

Advancing Diversity, Equity, and Inclusion in Cancer Clinical Trials: Where are We ?

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Disclosures:

- None



Advancing DEI in Cancer Clinical Trials

The Problem: Low numbers of minority patients participate in cancer clinical trials



Advancing DEI in Cancer Clinical Trials

- What is the scope of the problem with DEI in cancer clinical trials
- What are the reasons for this problem
- How can we address those issues to improve minority/underserved participation in cancer clinical trials?



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Low minority participation can lead to:

- 1. Non-representative results** which may not be applicable to all patient groups due to :
 - differences in drug metabolism,
 - somatic and germline mutations,
 - alternative RNA splicing

These differences can lead to differences in pharmacokinetics, drug resistance, response and toxicity.



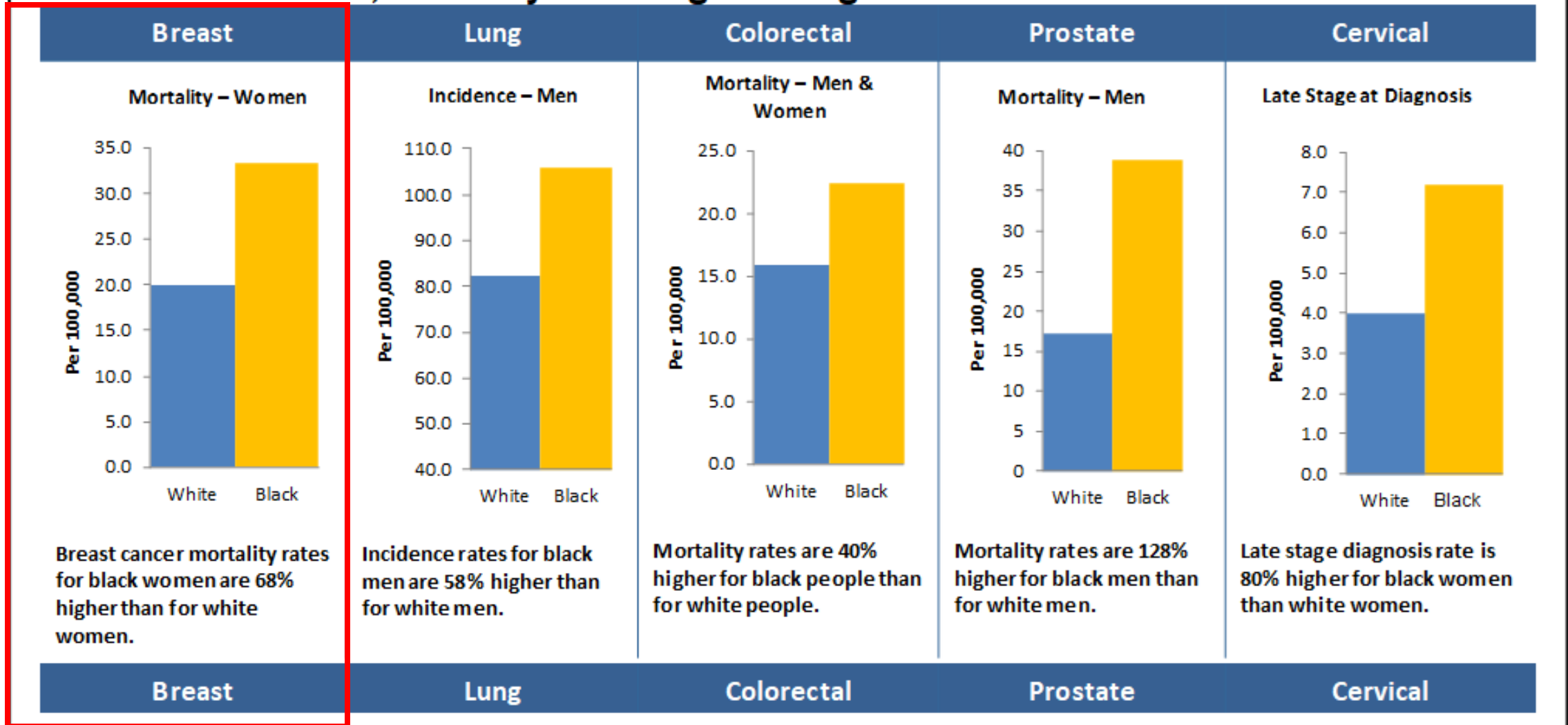
Advancing DEI in Cancer Clinical Trials

Low minority participation/lack of access: consequences

2. Minority / underserved patients do not get potentially beneficial therapies – they may be affected by some cancers to a greater degree (lung , colon, prostate)
 - **quality of life and survival can be compromised** by lack of trial access



Figure 2. Persistent and large racial disparities exist across all major cancers, in terms of incidence, mortality and stage at diagnosis.



