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Disparities and Trends in the Participation of Minorities, Women and the Elderly of Breast, Colorectal, Lung and Prostate Cancer Clinical Trials

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Precis: Minority, women, and the elderly remain underrepresented in clinical trials in recent years. However, some minority participation has increased in recent years.

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Abstract:

Background: 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. We evaluated patients in breast, colorectal, lung, and prostate cancer trials between 2000-2019. We determined the representation in a trial by race/ethnicity, sex, and age. Secondarily, we evaluated the change in trial participation by multivariable analysis by comparing years 2000-2004 to 2015-2019.

Results: The cohort included 242,720 participants, 197,320 (81.3%) Non-Hispanic White, 21,190 (8.7%) Black, 11,587 (4.8%), and Hispanic, 6,880 (2.8%). Black and Hispanic patients were underrepresented for colorectal [Odds Ratio (OR) 0.58, 95% Confidence Interval (CI) 0.50-0.67, p<0.001] and (OR 0.74, 95%CI 0.64-0.87, p<0.001) respectively, lung (OR 0.83, 95% CI 0.76-0.91, p<0.001), and (0.66, 95% CI 0.57-0.77, p<0.001) respectively, and prostate cancer trials (OR 0.85, 95% CI 0.79-0.92, p<0.001) and (OR 0.58, 95% CI 0.51-0.66, p<0.001) between 2015-2019. The odds of participation in 2015-2019 increased among Black patients in breast (OR 2.19, 95% CI 2.07-2.32, p<0.001], lung (OR 1.54, 95%CI 1.38-1.73, p<0.001), and prostate cancer trials (OR 1.14, 95% CI 1.04-1.26, p<0.001). The odds of participation in a trial among

Hispanic patients increased for breast (OR 3.32, 95% CI 3.09-3.56, p<0.001), colorectal (OR 2.46, 95% CI 2.04-2.96, p<0.001), lung (OR 3.88, 95%CI 3.20-4.69, p<0.001), and prostate cancer (OR 1.70, 95%CI 1.42-2.04, p=0.005).

Conclusions: In this study, we identified that Blacks and Hispanic patients remain underrepresented in trials, but in recent years participation increased. These findings indicate that minority participation has increased over time but that further efforts are needed.

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 two 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 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 1996-2002. The authors compared trials in 1996-1999 to 2000-2002 and identified that that in later years racial/ethnic minorities, women, and elderly, were less likely to enroll in trials when compared to whites, males, and patients who are younger in earlier years. Since, 2004 there have been two 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 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 2015-2019 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.

Methods

Data collection

This study followed the STROBE 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 – 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 the 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 (SEER) Program [12] combined with the CDC's National Program of Cancer Registries (NPCR) [13]. These statistics provide information on proportion of incident cancers and cover 100% of United States population [9] [12]. No institutional review board approval was required from our home institution (UC San Diego) and was therefore waived. Informed consent was waived 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, 2019 were included. We selected these four diseases based on the prior publication and because they remain amongst the four most common diseases for men and women [15]. We recoded patients as female (<40 patients) in prostate cancer clinical trials as 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, Phase I, Phase II, and Phase III. As some trials were categorized as Phase I/II and II/III 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 2000-2001 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]. Lastly, for sex patients were listed as male or female in the database.

Statistical Analysis

We defined enrollment fraction as described by Murthy et al. as the number of trial enrollees divided by the proportion of U.S. incident cancer cases in each subgroup in order 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 year 2015-2019 and performed Pearson's χ^2 of independence. To assess differences, we calculated crude odds ratios and 95% confidence interval for each subgroup. The Non-Hispanic White group was treated as the reference population.

