

KNOWLEDGE OF THE TUSKEGEE STUDY AND ITS IMPACT ON THE WILLINGNESS TO PARTICIPATE IN MEDICAL RESEARCH STUDIES

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The under-representation of racial/ethnic minorities among medical research participants has recently resulted in mandates for their inclusion by the National Institutes of Health (NIH). Therefore, there is a need to determine how history, attitudes, cultural beliefs, social issues, and investigator behavior affect minority enrollment in medical research studies.

From January 1998 to March 1999, 179 African-American and white residents of the Detroit Primary Metropolitan Statistical Area (PMSA) participated in a mail and telephone survey designed to examine impediments to African-American participation in medical research studies. Chi-square tests were performed to assess differences between the study groups using the Survey Data Analysis Program (SUDAAN).

Eighty-one percent of African Americans and 28% of whites had knowledge of the Tuskegee Study ($p = <0.001$). Knowledge of the Tuskegee Study resulted in less trust of researchers for 51% of African-Americans and 17% of whites ($p = 0.02$). Forty-six percent of African-Americans and 34% of whites indicated that their knowledge of the study would affect future research participation decisions ($p = 0.25$). Of these, 49% of African-Americans and 17% of whites would not be willing to participate in future medical research studies ($p = 0.05$).

This study confirms the need for medical researchers to confront the issue of the Tuskegee Study and its continuing impact on African-Americans' trust of medical research studies. (*J Natl Med Assoc.* 2000;92:563-572.)

Key words: Tuskegee Study, medical research

Recognition of the underrepresentation of African Americans and other racial/ethnic minorities

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among medical research participants has recently resulted in mandates for their inclusion by the National Institutes of Health (NIH).¹ Prior to the adaptation of the Belmont Report, racial/ethnic minorities had a disproportionately high representation among medical research study participants.²⁻⁵ Ethical principles outlined in the Belmont Report⁶ required recognition of an individual's right to choose to participate in research and required researchers to maximize benefits, reduce risks, and assure distributive justice to medical research participants. Adaptation of these principles substantially altered racial/ethnic minor-

ity presence among medical research subjects who were frequently unknowing participants in medical research studies.

Unfortunately, adaptation of the provisions in the Belmont report came too late to protect 400 unknowledgeable African-American men enrolled in the U.S. government-sponsored Tuskegee Study of untreated syphilis. The study, which began in 1932, was an examination of the natural history of syphilis in African American men. Participants were told that they were being treated, when in reality they received little if any treatment.⁷ This practice continued even after it was discovered that syphilis could be treated effectively with penicillin. In fact, the failure to treat the study group with penicillin even after the "antisiphilitic potency of penicillin was known," was presented as a positive feature of the study in at least two reports.^{8,9} In 1969, a panel was formed by the Centers for Disease Control and Prevention to review the Tuskegee Study. The panel voted to allow the study to continue to endpoint, that is until all subjects were brought to post-mortem, without any modification to the study protocol.¹⁰ The study was discontinued in 1972 as a result of public outcry after details of the study were made public.

Backlash from the Tuskegee Study is believed to continue to influence African-American beliefs and attitudes towards the medical and scientific establishment. Several investigators have suggested that the Tuskegee Study and resulting distrust are major impediments to African-American willingness to participate in medical research studies and disease prevention programs.^{3,11-16} Nonetheless, a review of the medical literature did not provide evidence of any studies that have actually examined prevalence of knowledge of the Tuskegee Study nor its influence on the willingness to participate in medical research studies. In light of the current difficulty in recruiting African Americans into research studies, it is important to evaluate the role of suspected barriers to their participation. This knowledge will alert researchers to the current challenges in the recruitment of African Americans and will help them appropriately tailor recruitment strategies. We examined racial differences, knowledge of the Tuskegee study, and the influence of this knowledge on the willingness of respondents to participate in medical research studies to evaluate the role of the Tuskegee Study.

