Beliefs of Women's Risk as Research Subjects: A Four-City Study Examining Differences by Sex and by Race/Ethnicity

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Abstract

Background: Given the history of vulnerability of women of childbearing age to medical treatments that have caused injury, for example, diethylstilbestrol (DES) and thalidomide, it is surprising that, to date, little research has directly examined attitudes of the general public regarding the vulnerability of women when they participate in biomedical research studies.

Methods: We asked three questions about beliefs of women as biomedical research subjects of 623 white, 353 black, and 157 Hispanic people in four U.S. cities: (1) Do you believe that women are more likely to be "taken advantage of" when they become subjects in a medical research project as compared to men? (2) Do you believe that women of childbearing age (15–45-year-olds) should become study participants in medical research projects? and, if the response was no or don't know/not sure, (3) Would you still say no or don't know/not sure to question 2 even if it meant that we would not know anything about the health and medical treatments for women aged 15–45 years?

Results: Overall, women were 60% more likely than men to state that women were more likely than men to be "taken advantage of," even when controlling for potential confounders, and both black and Hispanic participants were much more likely than white participants to state that this was the case. The majority of respondents (57.4%) said that women of childbearing age should not be research subjects; among women, both black and Hispanic people were less likely than white people to change their minds when prompted that this might mean that "nothing would be known about the health and medical treatments for women aged 15–45 years."

Conclusions: A substantial proportion of the participants reported knowledge of historical events, and this knowledge was related, particularly in black participants, to attitudes toward vulnerability of women as biomedical research subjects.

Introduction

IN LIGHT OF A HISTORY of unethical human experimentation in the United States (e.g., the Tuskegee Syphilis Study), it is not remarkable that much has been written about actual or perceived vulnerability of racial and ethnic minority research subjects.^{1–6} Given the history of vulnerability of women, specifically women of childbearing age, to medical treatments in the past that have caused injury not only to them but to their children, for example, diethylstilbestrol (DES)⁷ and thalidomide,⁸ it is surprising that, to date, little

research has directly examined attitudes of the general public about the vulnerability of women when they participate in biomedical research studies. Although investigations reporting on inclusion of women in studies have documented sex differences in clinical trial recruitment rates^{9–12} or have reported on reasons women decline to participate in clinical trials,^{13–16} there are no reports of beliefs and attitudes among the lay public regarding whether women, compared with men, are more likely to be "taken advantage of" when they become subjects in biomedical research studies, whether the benefits of including women of childbearing age outweigh

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the potential risks involved in their participation in these studies, and whether beliefs vary between the sexes or by race/ethnicity.

The purpose of this analysis was to examine (1) attitudes about women as subjects in biomedical research in a geographically, sociodemographically, ethnically, and racially diverse group of adults, (2) whether beliefs about perceived risks to women when they participate in biomedical research studies vary by sex or by race/ethnicity, and (3) the relationship of knowledge of two historical events (DES and thalidomide) to attitudes of whether women should participate in biomedical research studies.

Materials and Methods

The Tuskegee Legacy Project (TLP) questionnaire, a survey designed to examine reasons for lack of participation of racial and ethnic minorities, was administered via random-digit dial (RDD) telephone interviews to participants aged ≥ 18 years in four cities: Birmingham, Alabama; Tuskegee, Alabama; Hartford, Connecticut, and San Antonio, Texas. The TLP questionnaire, a 60-item instrument, primarily designed to address a range of issues related to the recruitment of minorities into biomedical studies, also contains questions related to inclusion of women in biomedical research. Details on the history and development of the TLP questionnaire and justifications of the methodological decisions both for the selection of the four cities and for the analysis of the TLP questionnaire have been published elsewhere.^{1,17} This study was approved by the Institutional Review Boards of the University of Connecticut Health Center and of New York University.

