

WILLINGNESS OF LATINX AND AFRICAN AMERICANS TO PARTICIPATE IN NONTHERAPEUTIC TRIALS: IT DEPENDS ON WHO RUNS THE RESEARCH

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Background: Inclusion of racial/ethnic minorities in cancer-related research remains inadequate, continuing to impact disparate health outcomes. Data regarding enrollment of racial/ethnic minorities in nontherapeutic, health-related research is sparse, and even less is known about enrollment of those with a double disparity of racial/ethnic minorities in rural settings.

Objective: To examine perspectives of Latinx and African American (AA) healthy volunteers from rural and urban settings in five southern US states and Puerto Rico regarding their trust in research and their willingness to participate in nontherapeutic research trials based on who conducts the research.

Methods: This study was conducted in 2013 in rural and urban communities across Alabama, Florida, Georgia, Mississippi, Louisiana, and Puerto Rico. A 38-item questionnaire based on the Tuskegee Legacy Project Questionnaire assessed willingness, motivators, and barriers to participation in nontherapeutic cancer-related research. The sample was segmented into four subgroups by urban/rural location and race/ethnicity.

Results: Of 553 participants (rural Latinx=151, urban Latinx=158, rural AA=122, urban AA=122), more than 90% had never been asked to participate in research, yet 75% of those asked agreed to participate. Most had positive views regarding health-related research. Trust in who conducted research varied by subgroup. Personal doctors and university hospitals were most trusted by all subgroups; for-profit and tobacco companies were least trusted. Both Latinx subgroups trusted pharmaceutical companies more than AAs; local hospitals and for-profit businesses were more trusted by AAs. Both rural subgroups trusted research by insurance companies more than their urban counterparts.

INTRODUCTION

Twenty-five years after the 1993 NIH Revitalization Act mandating inclusion of participants that adequately represent the US population,¹ it is apparent that researchers have not met this challenge successfully, with race/ethnic minority participation at <2% in clinical research trials funded by the National Cancer Institute.² This is particularly worrisome given the expected 25% and 40% increase in the Latinx and African American (AA) populations respectively over the next four decades.³ When these populations are under-represented in research trials, the generalizability of conclusions on a national or global scale are hindered.⁴ Therefore, the health applications to racial/eth-

nic minority individuals will remain inadequate, perpetuating continued disparate health outcomes. While therapeutic trials focus on treatments, and thus patients may directly benefit from their participation, non-therapeutic trials are not likely to provide direct benefits to participants. Also, non-therapeutic trials can range from completing health assessments or participating in behavioral interventions, which involve minimal risk, to Phase I trials, which may involve greater risk.

While inclusion of racial/ethnic minorities in therapeutic cancer trials is vital because some malignancies having a higher predominance and mortality among AA or Latinx compared with Whites,⁵ it is important for them to be included in nontherapeutic trials as well.² Significant dis-

Conclusions: If asked, rural and urban AA and Latinx healthy volunteers were willing to participate in health-related research, with personal doctors and university hospitals considered the most trusted sources to encourage/conduct research. *Ethn Dis.* 2021;31(2):263-272; doi:10.18865/ed.31.2.263

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parities occur in cancer morbidity and mortality rates for these populations, often explained by varying education levels, income, and place of residence.^{6,7} For instance, infection-related cancers (cervix, liver, or stomach), prostate, and breast cancer have higher incidence among Latinx, with cost-related factors and place of residence driving these disparities.⁸ Increased diversity in participants for behavior-

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al interventions, preventive screening, or Phase I studies could identify the social factors associated with disparate risk, early detection, and treatment.

Reasons for low participation rates remain unclear. Despite evidence from Katz and colleagues that Latinx and AAs have the same willingness to participate in research as their White counterparts,⁹ low levels of participation could stem from apprehension about how they might

be treated based on the lived experience of being a racial/ethnic minority in the United States¹⁰ or skepticism and distrust of medical procedures generally.¹¹ For some AAs, the sense of distrust can be traced back to incidents of medical maltreatment such as medical experimentation during slavery and the Tuskegee Syphilis Study.^{11,12} Some Latinx report similar fears of mistreatment¹³ and it appears that higher rates of language acculturation is correlated with increased reluctance to participate in clinical trials, possibly reflecting more negative experiences with the US health care system.¹⁴ Results from previous studies have suggested incorporating trust-building strategies into recruitment strategies such as clearly explaining trial procedures, using race/ethnicity matched study coordinators, acknowledging past mistreatment of racial/ethnic minorities, and assuring participants that safeguards are in place to prevent malfeasance.^{12,15,16}