METHODS

During 1998-1999, 198 residents of the Detroit Primary Metropolitan Statistical Area (Detroit PMSA) participated in a mail and telephone survey of impediments to African-American participation in medical research studies. Two pilot studies were conducted prior to this survey to evaluate the effectiveness of the sampling design, to provide estimates of stratum-specific response rates for use in sample allocation and to test three levels of participant incentives (data not presented).

A stratified multi-stage area probability sampling design was used to select households. The objective of the sampling design was to allocate the sample among strata with varying densities of households headed by African Americans to obtain approximately equal numbers of African-American and white households, without pre-screening for race (Fig. 1). This scheme was also believed to be stratification on income. The race of the householder and the percentage of African-American residents on a block were obtained from the 1990 U.S. Population Census and were used for primary- and second-stage stratification, respectively.

The 1990 U.S. Bureau of the Census computer file summary tape STF-1A¹⁷ of population and housing data was used to identify census tracts and summary tape STF-3A¹⁸ was used to identify census blocks. Street names and address ranges for the selected blocks were obtained from the Census of the Population Metropolitan Map Series and Enumeration District Maps¹⁹ and from the Rand-McNally Street Index for the Detroit PMSA.²⁰ Bressers Cross Index Directory²¹ was used to obtain addresses of occupied households in the Detroit PMSA and the names and telephone numbers of residents. Bressers Cross Index Directory is updated annually and is reported to have nearly 100% coverage.

Study envelopes were stamped "do not forward" so that letters would be returned when sent to the address of a vacant lot, unoccupied housing unit, incorrect street address, or when the resident was incorrectly identified. Reasons for letters returned were provided on all mail returned by the post office.

To be eligible to participate in this study, respondents had to be 18 years of age or older and a current resident of a selected household. Households were excluded if there were no eligible re-

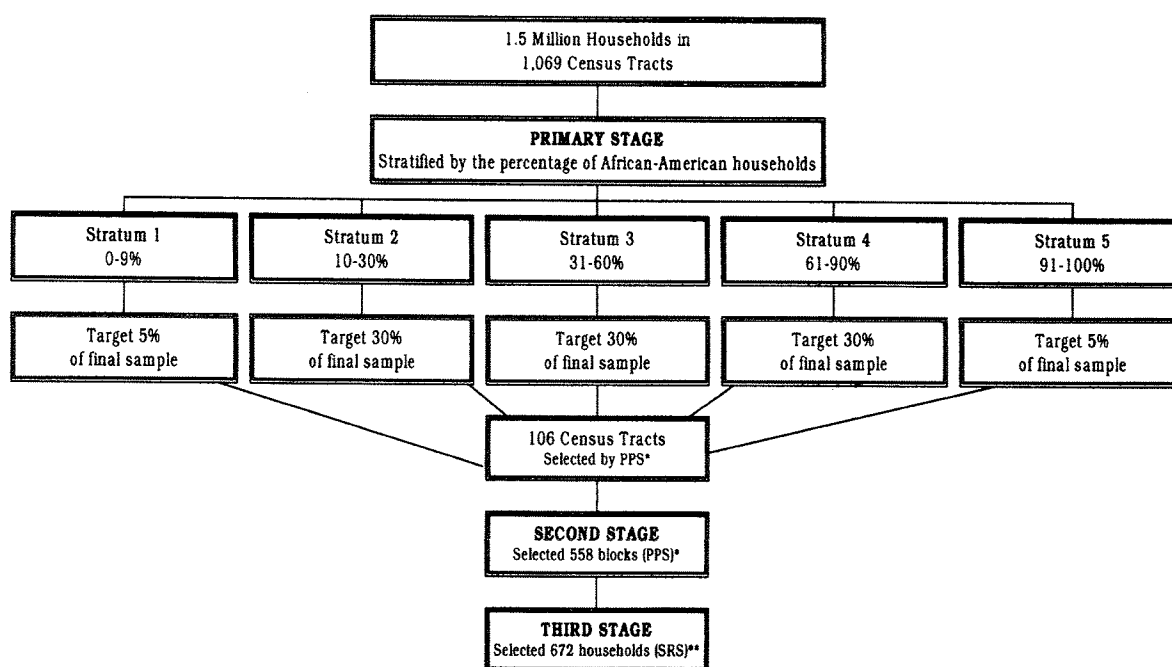


Figure 1. Summary of the sampling design for the IMPACT Study 1998–1999. PPS = sampling with probabilities proportional to size; SRS = simple random sampling.