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Is there really a Problem?

YES ! Multiple publications illustrate this.



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- The NIH Revitalization Act of 1993, PL 103-43, signed into law on June 10, 1993, directed the NIH to establish guidelines for inclusion of women and minorities in clinical research



Advancing DEI in Cancer Clinical Trials

- *Murthy et al, JAMA 2004*
- Evaluated enrollment data for NCI sponsored trials 1996-2002
- Approximately 75,000 patients
- Black patients significantly less likely to participate in trials for breast, colorectal and lung
- Overall minority participation was low



Advancing DEI in Cancer Clinical Trials:

Table 1. Participants in National Cancer Institute Cooperative Group Breast, Colorectal, Lung, or Prostate Cancer Therapeutic Trials, 1996-2002 (N = 75 215)*

Characteristic	Trial Participants, No. (%)	Proportion of Incident Cancer Patients, %†	Proportion of US Population, %†
Race/ethnicity			
White non-Hispanic	64 355 (85.6)	83.1	75.7
Hispanic	2292 (3.1)	3.8	9.1
Black	6882 (9.2)	10.9	10.8
Asian/Pacific Islander	1446 (1.9)	2.0	3.8
American Indian/Alaskan Native	240 (0.3)	0.2	0.7
Type of cancer			
Breast	40 788 (54.2)	27.9	
Colorectal	15 406 (20.5)	20.3	
Lung	9416 (12.5)	24.6	
Prostate	9605 (12.8)	27.1	
Age, y			
30-64	51 145 (68.0)	37.5	78.5
65-74	17 851 (23.7)	31.4	11.3
≥75	6219 (8.3)	31.2	10.2
Sex			
Male	24 104 (32.1)	51.0	47.6
Female	51 111 (67.9)	49.0	52.4

*Racial and ethnic groups are mutually exclusive.
†Estimated for the year 2000 among adults 30 years of age and older.



Advancing DEI in Cancer Clinical Trials

Table 5. Composition of Trial Enrollees According to Race/Ethnicity, 1996-2002

Group	1996	1997	1998	1999	2000	2001	2002	Enrollment vs Whites, 2000-2002 vs 1996-1998*	
								Relative Risk Ratio (95% CI)	P Value
Total No. of enrollees	8154	8974	9742	10710	11792	13359	12484		
Racial/ethnic group, % of total No. of enrollees									
White	83.0	84.2	84.0	86.0	87.4	86.3	86.6	1.0 (Referent)	
Hispanic	3.7	3.1	3.1	3.0	2.8	2.9	3.0	0.88 (0.72-1.08)	.23
Black	11.0	10.7	10.3	9.0	8.0	8.5	7.9	0.76 (0.65-0.89)	<.001
Asian/Pacific Islander	2.1	1.9	2.1	1.5	1.6	2.1	2.2	0.99 (0.83-1.18)	.91
American Indian/ Alaskan Native	0.3	0.2	0.5	0.5	0.3	0.3	0.3	0.80 (0.57-1.10)	.17

Abbreviation: CI, confidence interval.
 *Adjusted for age, sex, and cancer type using polychotomous logistic regression.

Murthy et al, JAMA 2004



Advancing DEI in Cancer Clinical Trials

- *Duma et al* -J Oncology Practice 2018
- Searched Clinicaltrials.gov 2003-2016: For completed trials in colon, breast, lung, prostate, renal and melanoma – 1012 trials found
- 55,689 pts
- **31% reported race**
- Sponsors: 44% Pharma, 25% NCI, 31% Academic
- Hispanics lowest participation in all trials except pancreas and lung where blacks had lower enrollment
- No significant differences noted in breast trials



Advancing DEI in Cancer Clinical Trials

Table 1. Participants in All Therapeutic Cancer Trials, 2003-2016 (N = 55,689)

Characteristic	Current Trial Participants		1996-2002 Trial Participants*		2013 Cancer Prevalence†	2010 US Census
	No.	%	No.	%	%	%
Race/ethnicity						
Non-Hispanic white	46,431	83.4	64,355	85.6	79.0	66.0
African American	3,270	6.0	6,882	9.2	10.0	12.6
Hispanic	1,484	2.6	2,292	3.1	7.0	16.0
Asian/Pacific Islander	2,982	5.3	1,446	1.9	3.3	4.8
American Indian/Alaskan Native	190	0.3	240	0.3	0.3	0.6
Other	1,332	2.4	NA			