We performed multivariable logistic regression analysis for each cancer type in order to determine the odds of participating in a clinical trial in 2015-2019 compared to 2000-2004. We adjusted for age, sex, and race/ethnicity. We performed a sensitivity analysis involving only Phase III 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 242,720 participants, including 197,320 (81.3%) Non-Hispanic White patients, 21,190 (8.7%) Black patients, 11,587 (4.8%) Hispanic patients, 6,880 (2.8%) Asian/Pacific Islander patients, 839 (0.30%) American Indian/Alaska Native patients, and 3,094 (2.0%) Other. Most patients were < 65 years old, 160,789 (66.2%) compared to patients ≤ 65 , 81,931 (33.8%) likely secondary to the large number of breast cancer patients. The median age and interquartile range for each organ system were the following, breast (median age 56, IQR: 48-6), colorectal (median age 60, IQR: 52-68),

lung (median age 65, IQR 58-71), and prostate (median age 68: IQR: 62-74). A majority of patients were female, 173,110 (71.7%) vs. 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 2015-2019 to proportion of cancer incidence 2015-2017 of non-Hispanic White patients to minorities for breast cancer, Black and Hispanic patients were more likely to participate in a clinical trials (OR 1.75, 95% CI 1.67-1.83, p<0.001), and (OR 1.19, 95%CI 1.12-1.25, p<0.001) (Table 2). For colorectal cancer trials, Black and Hispanic patients were underrepresented, (OR 0.58, 95% CI 0.50-0.67, p<0.001) and (OR 0.74, 95% CI 0.64-0.87, p<0.001). For lung cancer trials, Black and Hispanic patients were underrepresented (OR 0.83, 95% CI 0.76-0.91, p<0.001) and (OR 0.66, 95% CI 0.57-0.77, p<0.001) respectively. Lastly, for prostate cancer trials, Blacks and Hispanic participants were underrepresented (OR 0.58, 95% CI 0.51-0.66, p<0.001) and (OR 0.85, 95% CI 0.79-0.92, p<0.001).

When comparing clinical trial participation from 2015-2019 of elderly and non-elderly patients to proportion of cancer incidence 2015-2017 for breast cancer, patients older than 65 were underrepresented (OR 0.27, 95% CI 0.27-0.28, p<0.001) (Table 3). For colorectal cancer trial, patients older than 65 were underrepresented (OR 0.36, 95% CI 0.33-0.39, p<0.001). For lung cancer trials, patients older than 65 were less likely to participate in a trial (OR 0.59, 95% CI 0.56-0.62, p<0.001).

When comparing clinical trial participation from 2015-2019 of female and male patients to proportion of cancer incidence 2015-2017 for colorectal cancer, women were underrepresented (OR 0.73, 95% CI 0.67-0.79, p<0.001) (Table 4). For lung cancer clinical trials, women were underrepresented compared to men (OR 0.89, 95%CI 0.83-0.93, p<0.001).

We performed multivariable logistic regression analysis comparing the years 2000-2004 to 2015-2019 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<0.001), Hispanic patients (OR 3.32, 95% CI 3.09-3.56, p<0.001), Asian/Pacific Islander patients (OR 1.94, 95%CI 1.76-2.13, p<0.001). For colorectal

cancer, there was no change in participation of Black patients (OR 1.15, 95% CI 0.97-1.36, p=0.096) while Hispanic participation increased (OR 2.46, 95% CI 2.04-2.96, p<0.001) and there was also an increase in Asian/Pacific Islander patient participation (OR 2.48, 95% CI 2.00-3.08, p<0.001). Patients older than 65 were less likely to participate in a colorectal cancer clinical trial in recent years (OR 0.71, 95% CI 0.64-0.77, p<0.001) as well as women (OR 0.89, 95% CI 0.81-0.97, p=0.012). For lung cancer, there was an increase in participation of Black patients (OR 1.54, 95% CI 1.38-1.73, p<0.001), Hispanic patients (OR 2.21, 1.80-2.71, p<0.001), Asian/Pacific Islander patients (OR 3.88, 95% 3.2-4.69, p<0.001). Elderly participation increased in lung cancer trials (OR 1.38, 95% CI 1.29-1.47, p<0.001) as well as female participation (OR 1.17, 95% CI 1.10-1.24, p<0.001). Lastly for prostate cancer, there was an increase in participation of Black patients (OR 1.14, 95% CI 1.04-1.26, p<0.001) and Hispanic patients (OR 1.70, 95% CI 1.42-2.04, p=0.005), and Asian/Pacific Islander patients (OR 1.64, 95% CI 1.27-2.11, p<0.001). Participation of elderly patients increased in recent years (OR 1.15, 95% CI 1.07-1.24, p<0.001).