spondents (i.e. no respondent at least 18 years old, vacant housing units, respondent was too sick to participate or respondent did not speak English). Households that did not have telephones or those that had unlisted telephone numbers were excluded from the telephone survey follow-up portion of the study. The percentage of unlisted telephone numbers was the same for the City of Detroit and suburban areas (36% each).

The main study instrument was a mail survey containing 24 questions (long version). There was also short version of the mail survey, which contained 7 questions worded the same as the long version, addressed the main study objectives and collected demographic data (i.e., age and race). The third instrument was a telephone survey that contained all of the questions from the short mail survey and collected additional demographic data (i.e., education, income, and name).

One trained interviewer conducted all telephone interviews. Four attempts were made to contact each eligible household. These consisted of at least one phone call during business hours of a weekday, an

evening phone call, and a weekend phone call. Households for which a respondent was not reached after four telephone attempts were coded as refusals. The telephone interviewer was provided with a prepared script to assure that all participants were interviewed in the same manner.

Several contacts were made to each potential participant to encourage participation. First, an introductory letter was sent to introduce the study. Second, a cover letter, which described the study and its purpose, was sent with the first mailing of the long version of the questionnaire. A follow-up postcard was sent about two weeks after the mailing of the first survey. After two mailings of the long version of the survey, non-responders were mailed the short version. Nonresponders to the short version of the survey received telephone follow-up. Individuals who completed and returned a survey received a new two-dollar bill. The incentive was mailed after receipt of the completed mail survey or telephone interview.

To assess the prevalence of knowledge of the Tuskegee Study, we first asked "Have you ever heard

Table 1. Household Mail and Telephone Survey Response Rates

Survey type	Number attempted	Ineligible	Total eligible	Completed interviews	Refused	Response rate
Mail						
Long	672	42	630	114	516	18%
Short	516	NA	516	17	499	3%
Phone	284	80	204	67	137	33%
Overall	NA	NA	NA	NA	NA	36%

of the Tuskegee Syphilis Study or the study of syphilis in black men?" Respondents who answered no followed a skip pattern that did not include further questions on the Tuskegee Study. Respondents who answered yes were then asked "How did the men in the Tuskegee Study get syphilis?" and were given a list of three responses to choose from (See Table 4.) Third, respondents were asked "Will what you know about the Tuskegee Study affect your decision to participate in a medical research as a study subject in the future?" Fourth, the respondents were asked "How does what you know about the Tuskegee Study affect your trust in medical researchers?"

Statistical Analysis

The sample was weighted to estimate population parameters for the entire Detroit Metropolitan Statistical Area. Adjustments were made for unit non-response and for selection probability. The final adjusted weight was used to calculate estimates of the population parameters.

The Survey Data Analysis Program Version 7.5 [SUDAAN]²² was used for the analysis of all weighted data to produce estimates adjusted for clustering. Analyses that describe the demographic make-up of the sample were performed with SAS²³ and SPSS²⁴ on unweighted data. Chi-square tests were performed to assess differences in the distributions of proportions between study groups. A significance level of 0.05 (two-tailed) was used for all analyses. Race-stratified logistic regression analyses were used to model the influence of the Tuskegee Study on the willingness to participate in medical research studies.

Completing a mail questionnaire or a telephone interview constituted consent to participate in this study. The institutional review board of the University of Iowa (Committee A) approved the study protocol.

RESULTS

Six hundred seventy-two households were selected from the 1,069 occupied census tracts in the Detroit PMSA (Fig. 1). The third-stage sampling frame correctly identified the addresses of 630 of the 672 selected households (94%). A total of 42 households were coded as ineligible for the mail survey portion of the study (Table 1). The proportion of households coded as ineligible for the mail survey within the City of Detroit and suburban areas was about 6% for each.

