Original Article

Disparities and trends in the participation of minorities, women, and the elderly in breast, colorectal, lung, and prostate cancer clinical trials

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BACKGROUND: This study was done to determine the representation of minorities, women, and the elderly in National Cancer Institute (NCI) clinical trials. **METHODS:** This is an analysis in the NCI Clinical Data Update System. Patients were evaluated in breast, colorectal, lung, and prostate cancer trials from 2000 to 2019. Representation in a trial was determined by race/ethnicity, sex, and age. Secondarily, the change in trial participation by multivariable analysis by comparing years 2000 through 2004 to 2015 through 2019 was evaluated. **RESULTS:** The cohort included 242,720 participants: 197,320 Non-Hispanic White (81.3%), 21,190 Black (8.7%), 11,587 Hispanic (4.8%), and 6880 Asian/Pacific Islander (2.8%). Black and Hispanic patients were underrepresented for colorectal (odds ratio [OR], 0.58; 95% confidence interval [CI], 0.50-0.67; $P < .001$ and OR, 0.74; 95% CI, 0.64-0.87; $P < .001$, respectively), lung (OR, 0.83; 95% CI, 0.76-0.91; $P < .001$ and 0.66; 95% CI, 0.57-0.77; $P < .001$, respectively), and prostate cancer trials (OR, 0.85; 95% CI, 0.79-0.92; $P < .001$ and OR, 0.58; 95% CI, 0.51-0.66; $P < .001$) between 2015 and 2019. The odds of participation in 2015 to 2019 increased among Black patients in breast (OR, 2.19; 95% CI, 2.07-%2.32; $P < .001$), lung (OR, 1.54; 95% CI, 1.38-1.73; $P < .001$), and prostate cancer trials (OR, 1.14; 95% CI, 1.04-1.26; $P < .001$). The odds of participation in a trial among Hispanic patients increased for breast (OR, 3.32; 95% CI, 3.09-3.56; $P < .001$), colorectal (OR, 2.46; 95% CI, 2.04-2.96; $P < .001$), lung (OR, 3.88; 95% CI, 3.20-4.69; $P < .001$), and prostate cancer (OR, 1.70; 95% CI, 1.42-2.04; $P = .005$). **CONCLUSIONS:** This study identified that Black and Hispanic patients remain underrepresented in trials, but in recent years, participation has increased. These findings indicate that minority participation has increased over time, but further efforts are needed. ***Cancer* 2022;128:770-777**. © *2021 American Cancer Society*.

KEYWORDS: breast cancer, clinical trials, colorectal cancer, disparities, lung cancer, prostate cancer.

INTRODUCTION

The National Institutes of Health (NIH) first enacted the Revitalization Act in 1993, the goal of which was to encourage participation of women and minority patients in NIH-sponsored research.[1] This act was subsequently amended in 2001 and most recently amended in 2017.[1] The National Cancer Institute (NCI) has instituted multiple initiatives to address concerns about the heterogeneity of clinical trial participation.[2] The impact of these initiatives as well as the comprehensive characteristics of patients enrolled in cancer clinical trials has not been analyzed in nearly 2 decades.[3] The participation of minorities, women, and the elderly in cancer clinical trials is essential to determining not only the efficacy of treatments but also to improve the outcomes of these at-risk populations.[4] If there is not appropriate inclusion of these populations than health disparities will likely widen.[5] It should be noted that the participation of elderly patients in clinical trials compared to minorities and women might be fundamentally different as older patients are less likely to eligible for clinical trials due to existing comorbidities.[6]

Initially published in 2004, Murthy et al[3] evaluated the characteristics of all patients enrolled in therapeutic nonsurgical NCI Clinical Trial Cooperative Group trials on a year-to-year basis.[3] The authors' specific focus was within breast, colorectal, lung, and prostate cancer clinical trials from 1996 to 2002. The authors compared trials in 1996 to 1999 to trials in 2000 to 2002 and identified that in later years, racial/ethnic minorities, women, and elderly were less likely to enroll

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Brent S. Rose and Juan Javier-DesLoges had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

The Department of Defense was not involved in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

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in trials when compared to Whites, males, and patients who are younger in earlier years. Since 2004, there have been 2 additional studies on the characteristics of patients enrolling in clinical trials. However, both studies relied on the published results of completed trials, and because of their methodology, they were limited in their ability to identify trends in participation over time.[7,8] Trials can accrue for several years, and it remains unclear if participation disparities still exist today.