Discussion

In this study, we present an analysis of 20 years of clinical trial participation data, which includes nearly a 1/4 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. Lastly, we identified that the change in elderly participation varied by cancer type.

While 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 as 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 evaluated 75,215 patients from 1996-2002 who participated in NCI-sponsored cooperative group trials, the authors noted that Black patients were less likely to enroll in any clinical trial and that Hispanic and Black patients had lower enrollment fractions. Later reported in 2017, Duma et al. evaluated 55,689 patients from 2003-2016, 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 off of published results for trials that accrued for several years. In nearly two decades, no study has had access to or evaluated clinical trial participation data similar to that of Murthy et al. In this study of patients from 2000-2019, 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 were well represented for all cancer diagnoses. Due to 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 prior to 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 amongst the first to show that female participation in clinical trials has improved since the early 2000s. Duma et al. showed that when reviewing clinical trials from 2003-2016, there were 11,723 patients with lung cancer over the study period and 39.0% (n= 4,571) were female. Of note the authors did not compare years of participation or breakdown participation on an annual basis. In our study of 34,740, (48.4%) of patients were female we demonstrated that the participation of women in lung cancer clinical trials increased when comparing years 2000-2004 to 2015-2019 (OR 1.38, 95% CI 1.29-1.47, $p<0.001$). However, women overall were still underrepresented despite improvements (0.89, 95% CI 0.84-0.83, $p<0.001$). We identified similar underrepresentation in colorectal cancer trials. Strategies for recruiting women into trials have varied, and some studies have pointed towards web-based registration of patients as well as patient education and community outreach directed towards women to increase participation [22].

Finally, the participation of patients over the age of 65 according to most studies has declined over time. Ludmir et al. reviewed completed clinical trials for breast, colorectal, lung and prostate cancer from 1994-2015, which cumulatively accounted for 262,354. The authors identified significant differences between the median of the trial participants the population median age of the disease site [7]. Duma et. al found similar results, with elderly patients being underrepresented across all four 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 as many may not be eligible due to 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 we did not include industry sponsored clinical trial data and 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 2000-2019 [23].

However, there is a lack of uniform reporting measures and this data is 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]. Further, 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/sex. Lastly, we could not evaluate modality of treatment such as chemotherapy and surgery due to limitations of the dataset. Surgical clinical trials have not been studied in depth in the literature and further study is required.

Conclusion

In conclusion, in this analysis of 20 years of clinical trials, Black and Hispanic patients remain underrepresented but 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.

1. NOT-OD-18-014: Revision: NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research. Accessed February 5, 2021. https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-014.html
2. NCI Community Oncology Research Program (NCORP). Accessed February 5, 2021. https://ncorp.cancer.gov/