Duma et al JOP 2018



Advancing DEI in Cancer Clinical Trials

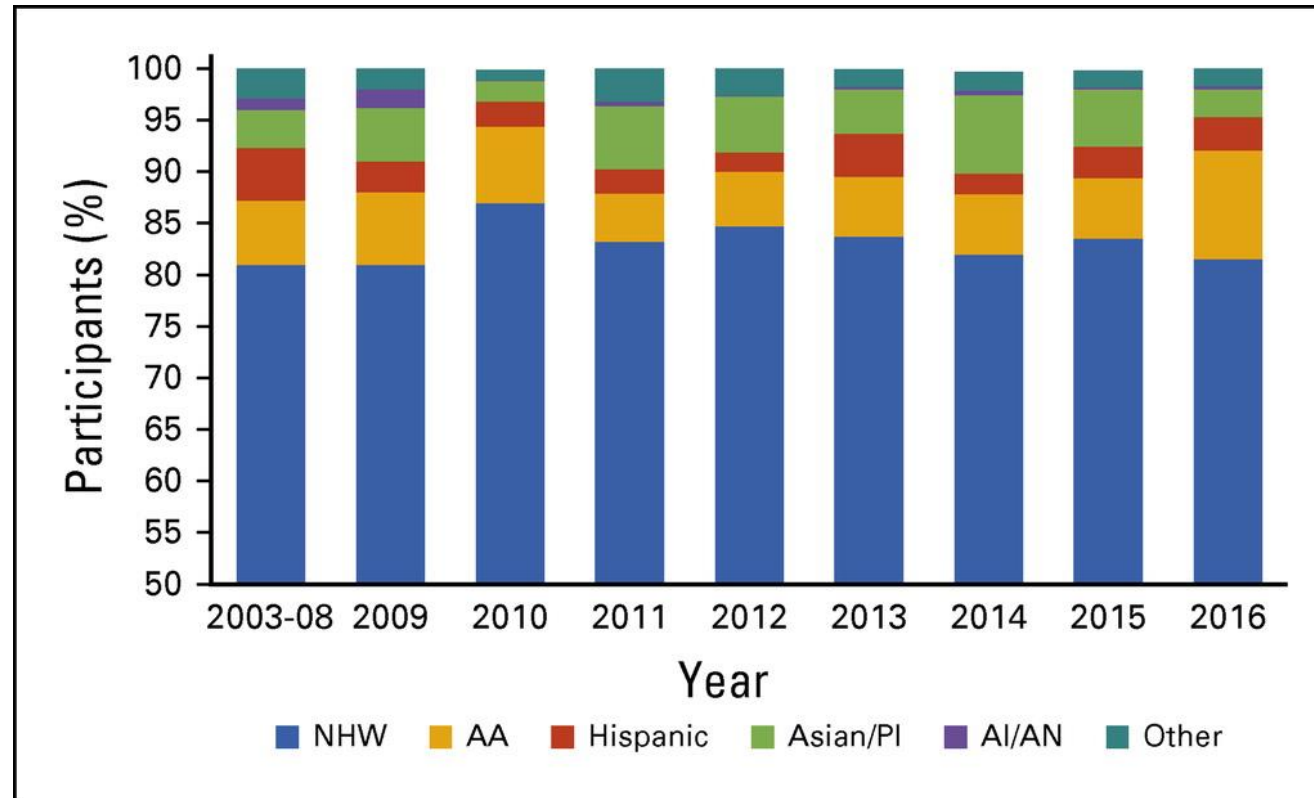


Fig 1. Composition of trial participants according to race/ethnicity, 2003-2016. AA, African American; AI/AN, American Indian/Alaskan Native; NHW, non-Hispanic white; PI, Pacific Islander.

Published in: Narjust Duma; Jesus Vera Aguilera; Jonas Paludo; Candace L. Haddox; Miguel Gonzalez Velez; Yucui Wang; Konstantinos Leventakos; Joleen M. Hubbard; Aaron S. Mansfield; Ronald S. Go; Alex A. Adjei; *Journal of Oncology Practice* 2018 14e1-e10.

DOI: 10.1200/JOP.2017.025288

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Advancing DEI in Cancer Clinical Trials

- *Ajewole et al, J Oncology Practice 2021*
- Analyzed trials for FDA approved **oral chemotherapy** drugs from 2009-2019
- 74 trials reported race, > 35,000 participants
- 26 (18%) trials were conducted mostly in the US