In addition to belonging to a racial or ethnic minority group, living in a rural area can result in a double disparity when it comes to participating in research trials. Rurality introduces unique challenges in recruitment; less than 10% of US physicians practice medicine in rural communities and access to adequate treatment can be challenging for the more than 20% of the US population residing in low-population areas.¹⁷ On an individual level, low income and the prohibitive cost of traveling to research sites impact participation decisions.¹⁸ On a hospital systems level, access to research is often determined by the quality and quantity of health care access and most research hospitals and

academic centers are located in urban areas.¹⁹ An internally reliant health care system with functional resources is necessary for research recruitment success, especially in enrolling racial/ethnic minority patients, and disparities in insurance coverage, inadequate staffing, and fewer resources can inhibit their likelihood of receiving care in rural settings.⁴ For participants with lower levels of educational attainment and/or limited English proficiency, participation in a rural community cancer center can be particularly difficult,¹³ highlighting the need for culturally relevant study designs. Evidence has shown that participant recruitment in these areas is most successful with involvement by trusted and familiar community and faith leaders and word-of-mouth promotion at barbershops, beauty shops, churches, and community centers.^{19,20}

The primary aim of our research was to examine differences in levels of trust of urban and rural Latinx and AA healthy volunteers and their willingness to participate in cancer-related nontherapeutic research based on who conducts the research.

MATERIALS AND METHODS

Conceptual Framework

We applied elements of Ford and colleagues' conceptual framework²¹ in our study. This model demonstrates the factors leading to acceptance or refusal to participate in a clinical trial, which require that, in order to make a decision of agreeing or refusing participation, individuals must be aware that the study is being conducted as well as have an opportunity to be a

participant. Barriers are categorized by whether they stem from lack of awareness or lack of opportunity and how they affect an individual's agreement to enroll. Specifically, we examined barriers related to awareness of benefits of research on population health, previous exposure to health research, living in a rural vs urban community, and levels of trust in research and the medical system.

Geographic Setting

We felt it was important to include rural areas to identify location-based differences in recruitment strategies for potential interventions, as the majority of studies regarding trust and participation in medical research among racial and ethnic minorities were conducted in urban areas.^{9,22-24} As well, the one rural locale included in the two previous Tuskegee Legacy Project (TLP) studies was the only site with a significant association between mistrust and participation.²⁵

This study was conducted in 2013 in rural and urban communities across Alabama, Florida, Georgia, Mississippi, Louisiana, and Puerto Rico as a collaborative effort between eight academic institutions: O'Neal Comprehensive Cancer Center at the University of Alabama at Birmingham; H. Lee Moffitt Cancer Center; University of Mississippi Cancer Center and Research Institute; Winship Cancer Institute of Emory University; Morehouse School of Medicine; Tuskegee University; Tulane University; and Ponce School of Medicine. These institutions are part of Region 3 of the Geographic Management Program (GMAP),²⁶ an NCI initiative established in 2011

to specifically focus on advancing research in cancer health disparities.

Study Design

Using the TLP^{9,22} as a foundation, a review team consisting of members from all participating institutions developed a 38-item questionnaire, written at a 4th grade reading level; the questionnaire was pilot tested among 40 rural and urban AAs and Latinx.

Questionnaires were interviewer-administered via iPad, matched by race/ethnicity to the participants, with the goal of reaching 100 participants per state (50 in rural counties/parishes and 50 in urban counties/parishes) and 60 Latinx in Puerto Rico (30 rural and 30 urban residents). Latinx were given the option of completing the questionnaire in either Spanish or English. Participants were compensated US\$20 cash for their time.

Eligibility criteria were: 1) aged ≥ 19 years (age of consent required to participate in research in Alabama at the time of the study); and 2) no personal history of cancer. Ten percent of interviews were flagged randomly by the computer for a re-test option to assess overall reliability.