The aim of this study was to evaluate the representation of patients by age, sex, and race/ethnic clinical trial participation for all NCI Clinical Trial Cooperative Group trials. We specifically focused on adequate representation in 2015 to 2019 and compared this to an earlier time period (2000-2004). We hypothesized that patient participation disparities may have improved when patients are stratified by age, sex, race/ethnicity, and participation year.

MATERIALS AND METHODS

Data Collection

This study followed the Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines for cohort studies. The data for this study was requested by the investigators through the Freedom of Information Act in coordination with the NCI.[9] Participation data for NCI-sponsored trials from 2000 to 2019 were obtained from the NCI Clinical Data Update System, a database that contains participation information about participants in NCI-sponsored Cooperative Group clinical trials.[10] Cancer Incidence Data (2000-2017) were obtained from United States Cancer Statistics, which is managed by the Centers for Disease Control and Prevention (CDC). The United States Cancer Statistics[11] includes cancer statistics from the NCI's Surveillance, Epidemiology, and End Results Program[12] combined with the CDC's National Program of Cancer Registries.[13] These statistics provide information on the proportion of incident cancers and cover 100% of the US population.[9,12] No institutional review board approval was required from our home institution (University of California, San Diego) and was therefore waived. Informed consent was waived, and trial-level data was publicly available and deidentified.

Study Participants

All patients who participated in a clinical trial with the lead disease being breast, colorectal, lung, or prostate cancer between the years January 1, 2000, and December 31,

TABLE 1. Participants in National Cancer Institute Cooperative Group Trials and Proportion of Incidence Cancer Patients in the United States According to Race/Ethnicity, Age, and Sex, 2000-2019

Characteristic	All Cancers, N = 242,720, No. (%)	Incident Cancer in United States, %	Breast Cancer, N = 145,366, No. (%)	Incident Cancer in United States, %	Colorectal Cancer, N = 30,383, No. (%)	Incident Cancer in United States, %	Lung Cancer, N = 34,740, No. (%)	Incident Cancer in United States, %	Prostate Cancer, N = 32,231, No. (%)	Incident Cancer in United States, %
Race/ethnicity										
Non-Hispanic White	197,320 (81.3)	78.5	118,080 (81.2)	77.9	24,844 (81.8)	77.4	29,657 (85.4)	83.1	24,740 (76.7)	75.3%
Black	21,190 (8.7)	11.6	11,828 (8.1)	10.7	2445 (8.1)	11.4	2678 (7.7)	10.2	4239 (13.1)	14.3%
Hispanic	11,587 (4.8)	5.9	8043 (5.5)	7.0	1554 (5.1)	6.9	824 (2.4)	3.8	1166 (3.6)	6.1%
Asian/Pacific Islander	6880 (2.8)	2.6	4381 (3.0)	3.3	1045 (3.4)	3.1	921 (2.7)	2.2	533 (1.7)	1.9%
Native American	839 (0.3)	0.5	497 (0.3)	0.5	123 (0.4)	6.9	130 (0.4)	0.5	89 (0.3)	0.4%
Other	4904 (2.0)	0.9	2537 (1.7)	0.6	358 (1.2)	0.6	530 (1.5)	0.2	1479 (4.6)	2.0%
Age, y										
<65	160,789 (66.2)	55.8	113,519 (78.1)	55.8	19,589 (64.5)	38.3	16,786 (48.3)	32.0	10,895 (33.8)	37.5%
≥65	81,931 (33.8)	44.1	31,847 (21.9)	44.1	10,780 (35.5)	61.6	17,954 (51.7)	67.9	21,351 (66.2)	60.2%
Sex										
Female	174,110 (71.7)	49.2	145,366 (100.0)	100.0	13,161 (43.3)	48.4	15,551 (44.8)	46.2	0 (0.0)	N/A
Male	68,610 (28.3)	50.7	0 (0.0)	0.0	17,208 (56.7)	51.6	19,189 (55.2)	53.7	32,246 (100.0)	100.00%

Abbreviation: US, United States.