Two hundred eighty-four households were initially identified for the telephone survey, of which 80 were later determined to be ineligible (Table 1). Of the ineligible households, 9% had telephone numbers that were not for the selected household, 12% had disconnected numbers, 2% had respondents that did not speak English, 1% the respondents were too sick to participate, and 1% did not meet the age eligibility criteria.

A total of 198 individuals participated in this survey. Ninety-one study participants (46%) were African-American and 88 (44%) were white. Fourteen participants (10%) were from other racial/ethnic groups (8 Hispanics, 4 Asian/Pacific Islanders, 2 Native Americans, and 5 refused to identify their race/ethnic group). Because of the small numbers, these 19 participants are excluded from this report.

African-American respondents were on the average younger than the white subjects ($p < 0.01$) and more frequently female ($p = 0.039$). There were no significant differences between African-Americans and whites in either education ($p = 0.169$) nor annual household income ($p = 0.43$) (Table 2).

Overall, study participants more frequently had heard of the Tuskegee Study or "the study of syphilis in black men" if they were African American. About 81% of African-Americans and 28% of whites had prior knowledge of the Tuskegee Study ($p =$

Table 2. Respondent Characteristics

Variable	African-Americans (n = 91)	Whites (n = 88)
Gender		
Male	39%	55%
Female	62%	45%
Age		
Mean age	41.9	50.2
Median age	42.0	47.0
Educational level		
Less than 8th grade	1%	2%
Between 8th and 11th	8%	13%
H.S. grad or GED	19%	24%
Some college/or College grad	73%	60%
Total household income		
Less than \$10,000	6%	9%
\$10,000 to \$19,999	17%	12%
\$20,000 to \$29,999	15%	17%
\$30,000 to \$49,999	18%	25%
\$50,000 or more	44%	38%

*Includes respondents who did not answer the race/ethnicity question.

<0.001). Knowledge of the Tuskegee Study was more prevalent among respondents with a high school education or more, males, and among respondents ages 30–39.

Among African Americans, there was no difference in knowledge of the Tuskegee Study by gender, education, income or residence (city of Detroit compared suburban areas). African-American respondents ages 30–49, however, were significantly more likely to have knowledge of the study than African-American respondents under age 30 (Table 3).

Among white respondents, there was no statistically significant difference in knowledge of the Tuskegee Study by gender, age, or income. White respondents with a college education more frequently had knowledge of the study than those with less than a high school education. There was also a nearly significant difference in the knowledge of the Tuskegee study between whites who resided in the City of Detroit compared to whites who resided in suburban areas, (Table 3).

Seventy-six percent of African Americans compared to 59% of whites who were familiar with the Tuskegee Study indicated that the men in the Tuskegee Study got syphilis from an injection by

researchers ($p = 0.26$). Only 6% of African Americans and 20% of whites believed that the men in the study got syphilis from having sex with an infected person. Nineteen percent of African Americans and 21% of white who were familiar with the Tuskegee Study indicated that they did not know how the men got syphilis. Among participants who believed that the men in the Tuskegee Study were injected with syphilis, 65% African Americans compared to 100% of whites indicated their future willingness to participate in a medical research study ($p = 0.01$).

There was also a significant racial difference in how knowledge of the Tuskegee Study affected trust of medical researchers among respondents. About 51% of African-Americans reported that their knowledge of the Tuskegee Study resulted in them having less trust, 48% reported that their trust had not changed, and 1% reported that they had more trust in medical researchers. In comparison, among white respondents, 17% responded that they had less trust, 83% had no change in their level of trust of medical researchers and none had more trust in medical researchers ($p = 0.02$).

Respondents whose knowledge of the Tuskegee Study resulted in a reduction of their level of trust in medical researchers were significantly less willing to participate in medical research when compared to respondents with no change in trust/increase in trust (OR, 0.19; 95% CI, 0.05–0.71). Respondents who had no knowledge of the Tuskegee study were less willing to participate in medical research than respondents who knew of the study and experienced no change in their level of trust, however, this was not a statistically significant difference (OR, 0.36; 95% CI, 0.06–2.07).