The Survey Research Unit (SRU) of the University of Alabama at Birmingham (UAB) administered the TLP questionnaire via RDD telephone interview. The target population was noninstitutionalized persons aged ≥ 18 years living in households with working telephones in the four targeted cities. The goal was to complete the 25-minute telephone interview with 900 adults in the following racial/ethnic groups: (1) 300 black respondents (100 in Hartford, 100 in Birmingham, 100 in Tuskegee, AL), (2) 100 Puerto Rican Hispanics (Hartford), (3) 100 Mexican Americans (San Antonio), and (4) 400 white adults (100 in Hartford, 100 in Birmingham, 100 in Tuskegee, 100 in San Antonio). A simple random sample was drawn based on the three-digit telephone exchange used for local calling areas within each city. SRU at UAB screened for nonworking and business numbers; unresolved numbers were retired after 20 attempts. A total of 13 interviewers were trained for the survey using computer-assisted telephone interview (CATI) technology; these interviewers were supervised at all times and randomly electronically monitored.

Key variables from the TLP questionnaire

Figure 1 shows the three questions from the TLP (the Women as Research Subjects questions, or WARS domain) that specifically explored attitudes about women's participation in biomedical studies. These questions were around the midpoint of the questionnaire (questions 34–36 of 60) directly after questions that explored attitudes regarding racial and ethnic minorities' vulnerability as biomedical research subjects. The general concept of vulnerability of women as research subjects is introduced in the first question, and the

1. Do you believe that WOMEN in the US are more likely to be "taken advantage of" when they become subjects in a medical research project as compared to MEN? Would you say that was:
☐ Always ☐ Most of the time ☐ Some of the time ☐ Rarely ☐ Never

2. Do you believe that women of childbearing age (15-45 year olds) should become Study participants in medical research projects?
☐ Yes ☐ No ☐ Don't know/Not sure

- IF the response to Q. #2 was "NO" or "Don't know/Not sure":

3. Would you still say . . .
 A) "NO" that women of childbearing age should NOT be subjects in medical research studies
 or
 B) "Don't know/not sure" whether women of childbearing age should be subjects in medical research studies
Even if it meant that we would not know anything about the health and medical treatments for women aged 15-45 yrs.?
☐ I would still say "NO" or "Don't know/Not sure"
☐ That changes my mind, so YES they should be included.

FIG. 1. Questions that explored attitudes toward the vulnerability of women as participants in biomedical research; TLP questionnaire.

second question specifically asks if women of childbearing age should be included in research studies. The third question is a probe for those who responded No or Not sure about whether they think women of childbearing age should be included in research studies; that is, the interviewer informed the respondent about the potential negative consequences of a total lack of knowledge about women's health for women of childbearing age that would inevitably result and inquired if this consideration changed their mind.

In addition, because we were also interested in determining if knowledge of DES and thalidomide was related to responses on the WARS domain questions, people were asked: Which of the following medical research studies have you heard about? Respondents answered either Yes, No, or don't know/not sure to a series of eight studies, one described as the DES or Diethylstilbestrol Study and another as the Thalidomide Study. For purposes of these analyses, we grouped those who stated No/don't know with those who responded No. We hypothesized that knowledge of DES and thalidomide would vary by age, by sex, by racial/ethnic group, and by education and income. Age was calculated using date of birth, and we classified education as either less than high school graduate, high school graduate alone or with some college vs. college degree or greater. We categorized income as <\$20,000 a year, ≥\$20,000 but <\$75,000 a year vs. ≥\$75,000 a year.

Statistical analysis

For bivariate analyses, study participants were stratified by sex and by racial/ethnic category and compared regarding the WARS domain questions using Pearson chi-square analyses and ANOVA. The responses to the WARS domain questions were collapsed for the purpose of bivariate and multivariate analyses. We collapsed responses of question 1 into two categories: Yes (all, most, and some of the time) vs. No (rarely and never). Questions 2 and 3 were also collapsed into two categories for the purpose of bivariate and logistic regression analyses: Yes vs. No (no and don't know/not

sure). We used logistic regression in order to control for potential confounders, including age, sex, race/ethnicity, education, income, and city/county. We report adjusted odds ratios (OR) and 95% confidence intervals (CI).