Figure 1. (A) Comparison of proportion of clinical trial enrollment versus proportion of cancer incidence by race/ethnicity for breast cancer trials. (B) Comparison of proportion of clinical trial enrollment versus proportion of cancer incidence by race/ethnicity for colorectal cancer trials. (C) Comparison of proportion of clinical trial enrollment versus proportion of cancer incidence by race/ethnicity for lung cancer trials. (D) Comparison of proportion of clinical trial enrollment versus proportion of cancer incidence by race/ethnicity for prostate cancer trials. Orange indicates proportion of patients with incident cancer. Blue indicates proportion of patients enrolled.

2019, were included. We selected these 4 diseases based on the prior publication and because they remain among the 4 most common diseases for men and women.[14,15] We recoded patients as female (<40 patients) in prostate cancer clinical trials because it was unclear if this was an error in recording or transgender. We included all patients over the age of 18 who participated in a clinical trial. Pediatric trials were excluded from the analysis. We included trials that completed participation and that are currently accruing patients. All phases of trials were included (ie, phase 1, phase 2, and phase 3). Because some trials were categorized as phase 1/2 and 2/3, we did not differentiate between phases in our analysis. Therapeutic modality such as chemotherapy, radiation, or surgery is not recorded in the database, and therefore we were unable to perform a subanalysis.

Designation of race and ethnicity was coded within the database provided by the NCI. For data from 2000 to 2001, the Cancer Therapy Evaluation Program (CTEP) assigned trial participants as White, Black, Asian/Pacific Islander, American Indian/Alaskan Native, or Hispanic. In 2002, CTEP changed their coding to include both race and ethnicity separately. Therefore, we created 5 mutually exclusive groups, non-Hispanic White, Black, Asian/Pacific Islander, American Indian/Alaska Native, multiracial/other, and Hispanic (any race).[3] For age, we categorized patients as older than 65 and younger than 65 as described in Duma et al.[8] Last, for sex, patients were listed as male or female in the database.

Statistical Analysis

We defined enrollment fraction as described by Murthy et al[3] as the number of trial enrollees divided by the proportion of United States incident cancer cases in each subgroup to define whether or not subgroups were underrepresented. We thus aimed to assess the relationship between enrollment fraction among various racial/ethnic, age, and sex groups in the years 2015 to 2019 and performed Pearson's χ^2 of independence. To assess differences, we calculated crude odds ratio (OR) and 95% confidence interval (CI) for each subgroup. The non-Hispanic White group was treated as the reference population.

We performed multivariable logistic regression analysis for each cancer type to determine the odds of participating in a clinical trial in 2015 to 2019 compared to 2000 to 2004. We adjusted for age, sex, and race/ethnicity. We performed a sensitivity analysis involving only phase 3 clinical trials with greater than 100 participants, which confirmed the findings of this study.

The statistical analysis was performed using IBM SPSS Version 27 and R version 3.6.1 using the "epitools" package.

RESULTS

When all cancer types were included, the final cohort for baseline characteristics of patients totaled 242,720 participants, including 197,320 non-Hispanic White patients (81.3%), 21,190 Black patients (8.7%), 11,587 Hispanic patients (4.8%), 6880 Asian/Pacific Islander patients (2.8%), 839 American Indian/Alaska Native patients (0.30%), and 3094 other patients (2.0%). A majority of patients were less than 65 years old (160,789; 66.2%) likely secondary to the large number of patients who were represented from breast cancer clinical trials. The median age and interquartile range for each organ system included breast (median age, 56 years; interquartile range [IQR], 48-64 years), colorectal (median age, 60 years; IQR, 52-68 years), lung (median age, 65 years; IQR, 58-71 years), and prostate (median age, 68 years; IQR, 62-74 years). A majority of patients were female (173,110; 71.7%) versus male (68,610; 28.3%) (Table 1). Minority group participation in clinical trials is compared to their respective cancer incidence in 5-year intervals in Figure 1.