Advancing DEI in Cancer Clinical Trials

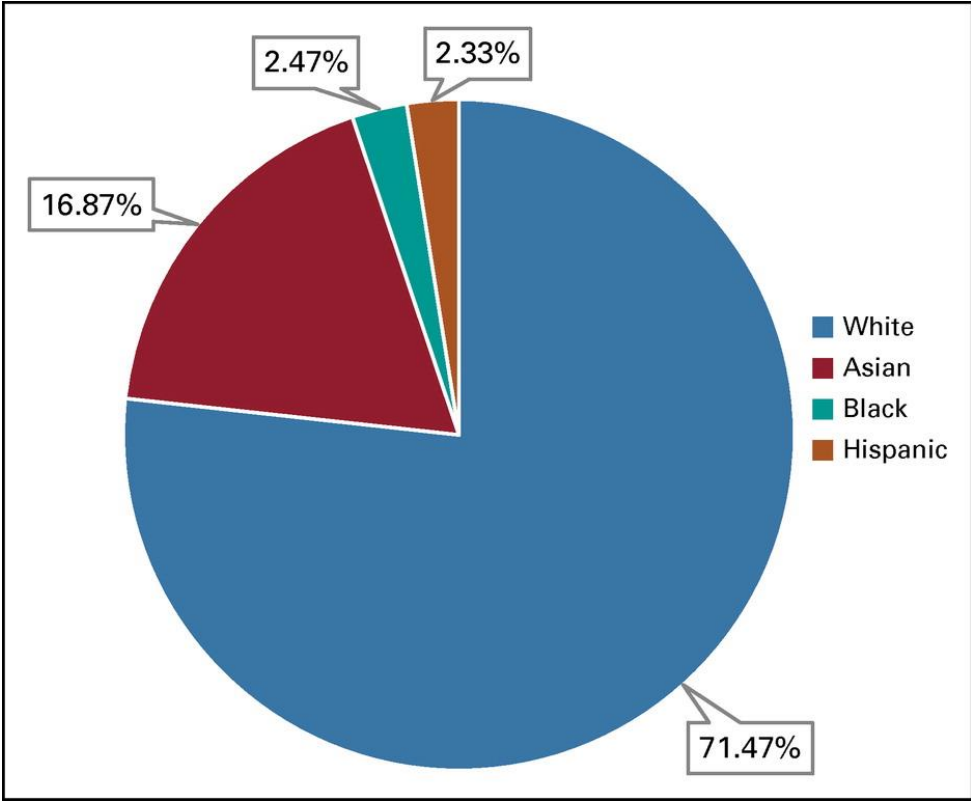


FIG 1. Black American representation in oral chemotherapy clinical trials, 2009-2019.

Published in: Veronica B. Ajewole; Oyinkansola Akindede; Uzoamaka Abajue; Okwuma Ndulue; Jazzmin J. Marshall; Yhenew T. Mossi; *JCO Oncology Practice* 2021 17e623-e628.
DOI: 10.1200/OP.20.01108
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Advancing DEI in Cancer Clinical Trials