Results

Characteristics of study participants

The TLP questionnaire was administered to 1133 adults in Birmingham, Tuskegee, Hartford, and San Antonio, with response rates of 70%, 65%, 49%, and 50%, respectively. The final study sample comprised 353 black (31.2%), 157 Hispanic (15.9%), and 623 white respondents (55.0%), and 51.7% of respondents were women. Hispanics self-identified as either Puerto Rican (24.8%) or Mexican American (75.2%). The demographic characteristics of the participants are shown in Table 1. Hispanic participants were younger than black and white participants (ANOVA, $p \leq 0.001$) and were more likely to be women than were white and black respondents (chi-square 7.0, $df\ 2$, $p = 0.03$). White participants were more educated (chi-square = 65.6, $df\ 4$, $p \leq 0.001$) and had higher incomes (chi-square 80.7, $df\ 4$, $p \leq 0.001$) compared to black or Hispanic participants.

Analysis of question 1: Do you believe that women in the United States are more likely to be "taken advantage of" when they become subjects in a medical research project as compared to men?

Overall, for the total respondent sample, a majority of persons (52.1%) stated that women, compared to men, were more likely to be "taken advantage of" as research subjects either always or most of the time (17.3%) or sometimes (34.8%) (Fig. 2). Overall, women were more likely to state that this was the case always, most of the time, or sometimes (19.1% of women vs. 15.5% of men; chi-square 13.0, $df\ 2$, $p = 0.002$). Blacks were nearly 5 times more likely as whites and Hispanics were nearly 3.5 times more likely as whites to state

TABLE 1. DEMOGRAPHIC CHARACTERISTICS OF STUDY PARTICIPANTS, TLP

	Race/ethnicity			
	White (n = 623)	Black (n = 353)	Hispanic (n = 157)	Total (n = 1133)
Sex (% women)	51.7%	47.9%	60.5%	51.7%
Age (years, mean $\pm$ SD)	53.8 $\pm$ 17.0	49.1 $\pm$ 16.5	41.5 $\pm$ 16.1*	50.6 $\pm$ 17.2
Education				
< High school graduate	11.8%	21.6%	26.1%	16.8%
High school graduate	51.3%	60.5%	58.6%	55.2%
≥ college graduate	36.9%*	17.9%	15.3%	28%
Income				
< \$20,000	21.3%	42.8%	41.7%	31.1%
\$20,000–74,999	58.4%	52.1%	52.5%	55.5%
≥ \$75,000	20.3%*	5.1%	5.8%	13.3%
Geographic location*				
Birmingham, AL	16.9%	29.5%	0.6%	18.5%
Tuskegee, AL	29.5%	30.0%	0.6%	25.7%
Hartford, CT	35.6%	30.6%	23.6%	34.1%
San Antonio, TX	18.0%	4.5%	75.2%	21.7%

*Significant at the $p \leq 0.05$ level.

FIG. 2. Response to question 1: Percentage, by race/ethnicity and gender, who believe either that women, compared to men, are more likely to be taken advantage of when they become research subjects ($n = 1133$).

that this was the case always or most of the time (blacks 32.7%, Hispanics 23.7% vs. whites 6.8%; chi-square 133.1, $df\ 4$, $p \leq 0.001$). When we examined differences by sex within each racial/ethnic category we found that among both white and black respondents, women were more likely than men to state that women as research subjects are more likely "taken advantage of" (whites: 46.1% of women vs. 32.2% of men, chi-square 11.8, $df\ 2$, $p = 0.003$; blacks: 77.1% of women vs. 63.9% of men, chi-square 7.4, $df\ 2$, $p = 0.024$). Among Hispanics, however, men and women did not significantly differ in their responses (62.0% of women vs. 61.7% of men, chi-square 0.30, $df\ 2$, $p = 0.88$).