When comparing clinical trial participation from 2015 to 2019 to the proportion of cancer incidence from 2015 to 2017 of non-Hispanic White patients to minorities for breast cancer, Black (OR, 1.75; 95% CI, 1.67-1.83; $P < .001$) and Hispanic (OR, 1.19; 95% CI, 1.12-1.25; $P < .001$) patients were more likely to participate in a clinical trials (Table 2). For colorectal cancer trials, Black (OR, 0.58; 95% CI, 0.50-0.67; $P < .001$) and Hispanic (OR, 0.74; 95% CI, 0.64-0.87; $P < .001$) patients were underrepresented. For lung cancer trials, Black (OR, 0.83; 95% CI, 0.76-0.91; $P < .001$) and Hispanic (OR, 0.66; 95% CI, 0.57-0.77; $P < .001$) patients were underrepresented. Last, for prostate cancer trials, Blacks (OR, 0.58; 95% CI, 0.51-0.66; $P < .001$) and Hispanic (OR, 0.85; 95% CI, 0.79-0.92; $P < .001$) participants were underrepresented.

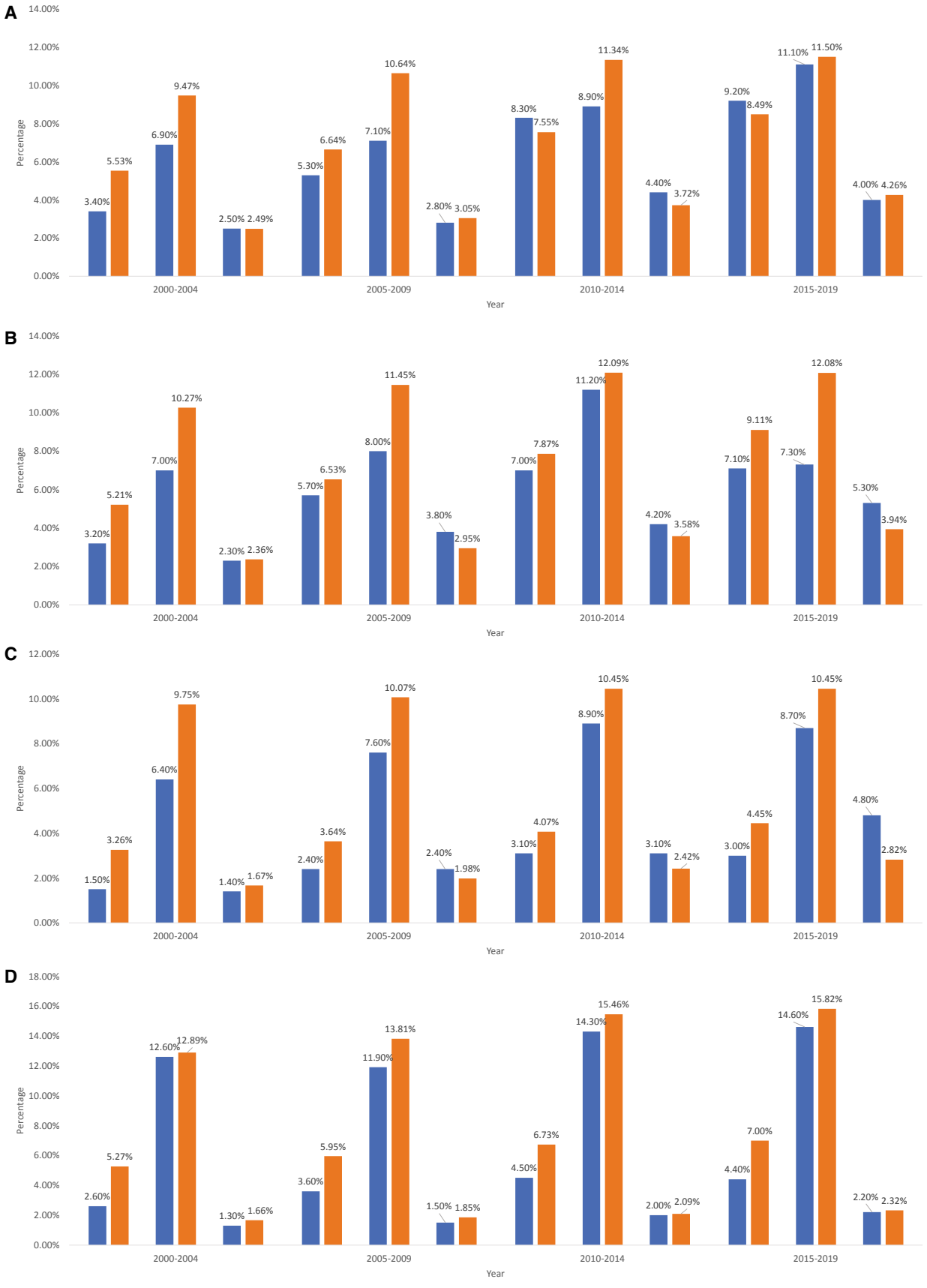
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TABLE 2. Trial Enrollment for Minorities Versus Non-Hispanic White for Breast, Colorectal, Lung, and Prostate Cancer Trials, 2015-2019