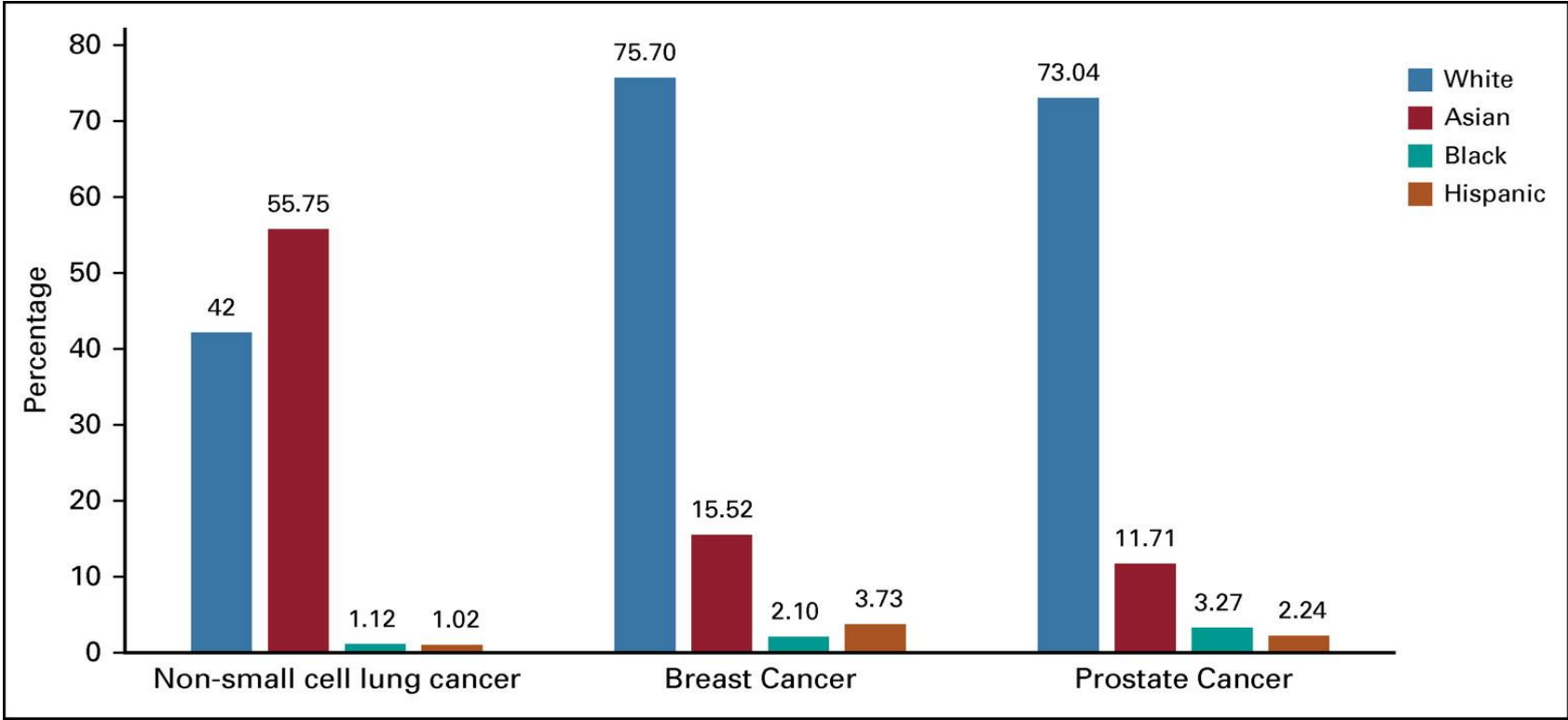


FIG 2. Black American inclusion in oral chemotherapy clinical trials involving top three disparity-related cancers among Black American populations 2009-2019.