When controlling for differences in age, income, and race/ethnicity between the sexes, the odds of believing that

women are more likely to be "taken advantage of" when they become subjects in a medical research study was 60% higher for women compared with men ($OR_{adjusted} = 1.6$, 95% CI 1.2, 2.1). When controlling for differences in age, income, education, and geographic location between racial/ethnic groups among women only, we found that the odds of believing that women compared to men are more likely to be "taken advantage of" when they become subjects in a medical research project were four times higher in black women ($OR_{adjusted} = 3.9$, 95% CI 2.5, 6.2) and two times higher in Hispanic women ($OR_{adjusted} = 1.9$, 95% CI 1.2, 3.1) compared to white women. For men, the odds of believing that women compared to men are more likely to be "taken advantage of" when they become subjects in a medical research project were also higher

FIG. 3. Response to question 2: Percentage, by race/ethnicity and gender, who believe either that women of childbearing age should not become research subjects or are not sure they should become research subjects ($n = 1133$).

in both black men ($OR_{\text{adjusted}} = 3.6$, 95% CI 2.3, 5.5) and Hispanic men ($OR_{\text{adjusted}} = 3.1$, 95% CI 1.7, 6.1) compared to white men.

When we examined responses to question 1 by sex within each race/ethnic group, we found that for white and black participants, women were more likely to believe that women would be "taken advantage of" when they become subjects in a medical research project compared to men (controlling for differences in sex in income level for whites and in age for Blacks) whites: $OR_{\text{adjusted}} = 1.7$, 95% CI 1.2, 2.4; blacks: $OR_{\text{adjusted}} = 1.8$, 95% CI 1.1, 3.0). For Hispanics, the odds of believing that women were more likely compared to men to be "taken advantage of" when they become subjects in a medical research project did not vary by sex in logistic regression analyses.

Analysis of question 2: Do you believe that women of childbearing age (15–45-year-olds) should become study participants in medical research projects?

Overall, 45.0% of the respondents said that women of childbearing age should not be research subjects, and an additional 12.4% were unsure whether they should be research subjects (Fig. 3). In order to test for differences by sex and by race/ethnicity when controlling for differences between groups, we grouped those who stated Don't know/not sure with those who stated No. We found no differences in the distribution of responses to question 2 between men and women, or between white, black, and Hispanic respondents in the overall sample in either bivariate or multivariate analyses, controlling for differences in age, geographic location, income, and education between the sexes (for women, compared to men, the $OR_{\text{adjusted}} = 1.1$, 95% CI 0.8, 1.4) and con-

trolling for differences in sex, age, and income between the racial/ethnic groups (for blacks, compared to whites, the $OR_{\text{adjusted}} = 1.0$, 95% CI 0.8, 1.4; for Hispanics, compared to whites, the $OR_{\text{adjusted}} = 1.2$, 95% CI 0.8, 1.9). In addition, when we examined responses to question 2 within each sex group, we found that for both men and for women, there was no significant difference by race/ethnicity (black women vs. white women, $OR_{\text{adjusted}} = 1.1$, 95% CI 0.7, 1.5; Hispanic women vs. white women, $OR_{\text{adjusted}} = 0.9$, 95% CI 0.5, 1.7; black men vs. white men, $OR_{\text{adjusted}} = 1.2$, 95% CI 0.7, 1.8; Hispanic men vs. white men, $OR_{\text{adjusted}} = 1.4$, 95% CI 0.6, 3.1). We also failed to find differences in responses by sex within each racial/ethnic group (white men vs. white women, $OR_{\text{adjusted}} = 1.2$, 95% CI 0.8, 1.8; black men vs. black women, $OR_{\text{adjusted}} = 0.8$, 95% CI 0.7, 1.1; Hispanic men vs. Hispanic women, $OR_{\text{adjusted}} = 0.5$, 95% CI 0.3, 1.1).