3. Murthy VH, Krumholz HM, Gross CP. Participation in cancer clinical trials: race-, sex-, and age-based disparities. *JAMA*. 2004;291(22):2720-2726. doi:10.1001/jama.291.22.2720
4. Kwiatkowski K, Coe K, Bailar JC, Swanson GM. Inclusion of minorities and women in cancer clinical trials, a decade later: Have we improved? *Cancer*. 2013;119(16):2956-2963. doi:https://doi.org/10.1002/cncr.28168
5. Heller C, Balls-Berry JE, Nery JD, et al. Strategies addressing barriers to clinical trial enrollment of underrepresented populations: A systematic review. *Contemp Clin Trials*. 2014;39(2):169-182. doi:10.1016/j.cct.2014.08.004
6. Lewis JH, Kilgore ML, Goldman DP, et al. Participation of patients 65 years of age or older in cancer clinical trials. *J Clin Oncol Off J Am Soc Clin Oncol*. 2003;21(7):1383-1389. doi:10.1200/JCO.2003.08.010
7. Ludmir EB, Mainwaring W, Lin TA, et al. Factors Associated With Age Disparities Among Cancer Clinical Trial Participants. *JAMA Oncol*. 2019;5(12):1769. doi:10.1001/jamaoncol.2019.2055
8. Duma N, Vera Aguilera J, Paludo J, et al. Representation of Minorities and Women in Oncology Clinical Trials: Review of the Past 14 Years. *J Oncol Pract*. 2017;14(1):e1-e10. doi:10.1200/JOP.2017.025288
9. Act (FOIA) F of I. FOIA.gov (Freedom of Information Act) Home Page. Accessed March 30, 2021. https://www.foia.gov/
10. NCI's National Clinical Trials Network (NCTN) - National Cancer Institute. Published May 29, 2014. Accessed March 30, 2021. https://www.cancer.gov/research/infrastructure/clinical-trials/nctn
11. United States Cancer Statistics | Cancer | CDC. Published March 10, 2021. Accessed April 8, 2021. https://www.cdc.gov/cancer/uscs/index.htm
12. SEER Incidence Data, 1975 - 2017. Accessed March 30, 2021. https://seer.cancer.gov/data/
13. National Program of Cancer Registries (NPCR) | CDC. Published March 31, 2021. Accessed April 8, 2021. https://www.cdc.gov/cancer/npcr/index.htm

14. Henley SJ, Singh SD, King J, Wilson RJ, O'Neil ME, Ryerson AB. Invasive Cancer Incidence and Survival - United States, 2013. *MMWR Morb Mortal Wkly Rep*. 2017;66(3):69-75. doi:10.15585/mmwr.mm6603a1
15. Common Cancer Types - National Cancer Institute. Published April 21, 2015. Accessed March 30, 2021. https://www.cancer.gov/types/common-cancers
16. Chen MS, Lara PN, Dang JHT, Paterniti DA, Kelly K. Twenty years post-NIH Revitalization Act: enhancing minority participation in clinical trials (EMPaCT): laying the groundwork for improving minority clinical trial accrual: renewing the case for enhancing minority participation in cancer clinical trials. *Cancer*. 2014;120 Suppl 7:1091-1096. doi:10.1002/cncr.28575
17. Heiney SP, Adams SA, Wells LM, Johnson H. Evaluation of Conceptual Framework for Recruitment of African American Patients With Breast Cancer. *Oncol Nurs Forum*. 2010;37(3):E160-E167. doi:10.1188/10.ONF.E160-E167
18. Ghebre RG, Jones LA, Wenzel J, Martin MY, Durant R, Ford JG. State-of-the-Science of Patient Navigation as a Strategy for Enhancing Minority Clinical Trial Accrual. *Cancer*. 2014;120(0 7):1122-1130. doi:10.1002/cncr.28570
19. McCaskill-Stevens W, Pinto H, Marcus AC, et al. Recruiting minority cancer patients into cancer clinical trials: a pilot project involving the Eastern Cooperative Oncology Group and the National Medical Association. *J Clin Oncol Off J Am Soc Clin Oncol*. 1999;17(3):1029-1039. doi:10.1200/JCO.1999.17.3.1029
20. Javier-DesLoges JF, Segal D, Khan A, et al. Urology Residency Training in Medically Underserved Areas through the Integration of a Federally Qualified Health Center Rotation. *Urology*. Published online January 6, 2021. doi:10.1016/j.urology.2020.11.057
21. Ramasubbu K, Gurm H, Litaker D. Gender bias in clinical trials: do double standards still apply? *J Womens Health Gend Based Med*. 2001;10(8):757-764. doi:10.1089/15246090152636514
22. Rivers DA, Pal T, Vadaparampil ST, Adams LA, Dash-Pitts L, Quinn GP. A community-academic partnership to explore informational needs of African American women as a primer for cancer clinical trial recruitment. *Ethn Health*. 2019;24(6):679-693. doi:10.1080/13557858.2017.1367762