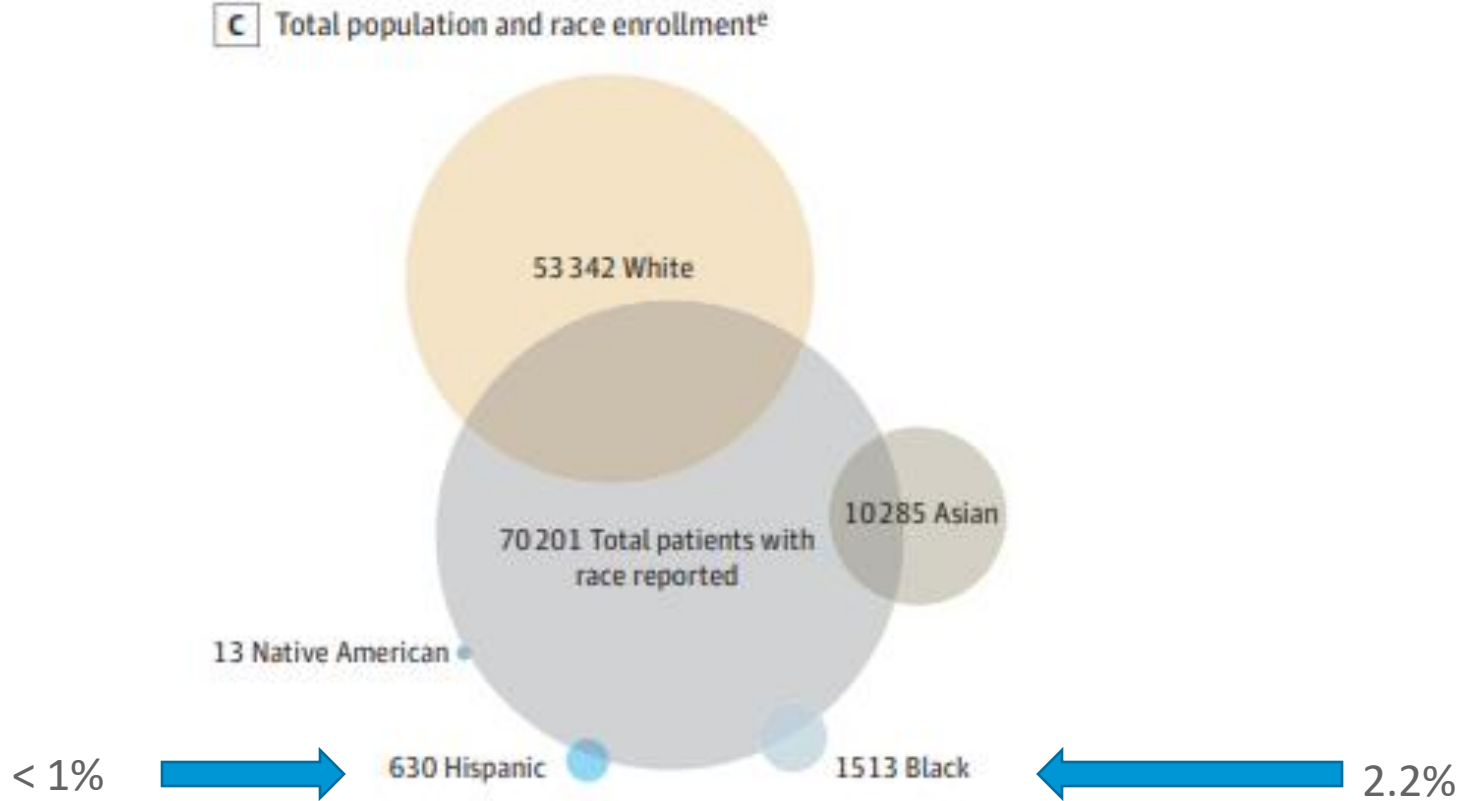


Advancing DEI in Cancer Clinical Trials

- *Loree et al*, JAMA Oncology 2019
- Reviewed Trials leading to FDA approvals for Oncology Drugs 2008-2018
- 63% of trials reported race(145/230)
- > 70,000 patients enrolled in trials reporting race



Advancing DEI in Cancer Clinical Trials



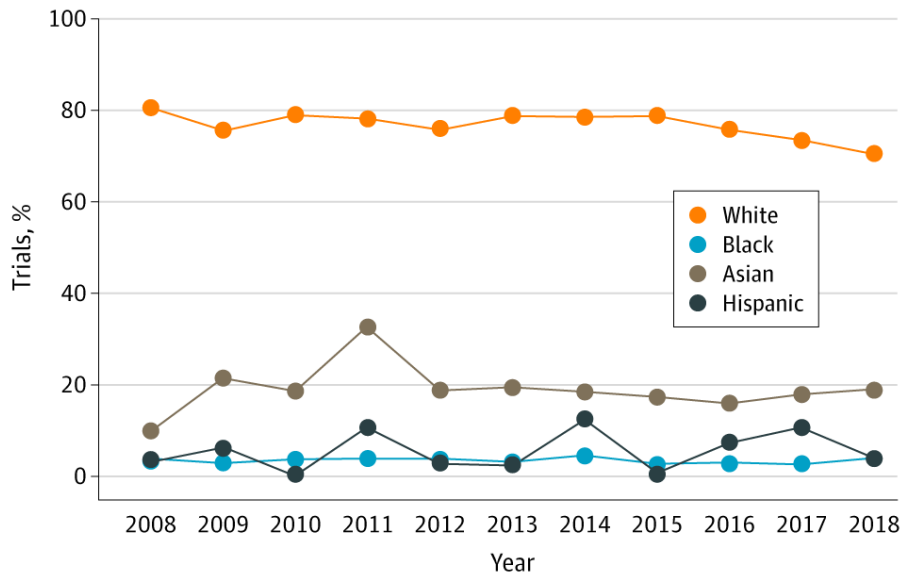
Loree et al, JAMA Oncology 2019



From: **Disparity of Race Reporting and Representation in Clinical Trials Leading to Cancer Drug Approvals From 2008 to 2018**

JAMA Oncol. 2019;5(10):e191870. doi:10.1001/jamaoncol.2019.1870

A Percentage of patients enrolled in FDA drug approval trials by race



B Comparison of incidence and mortality of patients with cancer vs trial enrollment

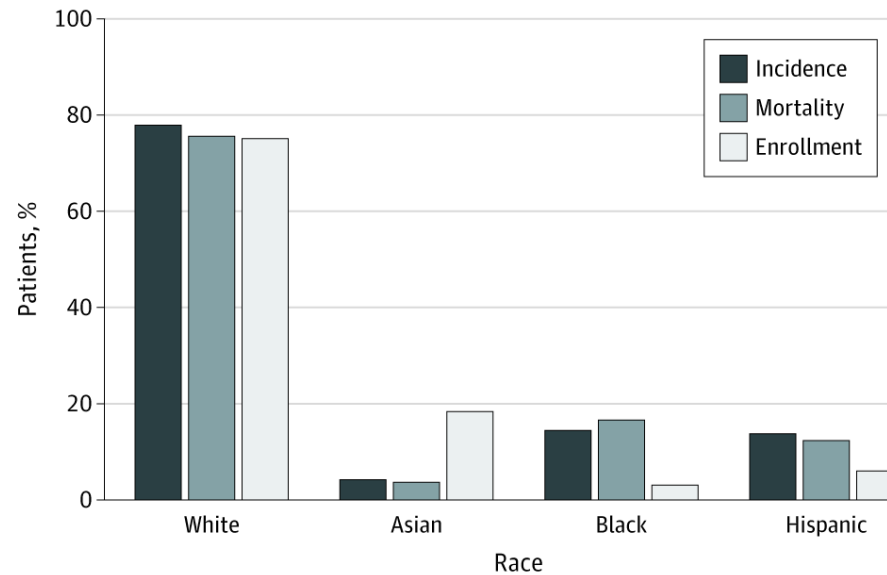


Figure Legend:

Differences in Incidence, Mortality, and Enrollment in Clinical Trials Leading to FDA Oncology Drug Approvals vs US Population With Cancer. A, Proportion of different races in trials for US Food and Drug Administration (FDA) approval from 2008 to 2018. B, Relative proportion of different races (pertaining to incidence and mortality) among patients with cancer in the United States was estimated using the Surveillance, Epidemiology, and End Results database and compared with trial participants in FDA approval trials between July 2008 and June 2018. Representation of black and Hispanic patients in pivotal FDA approval studies was low from 2008 to 2018.



Advancing DEI in Cancer Clinical Trials

Aldrighetti et al. JAMA open 2021

- Evaluated “Precision Cancer Studies” in Clinical Trials.gov 2020 (genomics, biomarkers etc)
- breast , lung, colorectal, prostate studies
- 93 studies with 5867 participants
- 82% white, 10% black, 4 % Asian, 3.4% hispanic



Advancing DEI in Cancer Clinical Trials:

So How are we doing Now?



Advancing DEI in Cancer Clinical Trials: Recent Breast Cancer Trials

Ribociclib as First-Line Therapy for HR-Positive, Advanced Breast Cancer

Gabriel N. Hortobagyi, M.D., Salomon M. Stemmer, M.D., Howard A. Burris, M.D., Yoon-Sim Yap, M.D., Gabe S. Sonke, M.D., Ph.D., Shani Paluch-Shimon, M.D., Mario Campone, M.D., Ph.D., Kimberly L. Blackwell, M.D., Fabrice André, M.D., Ph.D., Eric P. Winer, M.D., Wolfgang Janni, M.D., Ph.D., Sunil Verma, M.D., [et al.](#)

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Ribociclib Group (N=334)	Placebo Group (N=334)
Median age (range) — yr	62 (23–91)	63 (29–88)
Race — no. (%) †		
White	269 (80.5)	280 (83.8)
Asian	28 (8.4)	23 (6.9)
Black	10 (3.0)	7 (2.1)
Other or unknown	27 (8.1)	24 (7.2)

Hortobagyi et al NEJM 2016



Advancing DEI in Cancer Clinical Trials: Recent Breast Cancer Trials

Sacituzumab in Triple Negative Breast Cancer: Bardia et al, NEJM 2021

Subgroup	No. of Patients	Progression-free Survival		Hazard Ratio for Disease Progression or Death (95% CI)	
		Sacituzumab govitecan mo (95% CI)	Chemotherapy		
All patients	468	5.6 (4.3–6.3)	1.7 (1.5–2.6)		0.41 (0.32–0.52)
Age					
<65 yr	378	4.6 (3.7–5.7)	1.7 (1.5–2.5)		0.46 (0.35–0.59)
≥65 yr	90	7.1 (5.8–8.9)	2.4 (1.4–2.9)		0.22 (0.12–0.40)
Race					
White	369	5.7 (4.3–6.8)	1.7 (1.5–2.6)		0.39 (0.30–0.51)
Black	56	5.4 (2.8–7.4)	2.2 (1.5–2.9)		0.45 (0.24–0.86)
Asian	18	NE (1.3–NE)	1.5 (1.2–NE)		0.40 (0.08–2.08)

12% black



Advancing DEI in Cancer Clinical Trials: Recent Breast Trials

ORIGINAL ARTICLE

Pembrolizumab plus Chemotherapy in Advanced Triple-Negative Breast Cancer

Javier Cortes, M.D., Ph.D., Hope S. Rugo, M.D., David W. Cescon, M.D., Ph.D., Seock-Ah Im, M.D., Ph.D., Mastura M. Yusof, M.D., Carlos Gallardo, M.D., Oleg Lipatov, M.D., Carlos H. Barrios, M.D., Jose Perez-Garcia, M.D., Hiroji Iwata, M.D., Norikazu Masuda, M.D., Marco Torregroza Otero, M.D., et al., for the KEYNOTE-355 Investigators^{*}

- NEJM 2022
- Participants listed as Hispanic or Non-Hispanic !