Data Collection

Counties/parishes in each state were identified as rural or urban using 2010 US government geographic classification data.²⁷ Interviewers chose two rural and two urban counties/parishes per state/territory based on population for potential recruitment, ie, percentage of AAs or Latinx living within the counties and potential recruitment sites within each. Teams of interviewers were provided iPads programmed with the survey

in both English and Spanish and travelled in groups of two to four. To promote uniformity in data collection, recruitment sites were divided into three segments where adults gather: leisure (eg, church, social gatherings, and homes); work/school; and shopping. Post interview, participants who were flagged for retest were asked to provide a telephone number and address where they could be reached within two weeks. Participants who consented to retest were given an additional US\$20 cash.

Measures

The 38-item survey instrument was divided into several sections: 1) demographics; 2) general health; 3) health care access; 4) past exposure to research studies; 5) opinions about research; and 6) trust and willingness to participate in research on health and illness based on who would be conducting the research.⁸ In addition, we assessed willingness to participate in cancer-related research based on the level of involvement (eg, blood draw, completion of the survey); those findings are not addressed in this article. Items were adapted from the TLP,⁹ a valid and reliable measure of willingness to participate and levels of trust in medical research.^{22,28} The original questionnaire was translated to Spanish by a bilingual native Spanish speaker and independently back-translated to English by a bilingual native English speaker.

Adaptations were made to the TLP to update language and for clarity. Throughout the questionnaire we replaced the original phrase, medical research, with the phrase, research studies about health and illness, to clarify that our topic was nonthera-

peutic research among healthy volunteers. Questions regarding past exposure to research studies were reworded slightly from the TLP and presented in a different order by ascertaining first if they had ever been asked to participate in research about health and illness before asking what type of study and how positive/negative the experience was. To assess participants' research views on the benefits of research on population health, rather than ask the TLP question, "How much do you think medical research has improved the quality of medical care today?" we asked three questions, examining their perceptions of benefits to the general population, AAs, and Latinx. Response choices ranged from not at all to 100%. As a don't know response might have indicated lack of knowledge rather than response ambivalence,²⁹ we elected to include the response as a separate choice in order to inform possible interventions. In cancer research, choosing a don't know response can be accounted for by level of education and the lack of knowledge might be addressed in interventions with an educational component thereby reducing health disparities.^{30,31}

Perceptions of participants' trust in the researchers themselves and trust in research results were nearly identical to the TLP, with our asking, "How much trust do you have in the people who carry out (results that come from) research studies on health and illness?" with response categories the same as for the three questions regarding benefits to population health. Items regarding likelihood to participate based on who is carrying out the research (eg, personal doctor, a university research center, institutions)

were also nearly identical; although, we added two response choices: local hospital/clinic not affiliated with a university and for-profit business. Response categories for these ranged from very unlikely to very likely.

Statistical Analysis

Statistical analyses were performed to determine if levels of trust and willingness to participate are different among urban and rural Latinx and AA healthy volunteers with results segmented into four subgroups (urban and rural Latinx, urban and rural AAs). Demographic characteristics of study participants were summarized by descriptive statistics such as proportions and means with standard deviations. Chi-square tests compared characteristics between subgroups. ANOVA compared age and number of people supported by participants' household income. Previous exposure experience and participants' views on improved population health and trust levels of research among the subgroups were evaluated by presenting proportions and compared. Finally, distributions of participants' trust levels by subgroups were evaluated and presented by plotting proportions of trust by who was conducting the research. All statistical analyses were performed using SAS software, version 9.4.³² Results were determined to be statistically significant when the accompanying statistical test yielded a probability of $\leq .05$.

RESULTS

The sample consisted of 553 participants: rural Latinx (n=151), rural AA (n=122), urban Latinx (n=158),

and urban AA (n=122). Just over 30% were recruited at their work/school, 47.5% through leisure activities (home, church, social gatherings), and 22.3% at commercial establishments. More than 90% of Latinx answered the survey in Spanish. Number of participants per state were: Louisiana, 90; Alabama, 105; Mississippi, 102; Florida, 97; Georgia, 98; and Puerto Rico, 59. There were statistically significant differences between subgroups in most demographic variables (Table 1). For instance, while only 34% of participants were aged <30 years and the mean age for the entire sample was 37.9 (+14.6), rural and urban AAs were older than rural and urban Latinx. Most participants within all four sub-groups were between the ages of 30 and 50.