Analysis of question 3 (includes only those who stated No or don't know/not sure to question 2, $n = 659$): Would you still say No or Don't know/not sure that women of childbearing age should not be subjects in medical research studies, even if it meant that we would not know anything about the health and medical treatments for women aged 15–45 years?

Less than half of those who stated No or Don't know/not sure to question 2 (39.0%) changed their minds when reminded of the resulting negative consequences for knowledge about women's health that would result from barring women from clinical research (Fig. 4). The odds of changing one's mind did not vary by sex ($OR_{\text{adjusted}} = 1.4$ for women vs. men, 95% CI 1.0, 2.1), although the difference between the sexes overall did approach statistical significance

FIG. 4. Response to question 3: Percentage, by race/ethnicity and gender, who would still say No or Don't know/not sure whether women of childbearing age should become research subjects, even if it meant knowing nothing about the health and medical treatments for women aged 14–45 ($n = 659$).

($p = 0.06$). We found that both black women and Hispanic women were less likely than white women to change their minds when reminded of the negative consequences for women's health (blacks, $OR_{adjusted} = 0.5$, 95% CI 0.3, 1.0; Hispanics, $OR_{adjusted} = 0.5$, 95% CI 0.3, 1.0, both compared to whites), whereas among men, we found no difference in the proportion of those who changed their minds ($OR_{adjusted}$ for blacks 0.6, 95% CI 0.3, 1.1; $OR_{adjusted}$ for Hispanics, 1.0, 95% CI 0.4, 2.8).

Bivariate analysis of knowledge of historical events (knowledge of either thalidomide or DES) and demographic characteristics of participants

Of the total study sample, 12.0% of participants reported having heard of DES, and 22.7% reported having heard of thalidomide. Knowledge of neither thalidomide nor DES was related to sex. Black participants were less likely than white participants to report knowledge of thalidomide (33.4% of whites vs. 10.8% of blacks; chi-square 61.32, df 1, $p \leq 0.001$), but there was no difference between blacks and whites regarding knowledge of DES (14.7% of whites vs. 12.1% of blacks; chi-square 1.25, df 1, $p = 0.26$). Hispanics were less likely than whites to report knowledge of thalidomide (33.4% of whites vs. 7.7% of Hispanics; chi-square 61.32, df 1, $p \leq 0.001$) and of DES (12.1% of whites vs. 6.4% of Hispanics; chi-square 6.98, df 1, $p = 0.03$). Knowledge of thalidomide (but not DES) was related to age, with 30.7% of those age 50+ reporting knowledge of thalidomide vs. 14.0% of those age ≤ 49 (chi-square 43.57, df 1, $p \leq 0.001$). Knowledge of both thalidomide and DES was clearly related to both education and to income. Of those with "some college," 44.1% reported knowledge of thalidomide and 23.4% reported knowledge of DES. In contrast, of those with a high school education or less, only 14.7% knew of thalidomide (chi-square 51.23, df 1, $p \leq 0.001$) and 7.8% knew of DES (chi-square 110.56, df 1, $p \leq 0.001$). Of those with family incomes $\geq \$35,000$ per year, 33.3% reported knowledge of thalidomide and 16.4% reported knowledge of DES vs. 14.4% and 9.2%, respectively, of those with incomes $\leq \$34,000$ per year (for thalidomide, chi-square 50.25, df 1, $p \leq 0.001$; for DES, chi-square 11.79, df 1, $p \leq 0.001$). We found geographic differences in knowledge of thalidomide, with more respondents in Hartford (49.8%) than in Birmingham (13.2%), Tuskegee (16.3%), and San Antonio (20.6%) reporting knowledge of thalidomide (chi-square 41.16, df 3, $p \leq 0.001$). Geographic location was not related to knowledge of DES (chi-square 2.15, df 1, $p = 0.54$).