Because of the racial differences in the effects of the independent variables on the willingness to participate in medical research studies, race-stratified logistic regression analyses were performed. Among African Americans, there was no significant difference in the willingness to participate based on mere knowledge of the Tuskegee Study (Table 4). The willingness to participate in a research study was significantly lower, however, if the effect of knowledge of the Tuskegee Study was a reduction in the level of trust of medical researchers compared to no change in trust/increased level of trust (Table 4).

African Americans who did not know about the Tuskegee Study were significantly less willing to participate than those who knew about the study and had no change in their level of trust (OR, 0.13; 95%

Table 3. Characteristics of Respondents by Knowledge of the Tuskegee Study Race

Demographic variable	African-Americans					P value	Whites					P value
	Knew		Did not know		Knew		Did not know					
	%	n	%	n	%		n	%	n			
Gender												
Male	89.3	(25)	10.7	(3)	0.223	41.5	(17)	58.5	(24)	0.168		
Female	75.6	(34)	24.2	(11)		57.6	(19)	42.4	(14)			
Age												
<30	71.0	(22)	29.0	(9)	Ref*	42.1	(8)	57.9	(11)	Ref*		
30-49	96.4	(27)	3.6	(1)	<0.01	42.1	(8)	57.9	(11)	1.0		
50-64	81.5	(22)	18.5	(5)	0.351	60.7	(17)	39.3	(11)	0.246		
65+	1.4	(1)	0	(0)	0.525	42.1	(8)	57.9	(11)	1.0		
Education												
Less than high school	71.4	(5)	28.6	(2)	Ref*	30.8	(4)	69.2	(9)	Ref*		
High school grad or GED	66.7	(10)	33.3	(5)	0.613	25.0	(5)	75.0	(15)	1.0		
College	84.2	(48)	15.8	(9)	0.593	58.3	(28)	41.7	(20)	0.078		
Income												
Less than \$10,000	80.0	(4)	20.0	(1)	Ref*	42.9	(3)	57.1	(4)	Ref*		
\$10,000 to \$19,999	69.2	(9)	30.8	(4)	1.0	22.2	(2)	77.8	(7)	0.596		
\$20,000 to \$29,999	75.0	(9)	35.0	(3)	1.0	53.8	(7)	46.2	(6)	1.0		
\$30,000 to \$49,999	71.4	(10)	28.6	(4)	1.0	50.0	(9)	50.0	(9)	1.0		
Over \$50,000	87.9	(29)	12.1	(4)	0.527	51.7	(15)	48.3	(14)	1.0		
Residence												
City of Detroit	82.4	(61)	1.6	(13)	1.0	56.5	(26)	43.5	(20)	0.063		
Suburban	81.3	(13)	18.8	(13)		36.6	(15)	63.4	(26)			

CI, 0.04-0.49). There was no statistically significant difference in the willingness to participate when African Americans who did not know about the Tuskegee Study were compared to African Americans who knew about the study and had less trust in medical researchers (OR 0.74; 95% CI, 0.18-3.12).

Among whites, there was no statistically significant difference in the willingness to participate as a result of knowledge of the Tuskegee Study, effect of such knowledge on their trust of medical researchers, nor beliefs about how the men in the Tuskegee Study got syphilis (Table 4).

Among respondents familiar with the Tuskegee Study, 40.7% responded that their knowledge of the study would be a factor in their future decisions regarding medical research participation. About 46% of African Americans compared to 33.5% of whites who knew of the study indicated that it would influence future research participation decisions ($p = 0.25$). Forty-nine percent of African Americans and 17% of whites who indicated that the Tuskegee Study would be a factor in future medical research participation decisions also indicated that they

would not be willing to participate in a medical research study in the future ($p = 0.05$).