More than 90% of participants had never been asked to participate in research (2.0% rural Latinx, 12.4% rural AAs, 8.3% urban Latinx, and 10.8% urban AA; $P=.008$). Yet, 75% of those asked had agreed to participate (66.7% rural Latinx, 80% rural AAs, 83.84.6% urban Latinx, and 61.5% urban AAs; $P=.53$), and more than 90% had a positive experience. With regard to awareness of benefits of research on population health, respondents' views were largely positive. Rural and urban AAs agreed that research has improved the health of Americans overall and AAs health, while fewer felt research improved Latinx health to the same degree. More urban Latinx felt research improved American's health than their rural counterparts. (Table 2).

With regard to trust in research, urban Latinx placed the most trust in the people who carry out research

Table 1. Participant demographics by race/ethnicity and rural/urban locale (N=553)

	Rural		Urban		P
	LX	AA	LX	AA	
Sex, n=536	%	%	%	%	
Male	37.4	36.8	40.3	46.6	.381
Female	62.6	63.2	59.7	53.4	
Marital status, n=520	%	%	%	%	
Never married	23.7	45.6	28.0	59.8	<.001 ^b
Married/living with partner	66.9	27.2	56.0	20.5	
Divorced or separated	7.9	23.7	14.0	16.2	
Widowed	1.4	3.5	2.0	3.4	
Education level, n=520	%	%	%	%	
< High school	41.7	10.5	14.8	12.7	<.001 ^b
HS/GED	33.1	46.5	32.2	41.5	
Technical school/some college	10.8	28.1	28.9	31.4	
College degree	14.4	14.9	24.2	14.4	
Employment status ^a , n=520	%	%	%	%	
Full-time	37.0	28.1	42.7	36.4	<.001 ^b
Part-time or self-employed	28.3	19.3	26.0	21.2	
Unemployed	7.2	18.4	4.7	18.6	
Homemaker	21.0	4.4	11.3	0.8	
Student/retired/disabled	6.5	29.8	15.3	22.9	
Age, n=520	mean (SD)	mean (SD)	mean (SD)	mean (SD)	
	33.96 (±11.76)	41.87 (±16.14)	37.25 (±14.37)	39.68 (±15.28)	<.001 ^b
Income ^a , n=503	%	%	%	%	
<25,000	48.6	62.4	40.1	62.4	<.001 ^b
25,000-49,999	14.5	18.3	26.5	14.7	
50,000-74,999	0.7	5.5	7.5	11.0	
≥75,000	0.7	8.3	7.5	1.8	
Refused	35.5	5.5	18.4	10.1	
# People supported by income, n=513	mean (SD)	mean (SD)	mean (SD)	mean (SD)	
	3.67 (±2.25)	2.41 (±1.56)	3.59 (±1.71)	2.23 (±2.0)	<.001 ^b

LX, Latinx or people of Latin American descent; AA, African American.

a. Annual income in US\$.

b. Statistical significance, two-tailed test.

while urban AAs had the least. In general, the majority of all participants trusted the results of research at least some of the time (Table 3). We further explored if the entity conducting the study would impact participation (Figure 1). All four subgroups had the most trust in their own doctor, followed by a university hospital. The lowest percentage of trust overall was in tobacco companies and for-profit businesses. Both rural and urban Latinx had a higher percentage of trust

in pharmaceutical companies when compared to their AA counterparts.

DISCUSSION

According to Ford et al, in order to agree or refuse to participate in research, individuals must both be aware of a research study and have the opportunity to enroll and barriers to participation should fall within these confines.²¹ Although participants in

our study generally had positive, trusting views regarding research, they had not been given the opportunity to participate in health-related research as healthy volunteers, particularly rural and urban Latinx participants.