Analysis of relationship between DES and thalidomide and responses to the WARS domain questions

Results of the adjusted analysis of the relationship between knowledge of DES and thalidomide and responses to the WARS domain questions are shown in Table 2. Overall, knowledge of DES, but not of thalidomide, was independently, albeit moderately, increased in those who believed that women were more likely, compared to men, to be "taken advantage of" when controlling for potential confounders (sex, race/ethnicity, education, income, and geographic location), with those who stated that women, compared to men, are likely Always, Most of the time, or Sometimes to

be taken advantage 60% more likely to report knowledge of DES ($OR_{adjusted} = 1.58$, 95% CI 1.02, 1.93) compared to those who responded Never or Rarely.

Knowledge of DES, but not of thalidomide, was also independently related to whether one thought that women of childbearing age should participate in biomedical research as participants (question 2), with those who stated that women of childbearing age should not participate in biomedical research as participants less likely to report knowledge of DES ($OR_{adjusted} = 0.59$, 95% CI 0.41, 0.86). On further examination, we found that the relationship between stating that women of childbearing age should not participate in biomedical research as participants and being less likely to report knowledge of DES was evident only among black participants ($OR_{adjusted} = 0.59$, 95% CI 0.41, 0.86) and among men ($OR_{adjusted} = 0.51$, 95% CI 0.30, 0.87). In fact, we also found that blacks who stated that women of childbearing age should not participate in biomedical research as participants were also less likely to report knowledge of thalidomide ($OR_{adjusted} = 0.36$, 95% CI 0.17, 0.76).

Responses to question 3, whether one changed one's mind about women of childbearing age participating in biomedical research, given the consequences, were not related to knowledge of DES ($OR_{adjusted} = 0.91$, 95% CI 0.52, 1.63) or thalidomide ($OR_{adjusted} = 1.15$, 95% CI 0.77, 1.73) overall. However, this is likely due to the difference in directionality of response seen between men and women. Although the differences within the sexes were not statistically significant (perhaps because of reduced sample size), we found that among men, those who changed their minds from No or Not sure to Yes, women of childbearing age should be research subjects, given the negative consequences for women's health, were about two times more likely to report knowledge of DES and of thalidomide; among women, those who changed their minds were 60% less likely to report knowledge of DES and were 40% less likely to report knowledge of thalidomide.

Discussion

In the late 1970s, largely because of the recognition of the deleterious effects of two medications (thalidomide and DES) taken by thousands of pregnant women on both themselves and their fetuses, the Food and Drug Administration (FDA) prohibited women of childbearing age from participating in clinical research as research subjects.¹⁸ Within 10 years from their expulsion from clinical research, however, it was recognized by the U.S. Public Health Service Task Force on Women's Health that the subsequent fallout from women's exclusion from research was that women's health had been compromised because of lack of knowledge about women's health and treatment of diseases in women.¹⁹ It soon became apparent, for example, that certain diseases (e.g., cardiovascular disease) presented or behaved differently in women than in men and that drug metabolism might vary by sex, for example, with important side effects more prevalent in women than in men.²⁰ Despite this legislation, several reports have shown that in some cases, especially in the case of racial/ethnic minorities, women still may be underrepresented in biomedical research.^{10,21,22}

We examined beliefs and attitudes regarding vulnerability of women when they participate in biomedical research studies. Specifically, we examined whether people believed

TABLE 2. REPORTED KNOWLEDGE OF DES AND THALIDOMIDE: RELATIONSHIP TO QUESTIONS EXPLORING VULNERABILITY OF WOMEN AS BIOMEDICAL RESEARCH PARTICIPANTS, TLP^a