Cancer Type	Race/Ethnicity	No. of Trial Participants	Enrollment Fraction[a]	OR (95% CI)	*P*
Breast	Non-Hispanic White	12,159	2.18%	Referent	
	Black	2183	2.53%	1.75 (1.67-1.83)	<.001
	Hispanic	1646	2.58%	1.19 (1.12-1.25)	<.001
	Asian/Pacific Islander	691	2.16%	0.99 (0.91-1.07)	.846
	American Indian/Alaska Native	87	2.14%	0.96 (0.77-1.19)	.739
Colorectal	Non-Hispanic White	1969	0.63%	Referent	
	Black	190	0.36%	0.58 (0.50-0.67)	<.001
	Hispanic	184	0.47%	0.74 (0.64-0.87)	<.001
	Asian/Pacific Islander	136	0.81%	1.28 (1.07-1.52)	<.001
	American Indian/Alaska Native	25	0.80%	1.27 (0.86-1.89)	<.001
Lung	Non-Hispanic White	5175	0.95%	Referent	
	Black	559	0.80%	0.83 (0.76-0.91)	<.001
	Hispanic	190	0.64%	0.66 (0.57-0.77)	<.001
	Asian/Pacific Islander	307	1.63%	1.72 (1.53-1.93)	<.001
	American Indian/Alaska Native	34	0.86%	0.90 (0.64-1.27)	.565
Prostate	Non-Hispanic White	4160	0.98%	Referent	
	Black	792	0.84%	0.85 (0.79-0.92)	<.001
	Hispanic	240	0.57%	0.58 (0.51-0.66)	<.001
	Asian/Pacific Islander	119	0.86%	0.87 (0.72-1.04)	.148
	American Indian/Alaska Native	15	0.60%	0.61 (0.36-1.01)	.057

Abbreviations: CI, confidence interval; OR, odds ratio.
[a]Defined as patients enrolled in trials/total cancer incidence for corresponding years.

TABLE 3. Trial Enrollment Fraction for Elderly Versus Nonelderly Cancer for Breast, Colorectal, Lung, and Prostate Cancer Trials, 2015-2019

Age, y	No. of Trial Participants	Enrollment Fraction[a]	OR (95% CI)	*P*
Breast cancer				
<65	13,772	3.42%	Referent	
≥65	3352	0.95%	0.27 (0.26-0.28)	<.001
Colorectal cancer				
<65	1761	0.95%	Referent	
≥65	826	0.34%	0.36 (0.33-0.39)	<.001
Lung cancer				
<65	2703	1.33%	Referent	
≥65	3727	0.80%	0.59 (0.56-0.62)	<.001
Prostate cancer				
<65	1551	0.65%	Referent	
≥65	3888	1.07%	1.64 (1.55-1.74)	<.001

Abbreviations: CI, confidence interval; OR, odds ratio.
[a]Defined as patients enrolled in trials/total cancer incidence for corresponding years.