Despite the continued belief among providers and researchers that underrepresented racial/ethnic minorities are apprehensive of research trials due to past traumas such as the Tuskegee experiments,^{11,12} our study confirms that a positive attitude to-

Table 2. Participants' views on improved population health^a, N=553

		Rural		Urban		P
		LX, %	AA, %	LX, %	AA, %	
How much has health/illness research improved the general health of people in the United States?, n=550	100%	2.0	16.5	6.4	13.1	<.001 ^a
	A great deal	24.7	43.0	35.7	36.1	
	Some	20.0	24.8	27.4	29.5	
	A little	12.7	9.9	9.6	10.7	
	Not at all	2.0	0.8	4.5	8.2	
	DK/NS	38.7	5.0	16.6	2.5	
How much has health/illness research improved the health of AA in the United States today?, n=550	100%	1.3	14.9	5.1	6.6	<.001 ^a
	A great deal	13.3	33.9	19.7	36.1	
	Some	18.7	32.2	19.1	32.0	
	A little	8.0	15.7	13.4	16.4	
	Not at all	3.3	2.5	3.2	5.7	
	DK/NS	55.3	0.8	39.5	3.3	
How much has health/illness research improved the health of LX in the United States today?, n=550	100%	0.7	6.6	3.8	4.9	.001 ^a
	A great deal	15.3	17.4	24.8	16.4	
	Some	16.7	23.1	22.3	32.8	
	A little	26.0	19.0	24.2	17.2	
	Not at all	5.3	5.0	8.3	7.4	
	DK/NS	36.0	28.9	16.6	21.3	

LX, Latinx or people of Latin American descent; AA, African Americans; DK/NS, Don't know/Not sure.
 a. statistical significance, two-tailed test.

ward health-related research has emerged as an underlying theme over the past several years.^{9,28} Previous studies concluded that race/ethnic minority participants felt positive about research because of an awareness of the positive impact results have on medical care³³ and that their participation might help their own health, as well as the health of their families and others.³⁴ This sense of altruism was also suggested in our study with both rural and urban AAs believing that research improves the health of other AAs in the United States. However, results were mixed for Latinx participants with more than half feeling uncertain whether overall population health and, particularly, Latinx health, has improved because of research. Additionally, urban Latinx had more neutral responses regarding the impact of research on the Latinx population.

This neutrality may be due to a gap in culturally translated information regarding research that may undermine Latinx knowledge about research in general, the purpose of a study, and/or the availability of studies in which they can participate.¹⁴ According to London et al, in their study examining Latinas' willingness to participate in nontherapeutic preventive breast cancer research, only half had ever heard of clinical trials before.¹⁴ With more than 90% of Latinx participants in our study answering the survey in Spanish, it is possible that their uncertainty could be due to a language barrier or a lack of awareness that they were eligible to participate in research. For immigrants, this could be coupled with concern over eligibility for studies due to their legal status as only 33% of Latinx participants indicated the United

States as their country of birth (including participants in Puerto Rico).

It is interesting to note that, although three-quarters of respondents trusted research conducted by their own doctors, less than one in 10 had ever been asked to participate. This lack of exposure to research opportunities points to a double disparity of rurality and minority race/ethnicity. Our findings were similar to Katz et al with regard to levels of trust in who is conducting the research, with research by one's own doctor the most trusted.⁹ While the TLP studies found no statistically significant associations by race and ethnicity when it came to trust in medical research,^{9,22} it is important to note that they were conducted in urban areas, with the exception of Tuskegee, Alabama. Our findings reflected significant variations in levels

Table 3. Participants' levels of trust in research studies, N=553

		Rural		Urban		P
		LX, %	AA, %	LX, %	AA, %	
How much do you trust the people who carry out health/illness research?, n=548	100%	12.0	18.2	16.7	11.6	<.001 ^a
	A great deal	28.7	29.8	38.5	28.1	
	Some	26.0	33.1	21.2	43.8	
	A little	19.3	13.2	14.7	13.2	
	Not at all	2.0	4.1	1.3	2.5	
	DK/NS	12.0	1.7	7.7	0.8	
How much do you trust the results from health/illness research?, n=548	100%	12.7	15.7	16.0	10.7	.069
	A great deal	31.3	28.1	44.9	36.4	
	Some	32.0	39.7	21.2	32.2	
	A little	12.0	11.6	9.0	12.4	
	Not at all	1.3	1.7	2.6	2.5	
	DK/NS	10.7	3.3	6.4	5.8	
How often are research studies carried out today without people knowing they were part of a research study?, n=549	100%	4.0	14.0	2.6	8.2	.001 ^a
	A great deal	20.7	27.3	23.7	37.7	
	Some	14.7	42.1	19.9	34.4	
	A little	24.7	3.3	26.9	13.9	
	Not at all	2.7	1.7	6.4	4.1	
	DK/NS	33.3	11.6	20.5	1.6	

LX, Latinx or people of Latin American descent; AA, African Americans; DK/NS, Don't know/Not sure.
 a. statistical significance, two-tailed test.

of trust by race/ethnicity and between rural and urban participants with rural participants reporting less trust.