	<i>Reported knowledge of:</i>	<i>Men</i>	<i>Women</i>	<i>Whites</i>	<i>Blacks</i>	<i>Hispanics</i>	<i>Total</i>
Q1: Those who believe that women in the U.S. are more likely to be "taken advantage of" when they become subjects in a medical research project as compared to men always/most times/sometimes vs. rarely/never	DES	1.60 (0.84, 2.93)	1.43 (0.77, 2.64)	1.87^b (1.04, 3.36)	1.55 (0.74, 3.26)	1.73 (0.40, 7.38)	1.58 (1.02, 1.93)
Q2: Those who believe that women of childbearing age (15–45-year-olds) should not become study participants in medical research projects vs. those who say yes, they should participate	DES	0.51 (0.30, 0.87)	0.69 (0.41, 1.14)	0.98 (0.56, 1.70)	0.30 (0.16, 0.59)	1.09 (0.30, 4.04)	0.59 (0.41, 0.86)
Q3: Would you still say no, or don't know/not sure, that women of childbearing age should not be subjects in medical research studies <i>even if it meant that we would not know anything about the health and medical treatments for women aged 15–45 years?</i>	Thalidomide	0.67 (0.43, 1.06)	0.80 (0.50, 1.28)	0.88 (0.59, 1.31)	0.36 (0.17, 0.76)	0.72 (0.22, 2.35)	0.78 (0.57, 1.04)
	DES	2.37 (0.96, 5.85)	0.47 (0.21, 1.07)	1.43 (0.70, 2.92)	0.79 (0.14, 4.58)	0.96 (0.14, 6.57)	1.11 (0.65, 1.89)
	Thalidomide	1.91 (0.99, 3.65)	0.61 (0.34, 1.11)	1.45 (0.87, 2.40)	0.55 (0.14, 2.24)	0.29 (0.32, 2.58)	1.03 (0.67, 1.58)

^aOdds ratios.

^bBold indicates statistically significant results at a level of $p \leq 0.05$.

the benefits of including women of childbearing age outweigh the potential risks involved in their participation in these studies and if beliefs varied by sex or by race/ethnicity in a geographically and sociodemographically diverse group of adults. We found that a substantial proportion—roughly half—of participants in this RDD survey thought that women, compared to men, were more likely to be “taken advantage of” as research subjects and that most respondents (67%) were either against or unsure if women of childbearing age should participate as research subjects. When the interviewer informed these respondents about the potential negative consequences of a total lack of knowledge about women’s health for women of childbearing age that would inevitably result, fewer than half (39%) of respondents changed their minds about participation of women of childbearing age. Clearly, it is likely that this reluctance on the part of the general public to recognize the importance of inclusion of women in research studies could be one of the barriers in achieving the goals of the NIH mandate²³ and the legal obligation that all federally funded studies include women unless there is a clear reason to exclude them.²⁴

Those who stated that women were more likely to be taken advantage of were more likely to be either black or Hispanic. It has been widely reported that African Americans and other minority groups are more reluctant than white people to participate in biomedical research because of a history of research abuses against black people in this country.^{4,25,26} Although it is understandable that racial/ethnic minorities might be more suspicious of potential research abuses against women of childbearing age (a group whom many might view as especially vulnerable to exploitation or more likely to receive special protection due to their childbearing potential and the potential dangers to a developing fetus), it remains to be established whether knowledge of research abuses translates into hesitance or refusal to participate in biomedical research. Indeed, several investigations have found no difference between racial/ethnic minorities and white people in willingness to participate in biomedical research,^{1,27} and other investigators have found that racial/ethnic differences in biomedical research participation can be accounted for by differences in socioeconomic status.^{28,29} When we controlled for differences in socioeconomic status among the three racial/ethnic groups, however, the profound differences we found by race/ethnicity persisted: the odds of believing that women are more likely to be “taken advantage of” when they become subjects in a medical research project were almost 4 times as high for black respondents and 2.5 times as high for Hispanic respondents, compared to whites respondents.