23. Gresham G, Meinert JL, Gresham AG, Meinert CL. Assessment of Trends in the Design, Accrual, and Completion of Trials Registered in ClinicalTrials.gov by Sponsor Type, 2000-2019. *JAMA Netw Open*. 2020;3(8):e2014682. doi:10.1001/jamanetworkopen.2020.14682

Characteristic	All Cancers N=242,720	Percent Incident Cancer in U.S.	Breast Cancer N=145,366	Percent Incident Cancer in U.S.	Colorectal Cancer N=30,383	Percent Incident Cancer in U.S.	Lung Cancer N=34,740	Percent Incident Cancer in U.S.	Prostate Cancer N=32,231	Percent Incident Cancer in U.S.
Race/ethnicity	No (%)	%	No (%)	%	No (%)	%	No (%)	%	No (%)	%
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%	2,445 (8.1%)	11.4%	2,678 (7.7%)	10.2%	4,239 (13.1%)	14.3%
Hispanic	11,587 (4.8%)	5.9%	8,043 (5.5%)	7.0%	1,554 (5.1%)	6.9%	824 (2.4%)	3.8%	1,166 (3.6%)	6.1%
Asian/Pacific Islander	6,880 (2.8%)	2.6%	4,381 (3.0%)	3.3%	1,045 (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	4,904 (2.0%)	0.9%	2,537 (1.7%)	0.6%	358 (1.2%)	0.6%	530 (1.5%)	0.2%	1,479 (4.6%)	2.0%
Age, years										
<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%	13,161	48.4%	15,551	46.2%	0 (0.0%)	N/A

			(100.0%)		(43.3%)		(44.8%)			
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%

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

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

Race/Ethnicity	No. of Trial Participants	Enrollment Fraction[1]	Odds Ratio (95% CI)	P value
	Breast Cancer			
Non-Hispanic White	12,159	2.18%	Referent	
Black	2,183	2.53%	1.75 (1.67-1.83)	<0.001
Hispanic	1,646	2.58%	1.19 (1.12-1.25)	<0.001
Asian/Pacific Islander	691	2.16%	0.99 (0.91-1.07)	0.846
American Indian/Alaska Native	87	2.14%	0.96 (0.77-1.19)	0.739
	Colorectal Cancer			
Non-Hispanic White	1,969	0.63%	Referent	
Black	190	0.36%	0.58 (0.50-0.67)	<0.001
Hispanic	184	0.47%	0.74 (0.64-0.87)	<0.001
Asian/Pacific Islander	136	0.81%	1.28 (1.07-1.52)	<0.001
American Indian/Alaska Native	25	0.80%	1.27 (0.86-1.89)	<0.001

	Lung Cancer			
Non-Hispanic White	5,175	0.95%	Referent	
Black	559	0.80%	0.83 (0.76-0.91)	<0.001
Hispanic	190	0.64%	0.66 (0.57-0.77)	<0.001
Asian/Pacific Islander	307	1.63%	1.72 (1.53-1.93)	<0.001
American Indian/Alaska Native	34	0.86%	0.90 (0.64-1.27)	0.565
	Prostate Cancer			
Non-Hispanic White	4,160	0.98%	Referent	
Black	792	0.84%	0.85 (0.79-0.92)	<0.001
Hispanic	240	0.57%	0.58 (0.51-0.66)	<0.001
Asian/Pacific Islander	119	0.86%	0.87 (0.72-1.04)	0.148
American Indian/Alaska Native	15	0.60%	0.61 (0.36-1.01)	0.057

1. Enrollment Fraction – Defined as Patients Enrolled in Trials / Total Cancer Incidence for Corresponding Years

Table 3: Trial Enrollment Fraction for Elderly vs. Nonelderly Cancer for Breast, Colorectal, Lung, and Prostate Cancer Trials, 2015-2019

Age	No. of Trial Participants	Enrollment	Odds Ratio (95%	P value

		Fraction[1]	CI)	
Breast Cancer				
<65	13,772	3.42%	Referent	
>65	3,352	0.95%	0.27 (0.26-0.28)	<0.001
Colorectal Cancer				
<65	1,761	0.95%	Referent	
>65	826	0.34%	0.36 (0.33-0.39)	<0.001
Lung Cancer				
<65	2,703	1.33%	Referent	
>65	3,727	0.80%	0.59 (0.56-0.62)	<0.001
Prostate Cancer				
<65	1,551	0.65%	Referent	
>65	3,888	1.07%	1.64 (1.55-1.74)	<0.001