Living in a low-population area can be limiting as well. Our findings that only 2% of rural Latinx participants have ever been offered the opportunity to participate in a study magnifies the continued need to recruit within these populations in order to meet the NIH mandate of representing the US population accurately in research. Of those reporting they had participated, 88% found the experience extremely positive and only a few in the urban Latinx subgroup reported it as a solely negative experience.

The prevailing attitudes of trust in our rural populations led us to conclude that appropriate access to research is the missing link in enrollment of racial/ethnic minorities. These four subgroups have a will-

ingness to participate and a trust in health-related research, but they are simply not being asked to enroll. Interestingly, despite high levels of

Our study confirms that a positive attitude toward health-related research has emerged as an underlying theme over the past several years.^{9,28}

trust, more than a third of respondents believed that research could be carried out without an individual's knowledge. Education tailored to ra-

cial/ethnic minorities that covers general truths and misconceptions about clinical research is likely necessary to bolster reception and enrollment in research.³⁵ Thus, it will be important for study designs to include an educational component, perhaps during an informational meeting prior to study commencement.

The entity conducting health/illness research influenced the willingness to participate across our four subgroups, with local doctors and academic hospitals being the most trusted sources. Thus, it is critical to engage local providers when conducting non-therapeutic trials in rural and urban settings.

Study Limitations

There are a few limitations to note. Our four subgroups had significant demographic differences dem-