When comparing clinical trial participation from 2015 to 2019 of elderly and nonelderly patients to proportion of cancer incidence from 2015 to 2017 for breast cancer, patients older than 65 were underrepresented (OR, 0.27; 95% CI, 0.27-0.28; $P < .001$) (Table 3). For colorectal cancer trials, patients older than 65 were underrepresented (OR, 0.36; 95% CI, 0.33-0.39; $P < .001$). For lung cancer trials, patients older than 65 were less likely to participate (OR, 0.59; 95% CI, 0.56-0.62; $P < .001$).

When comparing clinical trial participation from 2015 to 2019 of female and male patients to proportion of cancer incidence from 2015 to 2017 for colorectal cancer, women were underrepresented (OR, 0.73; 95% CI, 0.67-0.79; $P < .001$) (Table 4). For lung cancer clinical trials, women were underrepresented compared to men (OR, 0.89; 95% CI, 0.83-0.93; $P < .001$).

We performed multivariable logistic regression analysis comparing the years 2000 to 2004 to 2015 to 2019 and adjusting for sex, age, and race/ethnicity (Table 5). For breast cancer, there was an increase in participation of Black patients (OR, 2.19; 95% CI, 2.07-2.32; $P < .001$), Hispanic patients (OR, 3.32; 95% CI, 3.09-3.56; $P < .001$), and Asian/Pacific Islander patients (OR, 1.94; 95% CI, 1.76-2.13; $P < .001$). For colorectal cancer,

TABLE 4. Trial Enrollment Fraction According for Sex for Colorectal and Lung Cancer Trials, 2015-2019

Sex	No. of Trial Participants	Enrollment Fraction[a]	OR (95% CI)	*P*
Colorectal cancer				
Male	1556	0.69%	Referent	
Female	1031	0.50%	0.73 (0.67-0.79)	<.001
Lung cancer				
Male	3507	1.08%	Referent	
Female	2923	0.84%	0.89 (0.84-0.93)	<.001

Abbreviations: CI, confidence interval; OR, odds ratio.
[a]Defined as patients enrolled in trials/total cancer incidence for corresponding years.

TABLE 5. Multivariable Logistic Regression[a] for Trial Enrollment Comparing 2000-2004 Versus 2015-2019

Characteristic	Breast, OR (95% CI)	*P*	Colorectal, OR (95% CI)	*P*	Lung, OR (95% CI)	*P*	Prostate, OR (95% CI)	*P*
Race/ethnicity								
Non-Hispanic White	Referent		Referent		Referent		Referent	
Black	2.19 (2.07-2.32)	<.001	1.15 (0.97-1.36)	.096	1.54 (1.38-1.73)	<.001	1.14 (1.04-1.26)	<.001
Hispanic	3.32 (3.09-3.56)	<.001	2.46 (2.04-2.96)	<.001	2.21 (1.80-2.71)	<.001	1.70 (1.42-2.04)	.005
Asian/Pacific Islander	1.94 (1.76-2.13)	<.001	2.48 (2.00-3.08)	<.001	3.88 (3.20-4.69)	<.001	1.64 (1.27-2.11)	<.001
American Indian/Alaska Native	2.28 (1.73-2.99)	<.001	3.92 (2.29-6.72)	<.001	2.03 (1.27-3.25)	.003	1.00 (0.53-1.88)	<.001
Other	1.59 (1.42-1.77)	<.001	4.26 (3.15-5.77)	<.001	2.12 (1.71- 2.64)	<.001	0.24 (0.20-0.30)	<.001
Age, y								
<65	Referent		Referent		Referent		Referent	
≥65	0.98 (0.94-1.03)	.548	0.71 (0.64-0.77)	<.001	1.38 (1.29-1.47)	<.001	1.15 (1.07-1.24)	<.001
Sex								
Female	N/A		0.89 (0.81-0.97)	.012	1.17 (1.10-1.24)	<.001	N/A	
Male			Referent		Referent			

Abbreviations: CI, confidence interval; N/A, not applicable; OR, odds ratio.
[a]Multivariable model adjusts for age, sex, and race/ethnicity.