1. Enrollment Fraction – Defined as Patients Enrolled in Trials / Total Cancer Incidence for Corresponding Years

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

Sex	No. of Trial Participants	Enrollment Fraction[1]	Odds Ratio (95% CI)	P value
Colorectal Cancer				
Male	1,556	0.69%	Referent	
Female	1,031	0.50%	0.73 (0.67-0.79)	<0.001
Lung Cancer				
Male	3,507	1.08%	Referent	
Female	2,923	0.84%	0.89 (0.84-0.93)	<0.001

1. Enrollment Fraction – Defined as Patients Enrolled in Trials / Total Cancer Incidence for Corresponding Years

Table 5: Multivariable Logistic Regression[1] for Trial Enrollment Comparing 2000-2004 vs. 2015-2019

Characteristic	Breast	P value	Colorectal	P value	Lung	P value	Prostate	P value
Race/Ethnicity	OR (95% CI)		OR (95% CI)		OR (95% CI)		OR (95% CI)	
Non-Hispanic White	Referent		Referent		Referent		Referent	
Black	2.19 (2.07-	<0.001	1.15 (0.97-1.36)	0.096	1.54 (1.38-	<0.001	1.14 (1.04-	<0.001

	2.32)				1.73)		1.26)	
Hispanic	3.32 (3.09-3.56)	<0.001	2.46 (2.04-2.96)	<0.001	2.21 (1.80-2.71)	<0.001	1.70 (1.42-2.04)	0.005
Asian/Pacific Islander	1.94 (1.76-2.13)	<0.001	2.48 (2.00-3.08)	<0.001	3.88 (3.20-4.69)	<0.001	1.64 (1.27-2.11)	<0.001
American Indian/Alaska Native	2.28 (1.73-2.99)	<0.001	3.92 (2.29-6.72)	<0.001	2.03 (1.27-3.25)	0.003	1.00 (0.53-1.88)	<0.001
Other	1.59 (1.42-1.77)	<0.001	4.26 (3.15-5.77)	<0.001	2.12 (1.71-2.64)	<0.001	0.24 (0.20-0.30)	<0.001
Age								
<65	Referent		Referent		Referent		Referent	
>65	0.98 (0.94-1.03)	0.548	0.71 (0.64-0.77)	<0.001	1.38 (1.29-1.47)	<0.001	1.15 (1.07-1.24)	<0.001
Sex								
Female	N/A		0.89 (0.81-0.97)	0.012	1.17 (1.10-1.24)	<0.001	N/A	
Male			Referent		Referent			

1. Multivariable Model adjusts for Age, Sex, and Race/Ethnicity

Figure Legends

Figure 1A: Comparison of Proportion of Clinical Trial Enrollment vs. Proportion of Cancer Incidence by Race/Ethnicity for Breast Cancer Trials