To assess what, if any, impact nonresponse might have on study outcomes, we first compared early responders (respondents to the long version of the mail survey) to late responders (respondents to the short mail survey or the telephone interview). The underlying theory was that late responders were likely to be more similar to nonresponders than early responders.²⁵ This is especially appropriate methodology for this study because late responders were initially refusals to either one or both mail surveys.

Late responders were significantly less likely than early responders to be willing to participate in a medical research study. There were no significant differences between early and late responders in gender distribution or median age of respondents for whom these data were collected. Early responders did not significantly differ from late responders with regard to neither having had a previous opportunity to participate in a medical research study nor having knowledge of the Tuskegee Study. There was

Table 4. Univariate Logistic Regression Models of Willingness to Participate in a Medical Research Study Stratified by Race

Variable	Odds ratio	95% CI
African Americans		
Knowledge of the Tuskegee Study		
Knew about the study (n = 74)	2.7	0.99–7.40
Didn't know about the study (n = 16)	1.0	Ref*
Effect on knowledge of the Tuskegee Study on trust of Medical researchers		
Less trust in researchers (n = 19)	0.2	0.04–0.8
Same or more trust in researcher* (n = 22)	1.0	Ref*
Beliefs about how the men in the Tuskegee Study got syphilis		
From sex with an infected individual (n = 3)	—	—
Injected with it by researchers (n = 32)	0.32	0.04–2.57
Don't know how they got it (n = 5)	1.0	Ref*
Whites		
Knowledge of the Tuskegee Study		
Knew about the study (n = 41)	1.6	0.2–11.4
Didn't know about the study (n = 46)	1.0	Ref*
Effect on knowledge on trust of medical researchers		
Less trust in researchers (n = 6)	NA†	
Same or more trust in researcher* (n = 20)	1.0	Ref*
Beliefs about how the men in the Tuskegee Study got syphilis		
From sex with an infected individual (n = 6)	0.62	0.02–17.19
Injected with it by researchers (n = 17)	NV‡	—
Don't know how they got it (n = 4)	1.0	Ref*
Total		
Knowledge of the Tuskegee Study		
Knew about the study (n = 115)	0.95	0.20–4.61
Didn't know about the study (n = 62)	1.0	Ref*
Effect on knowledge on trust of medical researchers		
Less trust in researchers (n = 25)	0.19	0.05–0.71
Same or more trust in researcher* (n = 42)	1.0	Ref*
Beliefs about how the men in the Tuskegee Study got syphilis		
From sex with an infected individual (n = 9)	0.28	0.04–2.09
Injected with it by researchers (n = 49)	0.55	0.12–2.58
Don't know how they got it (n = 9)	1.0	Ref*

*Reference group.

†Sample size too small to calculate odds ratio.

‡Unable to calculate odds ratio because all respondents were willing to participate.

also no significant difference in the distribution of African Americans and whites among early and late responders (data not presented).

DISCUSSION

Generally, having knowledge of the Tuskegee Study alone did not significantly impact the willingness of study subjects to participate in a medical

research study. Nevertheless, this study confirms investigator suspicion^{3,11–16} that distrust arising from knowledge of the Tuskegee Study negatively impacts the willingness of African Americans to participate in medical research studies. African Americans whose knowledge of the study resulted in less trust in medical researchers were significantly less likely to be willing to participate in a medical re-

search study. After controlling for the influence of the Tuskegee Study on the trust of medical researchers, the willingness to participate in medical research was actually higher among African Americans with knowledge of the study than among African Americans who did not know about the study.

Despite the importance of the Tuskegee Study to medical ethics and recent publicity about the study, the overall proportion of white respondents who had knowledge of the Tuskegee Study was low. Whites who had attended college compared to those who had not were more often had knowledge of the study, which suggests that they may have been exposed to information on the study on college campuses or in their professional work.