there was no change in participation of Black patients (OR, 1.15; 95% CI, 0.97-1.36%, $P = .096$) whereas Hispanic participation increased (OR, 2.46; 95% CI, 2.04-2.96; $P < .001$) and there was also an increase in Asian/Pacific Islander patient participation (OR, 2.48; 95% CI, 2.00-3.08; $P < .001$). In recent years, patients older than 65 (OR, 0.71; 95% CI, 0.64-0.77; $P < .001$) and women (OR, 0.89; 95% CI, 0.81-0.97%, $P = .012$) were less likely to participate in a colorectal cancer clinical trial. For lung cancer, there was an increase in participation of Black patients (OR, 1.54; 95% CI, 1.38-1.73; $P < .001$), Hispanic patients (OR, 2.21; 95% CI, 1.80-2.71; $P < .001$), and Asian/Pacific Islander patients (OR, 3.88; 95% 3.2-4.69; $P < .001$). Elderly participation (OR, 1.38; 95% CI, 1.29-1.47; $P < .001$) as well as female participation (OR, 1.17; 95% CI, 1.10-1.24; $P < .001$) increased in lung cancer trials. For prostate cancer, there was an increase in participation of Black patients (OR, 1.14; 95% CI, 1.04-1.26; $P < .001$), Hispanic patients (OR, 1.70; 95% CI, 1.42-2.04%, $P = .005$), and Asian/Pacific Islander patients (OR, 1.64; 95% CI, 1.27-2.11; $P < .001$). Participation of elderly patients increased in recent years (OR, 1.15; 95% CI, 1.07-1.24; $P < .001$).

DISCUSSION

In this study, we present an analysis of 20 years of clinical trial participation data that includes nearly a quarter million patients participating in 766 clinical trials. We found that Black and Hispanic participants were underrepresented in colorectal, lung, and prostate cancer trials. Elderly patients were underrepresented in breast, colorectal, and lung cancer trials, and women were underrepresented in colorectal and lung cancer trials. We found that compared to earlier years, Hispanic and Black patients were more likely to participate in breast, lung, and prostate cancer trials in recent years. Additionally, women were less likely to participate in a colorectal cancer trial and more likely to participate in a lung cancer trial. Last, we identified that the change in elderly participation varied by cancer type.

Although some studies have indicated a lack of participation of minorities, women, and the elderly in clinical trials, this study is the first to indicate that some participation disparities are improving.[8,16] However, disparities still exist, and it remains essential that all investigators involved with clinical trials seek to diversify their participation because such efforts will further benefit patients and enhance the credibility of these studies.

The NIH Revitalization Act initially passed in 1993 mandated that minorities and women be appropriately included in all NIH-funded research. Since that time, studies have shown the persistently low participation of minorities in clinical trials.[3,8,16] Initially reported in 2004, Murthy et al[3] evaluated 75,215 patients from 1996 to 2002 who participated in NCI-sponsored cooperative group trials. The authors noted that Black patients were less likely to enroll in any clinical trial, and Hispanic and Black patients had lower enrollment fractions. Reported in 2017, Duma et al[8] evaluated 55,689 patients from 2003 to 2016. The authors noted that Black and Hispanic patients were less likely to be enrolled in clinical trials. The major limitation of this study was that the authors based their findings on published results for trials that accrued for several years. In nearly 2 decades, no study has had access to, or evaluated, clinical trial participation data similar to that of Murthy et al.[3] In this study of patients from 2000 to 2019, we evaluated 242,720 patients and found that Black and Hispanic participants were not well-represented, but their participation has increased over time.

The participation of Asian/Pacific Islander patients increased for each cancer-specific diagnosis compared to earlier years and was well-represented for all cancer diagnoses. Because of the overall small number of patients who were American Indian/Alaska Native or other/multiracial, limited conclusions can be drawn from these data. These findings indicate the importance of cancer-specific statistics for clinical trial participation for reaching a broad community of patients and researchers.[8]

The recruitment of minorities into clinical trials has shown to be particularly successful for Black women with breast cancer using the Heiney-Adams Recruitment Framework.[17] This framework focuses on social media marketing and relationship building. Other studies have suggested patient navigation as one approach to enhance the diversity of accrual to cancer clinical trials.[18,19] Innovative strategies include partnership with community and patients before protocol development, hiring research staff from the community, and involvement of primary care practices. Moreover, recruitment of bilingual staff and culturally sensitive material have also shown to be effective in improving clinical trial participation.[5,20] Additional efforts are needed to identify successful strategies for minority recruitment.