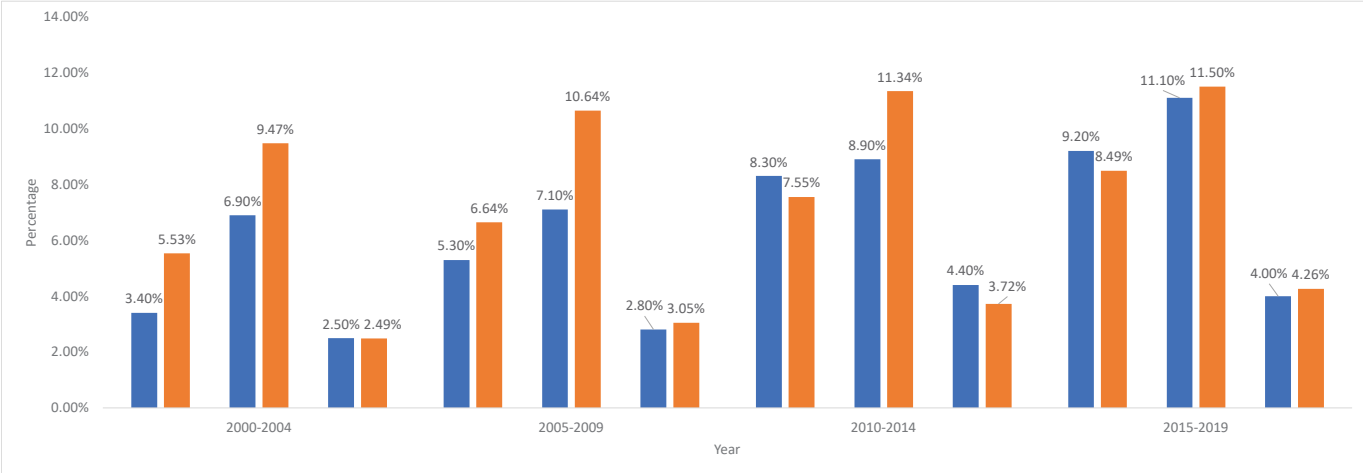
Figure 1B: Comparison of Proportion of Clinical Trial Enrollment vs. Proportion of Cancer Incidence by Race/Ethnicity for Colorectal Cancer Trials

Figure 1C: Comparison of Proportion of Clinical Trial Enrollment vs. Proportion of Cancer Incidence by Race/Ethnicity for Lung Cancer Trials

Figure 1D: Comparison of Proportion of Clinical Trial Enrollment vs. Proportion of Cancer Incidence by Race/Ethnicity for Prostate Cancer Trials

Orange = Proportion of Patients with Incident Cancer

Blue = Proportion of Patients Enrolled



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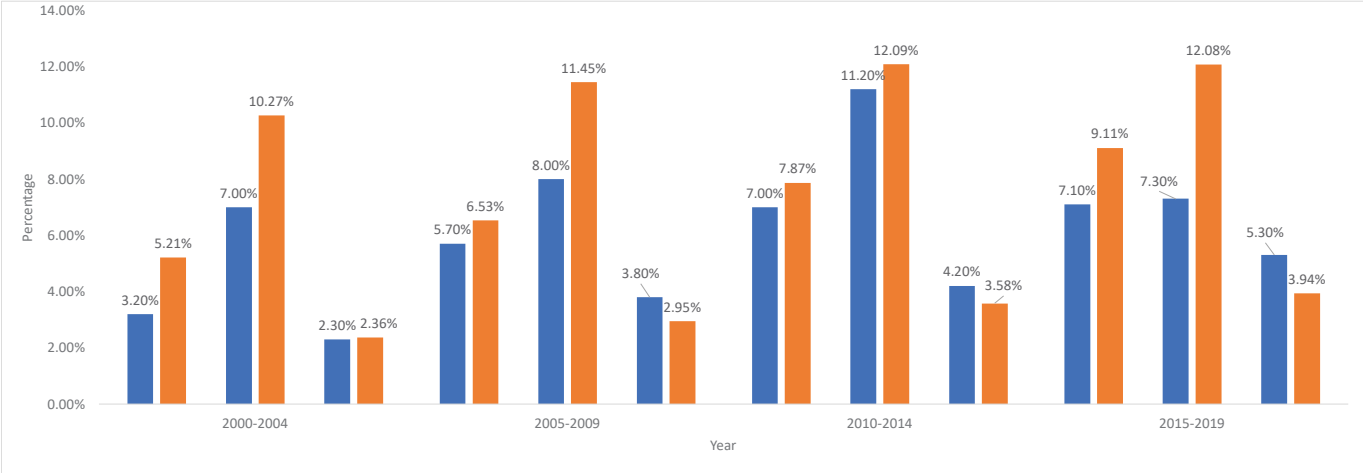