Perhaps one of the most surprising findings of this study was the difference between African Americans and whites in how respondents' knowledge of the Tuskegee Study affected their trust in medical researchers. Despite racial similarities in the belief that the men in the Tuskegee Study were injected with syphilis by researchers, African Americans, more frequently than whites, indicated that the Tuskegee Study would influence future decisions to participate in medical research studies and that they would not be willing to participate. Racial differences in response to beliefs about the Tuskegee Study may lie in the fact that the study only involved African-American men. African-Americans respondents were likely more able than whites to identify with Tuskegee Study 'participants,' which would explain differences in its impact on future medical research participation. Further, the disproportionately high representation of African Americans among medical research abuse victims²⁶⁻³⁰ may make it difficult for whites to perceive themselves as potential victims and is likely the underlying reason for the absence of any change in their trust of medical researchers as a result of their knowledge of the Tuskegee Study. Alternatively, it is also possible that changes in rules governing research conduct may have been more successful in restoring the confidence of whites than African-Americans.

It is also worth noting that African Americans who responded that the Tuskegee Study caused no change in their level of trust of medical researchers also less frequently indicated a willingness to participate in medical research in the future than did whites. The strong association of distrust and African American unwillingness to participate in medical research found in this study suggests that the

Tuskegee Study is only a symbol of the pervasive distrust of medical researchers by African Americans. Other evidence of medical misuse of minority and other disenfranchised groups^{4,26-32} lend support to this theory.

LIMITATIONS

A possible source of bias for this study is the age of the census data used for sampling. The most recent census data available were nearly 10 years old. Noncoverage errors may have occurred due to an increase in new housing construction that may have resulted in the creation of new census tracts or blocks that were not included as sampling units for this study. There has been a net decrease in the number of housing units and an exodus of individuals from Detroit while the opposite is true for suburban areas.³² The population of Detroit decreased by 5.7% between 1995 and 1998, while the population of some suburban areas increased as much as 20%.³³ These data suggest that bias from coverage errors are more likely to have occurred in suburban areas. This could have resulted in the overweighting of responses from Detroit residents and the underweighting of responses from suburban areas. Since the majority of white respondents resided in suburban areas and African Americans resided in Detroit, bias arising from noncoverage could potentially result in the underestimation the prevalence of study variables among white residents and the overestimation of the prevalence among African Americans, thus inflating the magnitude of the difference between the two groups.

Nonresponse was another possible source of bias. Nonresponse jeopardizes the ability to generalize results to the target population when non-responders differ from responders among important study characteristics. The fact that late responders were significantly less willing to participate in medical research suggests that nonresponse bias would likely result in an underestimation of the overall prevalence of individuals who were unwilling to participate in medical research. Because there was no difference in the racial distribution and knowledge of the Tuskegee Study between early and late responders, it is also likely that nonresponse did not bias racial comparisons nor comparisons based on knowledge of the study. Nevertheless, because nonresponders were not actually compared to participants, nonresponse bias cannot be ruled out.

CONCLUSION

This study suggests a need for medical researchers to be aware of and confront the issue of African-American distrust of medical researchers if African-American representation among study participants is to increase. The Tuskegee Study is symbolic of the larger problem of African-American distrust of the largely white medical establishment which has evolved in the presence of racial discrimination, racial inequities in quality of care received, and a previous history of medical research misuse.

Researchers must establish trusting relationships with African Americans built on service and mutual respect prior to the onset of a research program. Establishing trust will be further enhanced by encouraging open dialogue on the past misuse of minority participants that has generated the overall distrust of researchers. Individual researchers should state their commitment to ethical research conduct and describe provisions that they have made to protect participants in their particular studies. Researchers should also provide frank explanations for studies and initiatives that specifically target racial/ethnic minorities or that are likely to result in the disproportionate representation of racial/ethnic minorities among study participants. Most importantly, researchers must adhere to ethical rules for research conduct.

ACKNOWLEDGEMENTS

This study would not have been possible without the cooperation and interest of the study participants. This manuscript was funded in part by grant R03HS09597-01 from the Agency for Health Care Policy and Research and grants 1F31 CA 72125-01A1 and 2 T32 CA09314-19 from the National Cancer Institute, National Institutes of Health, Bethesda, MD.

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