout the interviews, suggestions for eliminating barriers to recruitment and participation in research/CTs emerged. These suggestions, in general and specifically, relating to the issues of relationships, messages, trust and strategies, which address perceived obstacles to involving the African American community in research.

Trusted sources of information

Faith leaders have a significant role in communication, education, and advocacy. An example of this leadership is a curriculum for seminarians to better educate them about issues of health and health care in African American populations [20,39]. This curriculum is an important advance already said to be underway. However, it is important to understand how difficult it may be to reach some faith leaders and clergy. African American care providers that work in the community have significant potential to promote participation by educating patients about CTs and the personal and community advantages of tailored research. The content of education and messages about research and CTs were also discussed. Health literacy was identified as an important obstacle, crucial for recruitment as well as adherence and retention in CTs, e.g., *"This must be achieved at two levels, knowing about medications and an understanding of the body and disease."*

Motivation to Participate

Respondents felt that recruitment must consider the perceived motivation for participation, for example, whether individuals have a personal or family experience of disease is often crucial to participation in specific CT research. As explained by one of the medical leadership:

"I think a lot of this with participating in clinical trials with African Americans depends sometimes on the disease, what the clinical trial is about. Getting them to participate depends on what stage of a condition they're in."

Type and amount of reward/incentive

The issue of incentives for research participation was carefully considered, with differences of opinion noted, including whether to offer payment for participation. Other types of rewards and incentives were also discussed with

interviewees, including the importance of altruism, and how participation can be seen as a benefit to the community:

"I think people have to see an investment, a return on investment. They have to see a need that they're helping someone else, whether it be a family, a community, and they have to be able to have a reward to know that they made a difference by participating."

Recruitment strategies

Critical issues to consider included:

- appropriateness of the recruiter;
- the reputation of the institution recruiting;
- the message/explanation being given;
- the need for details about what is being tested;
- and recruitment in small hospitals and public health centers.

Distinguish long term and short-term goals for participation

Tailored strategies were needed to support participation reflecting long term and short-term goals. Long term, for example, was said to be training of Black doctors and educators in seminaries. Short term was peer recruitment; contact at support groups, information at community clinics, provision of information to community doctors and navigators, videos with explanation of CTs as well as education about the need for tailored medications.

Conclusion

This qualitative study is a vanguard effort because data were obtained from the leadership of the African American community in the US, regarding their perceptions of, and reasons for, obstacles to participate in human subjects research by African Americans, specifically CTs. Reaching these experienced and knowledgeable individuals in face-to-face interviews across the country was facilitated because of the reputation of the National Center for Bioethics in Research and Health Care and the respect and trust which the Director holds among his peers. The research team is confident in the validity and importance of the interviewee responses given concerns about Pharma sponsored studies.

What we have seen in these timely interviews is that *trust and trustworthiness are critical issues, identified in the literature as obstacles, and in these interviews as solutions.* The leadership, aware of the objective of the study, were generous in their suggestions for improving the participation of their constituencies because they understand the need for tailored medical/health interventions that will address the long-standing and unacceptable health disparities in the US. They discussed, as does the literature, the importance of the history of unethical research and the sequelae of truth and myths. They also recognized, not well addressed in the literature, that there are important generational differences in the reasons for medical/health distrust. They highlight the need for the education of the health professions community, especially Black physicians in the community and in

institutions, so that there will be a better understanding of the need for such research and what it entails.

The leadership also stressed the need for reaching the faith leaders as well as the difficulty in gaining their understanding, and especially, their trust when the trustworthiness of the research community is not evident. This is true for both public and private sector efforts. Interestingly, the leadership placed emphasis on relationships between institutions, individuals, and the community as key to developing trustworthiness and trust.

The perceived pharmaceutical industry's objective as primarily profit was seen as undermining any attempts at developing these critical relationships. "Show that you care" was a salient theme. We would say, "prove" that there is a real commitment to African American health by developing culturally sensitive strategies for informing all constituencies. Understanding the history and values of the African American populations (plural because we stress generational issues) should be paramount in promotional efforts toward recruitment and participating in clinical trials.

The conclusion that we would draw from the study's findings is that the history of unethical research, while important, is not the predominate factor operating to limit participation. There needs to be far better understanding of what, how, and who should carry out recruitment and provide the leadership. Appropriate and effective information must be disseminated by trusted sources of information who may not necessarily be receptive to collaboration. Relationships that build trust require commitment and understanding. Motivation for participation needs to be explored and built upon, and incentives and rewards need careful consideration, not simply IRB or institutional approvals. Finally, trust, and thus participation, will not occur if the institution and its representatives are not seen as trustworthy.

The paradigm must change so that trustworthiness, not trust, is what is expected first.

Limitations: while this study provided a unique opportunity to learn from the African American leadership in the U.S., there were clear limitations and biases, which must be noted. This study was designed specifically to explore gatekeeper/expert knowledge and suggestions to enhance recruitment, retention, and reward among the African American population. The leadership interviewed represent senior and experienced individual men and women. Thus, perspectives of their constituents and the youth populations are not represented. Although small samples are typical for exploratory, qualitative studies, the lack of a representative sample and the convenience nature of the selection of respondents, clearly limits generalizability to even these leadership sectors.

Additionally, the respondents understood that they were advising Pharma, which may have biased their discussions. Finally, the interview involved one of their peers as the interviewer, so issues of trust and confidentiality may have affected the data both positively and negatively regarding validity. Nevertheless, the insights and perspectives of these key members of the leadership should guide the development of strategies to improve recruitment among African American communities.

Disclosure of interest

The authors declare that they have no competing interest.

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