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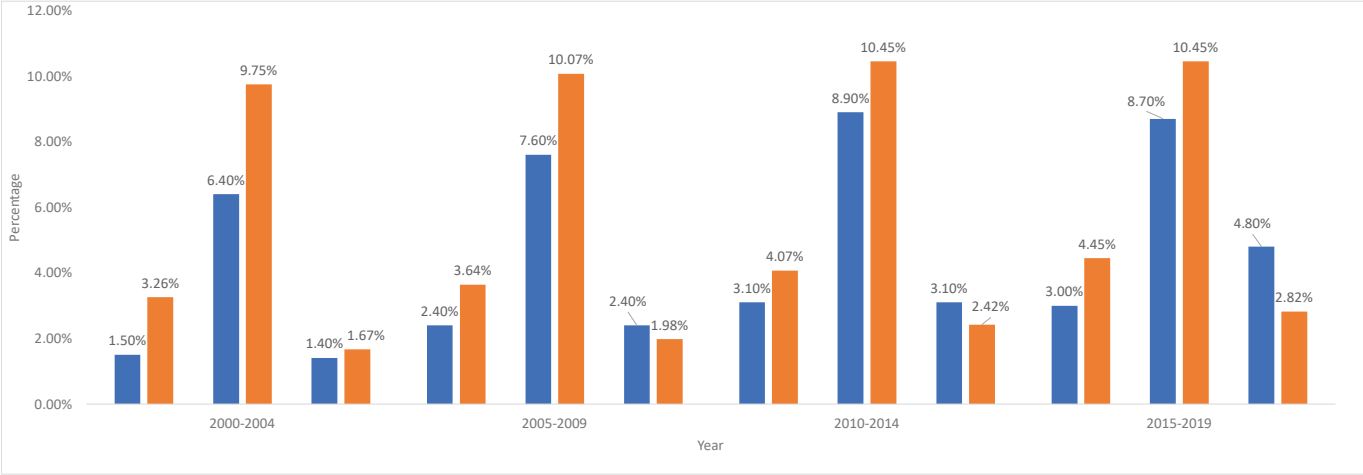

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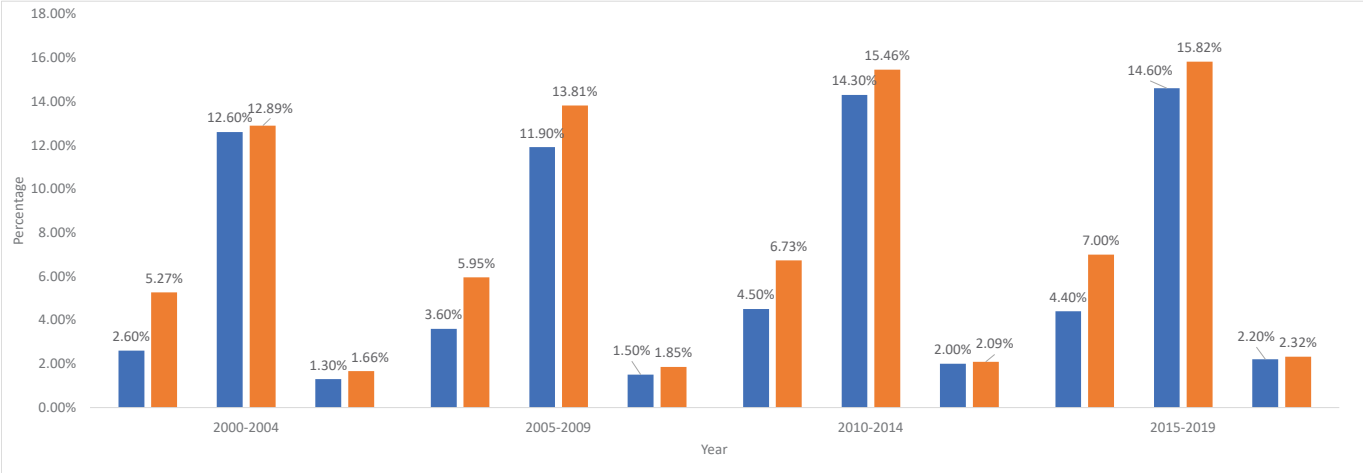

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