Women were more likely than men to believe that women were more likely to be “taken advantage of” than men as participants in biomedical studies. Given the power imbalance by gender that exists in the United States, it is not surprising that most women would be more suspicious of research abuses on women than would men. We found this attitudinal difference by sex, however, only among white and black people, but not among Hispanics. Despite the fact that Hispanics are now the nation’s largest ethnic minority group, comprising 14% of the nation’s total population, and the fact that higher rates of certain prevalent diseases, for example, diabetes, are found in Hispanics, data on recruitment of Hispanic women in biomedical research are sparse.^{9,10,30} Further research should determine if the NIH Revitalization Act, which, since 1993 has required federally funded stud-

ies to include women of childbearing potential unless there was clear justification for exclusion, has caused a substantial change in recruitment of women, especially those who are racial and ethnic minorities.

We found that a substantial proportion of the participants reported knowledge of historical events that have caused *in utero* or subsequent medical harm to the children of pregnant women who took thalidomide or DES during pregnancy and that knowledge of DES, in particular, was more common in those who stated that women were more likely to be “taken advantage of” and to beliefs of whether women of childbearing age should participate in biomedical research studies. Interestingly, those who stated that women are more likely than men to be “taken advantage of” were more likely to report knowledge of DES, although on further analysis, we found that this was the case only among white participants. Those who stated that women of childbearing age should not participate in biomedical research were actually less likely to report knowledge of DES. We found this relationship, however, only in men and only in black respondents, for whom, in particular, knowledge of either historical event was independently, inversely, and strongly related (thalidomide: $OR_{adjusted} = 0.36$, 95% CI 0.17, 0.74; DES: $OR_{adjusted} = 0.32$ 95% CI 0.16, 0.63); that is, those who stated that women of childbearing age should not participate in biomedical research as participants were, as was the case of the overall analysis, less likely to report knowledge of thalidomide or DES. One explanation for the directionality of the relationship between knowledge of DES and stating that women should be participants is that persons who knew of the DES study were aware of details, including the lack of testing performed on DES and the recognition that it was the lack of appropriate testing and use of this drug that caused subsequent harm. This finding supports the view that black people might be more sensitive than white people to issues surrounding clinical research in the United States.

To our knowledge, this is the first large-scale study to document high levels of wariness and differences in attitudes, by sex and by race/ethnicity, regarding women’s participation in biomedical research in a large, racially/ethnically diverse group of American adults and to examine if knowledge of past historical events that caused in harm to offspring influences these beliefs. Although level of education has been found to be a predictor of participation in biomedical research,¹⁵ further investigation into the relationship of race/ethnicity (and other demographic factors), beliefs, and attitudes toward biomedical research, and willingness to participate in clinical studies is clearly warranted. Also, studies that examine the relationship among sex, race/ethnicity, and participation should include measures of socioeconomic status in their analysis, as differences in socioeconomic status between the sexes and between the various racial and ethnic groups in the United States tend to be profound. Cultural differences and gender differences (i.e., beliefs and attitudes that vary between men and women as a result of the roles they play in society) should also be addressed.¹³ Indeed, studies have found recruitment strategies to be more successful when they are culturally appropriate and directed toward a particular subgroup of the population, for example, high-risk persons.³¹

In 1994, the Institute of Medicine, at the request of the NIH, issued a report on Women in Health Research, in which they explained that their report was focused on “justice,” that is, that “women and men should have the opportunity to par-

ticipate equally in the benefits and burdens of research."³² Although one should bear in mind the principal arguments to support the NIH policy of increased representation of women (first, to increase generalizability and to allow for valid analyses of differences by sex, and, second, because participation in biomedical research is often seen as advantageous to participants), our findings are parallel to those of others, who have suggested that more needs to be understood about whether both men and women, perhaps especially those who are racial/ethnic minorities, find these arguments compelling.³³

Disclosure Statement

The authors have no conflicts of interest to report.

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