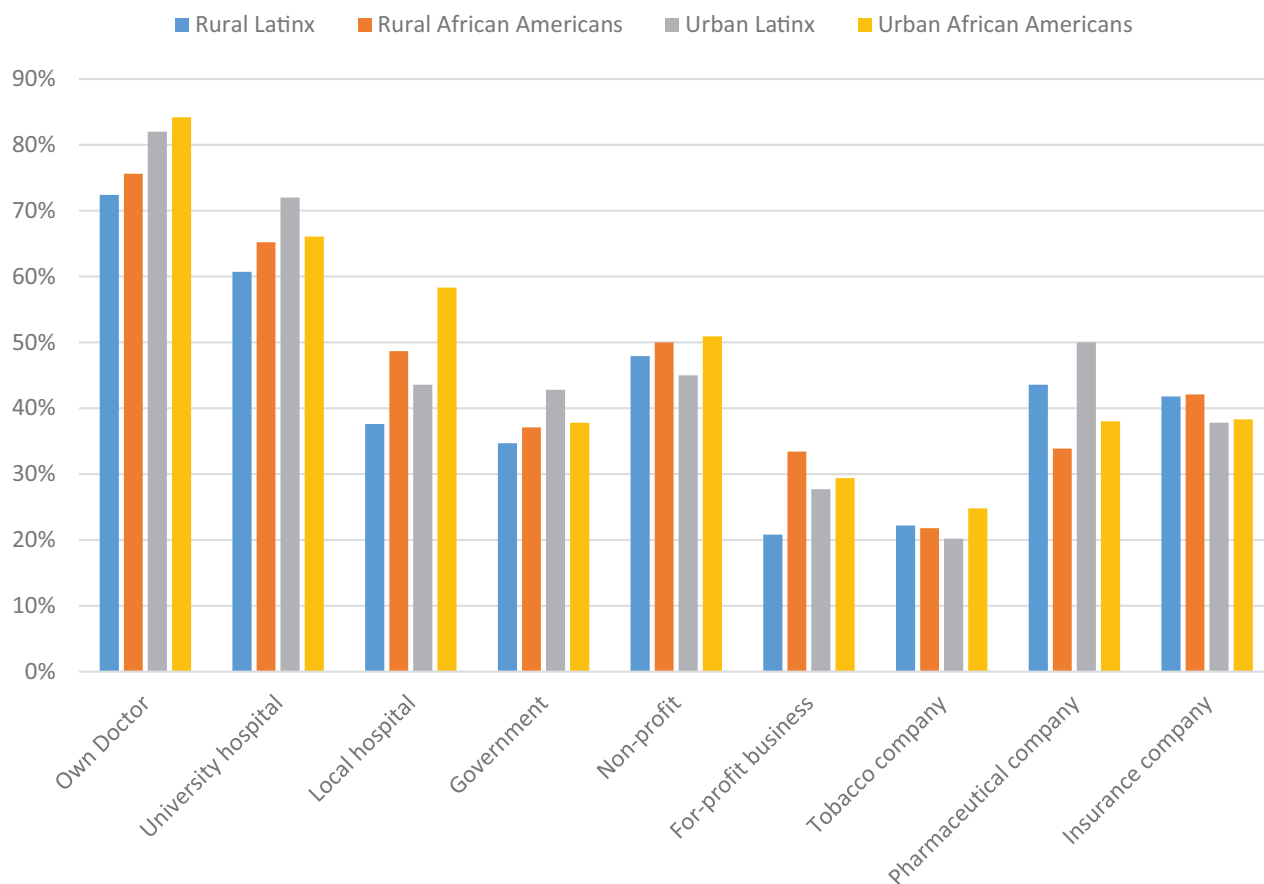


Figure 1. Likelihood of participation of urban and rural African American and Latinx patients in research studies about health and illness based on who conducted the study, %

onstrating diversity; however, they were representative of their respective populations. Our study was subject to selection and self-reporting biases due to the cross-sectional nature and use of surveys. However, we sought to minimize external bias by recruiting volunteers in comfortable places such as leisure, work/school, or shopping sites and utilizing surveys in Spanish or English. Also, our study was completed in 2013 and we cannot be sure how the intervening seven or so years would change responses. We have chosen to compare the findings across race/ethnicity and urban/rural but

given the demographic differences, it is possible that age also may play a role in the obtained findings as most participants were aged between the 30 and 50 years, which represents an age group who were unlikely to have chronic illnesses. It is possible that older or younger participants may have different perceptions in terms of participation in non-therapeutic trials as well as trust in research. Future studies with larger sample sizes and representation across the lifespan are needed, particularly to understand barriers and facilitators to health-related research among healthy volunteers.

Study Contributions

Despite these limitations, our study has two relevant contributions. The results provide additional insight into the motivations and attitudes of trust among racial/ethnic minority healthy volunteers toward participation in research. This is essential for inclusive enrollment in nontherapeutic trials. Our study also examines the impact of double disparities of racial/ethnic minorities in rural environments. The inclusion of rural racial/ethnic minorities provides relevant data that can be used for the future direction of research about health and illness.

Therefore, we conclude that inclusive enrollment is an attainable goal regardless of locale, particularly if studies are designed in a culturally relevant manner, address barriers to participation, and engage local health care providers.

CONCLUSION

Because of the shameful history of mistreatment of racial/ethnic minorities in medical research, it is not surprising that many medical providers may believe that it is fruitless to ask patients to volunteer for studies. Consequently, they may feel reluctant to offer research opportunities to their AA and Latinx patients. The primary reason why AA and Latinx individuals, in both rural and urban areas, did not previously participate in biomedical research was identified as not being invited to participate. Thus, our study provides evidence that trust in research, particularly trust in physicians, is established among these populations. Armed with this information, researchers, both therapeutic and non-therapeutic alike, should redouble their efforts to recruit members of underrepresented groups. This is especially true for those in rural areas as they report higher levels of trust and are more likely to agree to participate. Designing studies to address the barriers endemic to those impacted by the double disparity of minority race/ethnicity and rurality can help enrollment be more inclusive and, ultimately, more representative of the US population. In particular, reasons why providers fail to invite racial/ethnic minority individuals to participate in research studies should continue to be studied.

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CONFLICT OF INTEREST

No conflicts of interest to report.

AUTHOR CONTRIBUTIONS

Research concept and design: Thetford, Gillespie, Scarinci; Acquisition of data: Thetford, Gillespie; Data analysis and interpretation: Gillespie, Kim, Hansen, Scarinci; Manuscript draft: Thetford, Gillespie, Kim, Hansen, Scarinci; Statistical expertise: Kim, Hansen; Acquisition of funding: Scarinci; Administrative: Thetford, Gillespie, Hansen, Scarinci; Supervision: Scarinci

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