The participation of women in clinical trials has been studied in previous reports, and women are consistently underrepresented in clinical trials.[8,21] Our study is among the first to show that female participation in clinical trials has improved since the early 2000s. Duma et al[8] showed that when reviewing clinical trials from 2003 to 2016, there were 11,723 patients with lung cancer over the study period and 39.0% (n = 4571) were female. Notably, the authors did not compare years of participation or breakdown participation on an annual basis. In our study, 34,740 (48.4%) patients were female, and we demonstrated that the participation of women in lung cancer clinical trials increased when comparing years 2000 to 2004 to 2015 to 2019 (OR, 1.38; 95% CI, 1.29-1.47; $P < .001$). However, women overall were still underrepresented despite improvements (OR, 0.89; 95% CI, 0.84-0.83; $P < .001$). We identified similar underrepresentation in colorectal cancer trials. Strategies for recruiting women into trials have varied, and to increase participation, some studies have pointed toward web-based registration of patients as well as patient education and community outreach directed toward women.[22]

Finally, the participation of patients over the age of 65 according to most studies has declined over time. Ludmir et al[7] reviewed completed clinical trials for breast, colorectal, lung, and prostate cancer from 1994 to 2015, which cumulatively accounted for 262,354 patients. The authors identified significant differences between the median of the trial participants the population median age of the disease site.[7] Duma et al[8] found similar results, with elderly patients being underrepresented across all 4 cancers. Similar to both studies, we did identify disparities for age of participation. Notably, older patients were unrepresented for breast, colorectal, and lung cancer. The participation of elderly patients in clinical trials is complex because many may not be eligible because of associated toxicities.[6] Thus, it remains critical to develop therapies with minimal toxicity as therapeutics may not benefit the majority age group of these diseases.

Study Limitations

Our study is not without limitations. One of the notable limitations of this study is that we did not include industry-sponsored clinical trial data, and we only characterized NCI-sponsored cooperative group clinical trials. Industry clinical trials continue to make up an increasing percentage of clinical trials with estimates of 36% from 2000 to 2019.[23] However, there is a lack of uniform reporting measures, and these data are not recorded by the NCI. Not all industry trials publish their results if they fail to accrue and do not publish year-to-year data. Currently, there is no accurate way to study trends in patient participation for industry trials over time. Previous studies have either cumulatively counted patients over decades or assigned patients who accrued for several

years in their final year of participation.[5,6] Furthermore, regulatory measures are needed to address the reporting of industry-related clinical trials.[3] Another limitation of our study is that we could not account for errors in the coding of race/ethnicity, age, and sex. Last, we could not evaluate modality of treatment, such as chemotherapy and surgery, because of limitations of the data set. Surgical clinical trials have not been studied in depth in the literature, and further study is required.

In conclusion, in this analysis of 20 years of clinical trials, Black and Hispanic patients remain underrepresented, however, when compared to earlier trials, their participation has increased. We also found that women and the elderly remain underrepresented in clinical trials. Our findings indicate a need for further study into successful recruitment strategies of these underrepresented populations.

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AUTHOR CONTRIBUTIONS

Juan Javier-DesLoges: Conceptualization, data curation, formal analysis, investigation, methodology, writing–original draft, and writing–review and editing. **Tyler Nelson:** Data curation. **James Murphy:** Writing–review and editing. **Rana R. McKay:** Writing–review and editing. **Elizabeth Pan:** Writing – review and editing. **J. Kellogg Parsons:** Writing–review and editing. **Christopher J. Kane:** Writing–review and editing. **Karim Kader:** Writing–review and editing. **Jesse Nodora:** Writing–review and editing. **Ithaar H. Derweesh:** Writing–review and editing. **Sandip P. Patel:** Writing–review and editing. **Elena Maria Martinez:** Writing–review and editing. **Brent S. Rose:** Conceptualization, project administration, resources, supervision.

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