Advancing DEI in Cancer Clinical Trial: Recent Breast Trials

ORIGINAL ARTICLE

Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer

Shanu Modi, M.D., William Jacot, M.D., Ph.D., Toshinari Yamashita, M.D., Ph.D., Joohyuk Sohn, M.D., Maria Vidal, M.D., Ph.D., Eriko Tokunaga, M.D., Ph.D., Junji Tsurutani, M.D., Ph.D., Naoto T. Ueno, M.D., Ph.D., Aleix Prat, M.D., Ph.D., Yee Soo Chae, M.D., Ph.D., Keun Seok Lee, M.D., Ph.D., Naoki Niikura, M.D., Ph.D., *et al.*, for the DESTINY-Breast04 Trial Investigators*

Table 1. Demographic and Clinical Characteristics of the Hormone Receptor–Positive Cohort and All Patients at Baseline.*

Characteristic	Hormone Receptor–Positive Cohort		All Patients	
	Trastuzumab Deruxtecan (N=331)	Physician's Choice of Chemotherapy (N=163)	Trastuzumab Deruxtecan (N=373)	Physician's Choice of Chemotherapy (N=184)
Median age (range) — yr	56.8 (31.5–80.2)	55.7 (28.4–80.0)	57.5 (31.5–80.2)	55.9 (28.4–80.5)
Female sex — no. (%)	329 (99.4)	163 (100)	371 (99.5)	184 (100)
Region — no. (%)				
Europe or Israel	149 (45.0)	73 (44.8)	166 (44.5)	85 (46.2)
Asia	128 (38.7)	60 (36.8)	147 (39.4)	66 (35.9)
North America	54 (16.3)	30 (18.4)	60 (16.1)	33 (17.9)
Race — no. (%)†				
White	156 (47.1)	78 (47.9)	176 (47.2)	91 (49.5)
Black	7 (2.1)	2 (1.2)	7 (1.9)	3 (1.6)
Asian	131 (39.6)	66 (40.5)	151 (40.5)	72 (39.1)
Other	37 (11.2)	16 (9.8)	39 (10.5)	17 (9.2)

NEJM 2022



Advancing DEI in Cancer Clinical Trials

- So, we can conclude that: Under-representation is a long standing and long discussed problem
- Why has it been so challenging to address?
- What are the barriers faced?



Advancing DEI in Cancer Clinical Trials: Barriers to Participation

- Investigator
- Patient
- Institutional
- Geographic



Advancing DEI in Cancer Clinical Trials: Barriers to Participation - Investigator

- Implicit Bias of the Investigator
- Patients won't accept if offered
- Patients won't comply
- Limited clinician time – especially in underserved clinics
- Lack of research sources for the investigator
- Lack of available trials
- Lack of Institutional commitment



Advancing DEI in Cancer Clinical Trials: Barriers to participation - Patients

- Lack of information
- Social determinates of health: travel, childcare, work, financial
- Geography – access in rural areas
- Lack of trust
- Literacy, language, communication
- Digital barriers – access to internet, smartphones



Advancing DEI in Cancer Clinical Trials: Barriers to participation – Financial Toxicity

- *Nipp et al, Oncologist 2019*
- Patients on therapeutic Cancer clinical trials at Mass General 2015-2017 who reported financial concerns
- Those patients reported increased rates of :
 - 1) foregoing medical care due to cost
 - 2) using savings to pay for care
 - 3) selling possessions to pay for care
 - 4) taking on credit card debt to pay for care



Advancing DEI in Cancer Clinical Trials: Barriers to Participation - Trials

- Eligibility criteria (50% of potentially eligible patients lost here)
 - 1) laboratory requirements
 - 2) Functional status
 - 3) need for additional testing / biopsies
- Trials don't match type and stage of most prevalent diseases



Advancing DEI in Cancer Clinical Trials: Barriers to Participation - Eligibility

- *Riner et al J Clin Oncology 2022*
- Evaluated pancreatic cancer patients at Massey Cancer Center 2010-2019
- 676 patients identified – 42% Black, 52% White
- Utilized eligibility criteria from ClinicalTrials.gov for pancreatic cancer trials 2010-2017 (common inclusion/exclusion criteria across trials)



Advancing DEI in Cancer Clinical Trials: Barriers to Participation - Eligibility

- *Riner et al*, J Clin Oncology 2022
- 58% had stage III/IV disease, 65% of Blacks and 51% of Whites
- Using traditional trial eligibility criteria, Blacks were more likely to be ineligible due to hypoalbuminemia, HIV, Hepatitis C
- Blacks also had a higher rate of exclusion due to coronary stenting in last 6 months and prior cancer treatment (co-morbidities)
- Overall rate of ineligibility was 42% for blacks and 33% for whites



Advancing DEI in Cancer Clinical Trials: Barriers to Participation - Institutional

- Lack of Diversity of Research Staff – do we mirror our patients ?
- Costs associated with Research (especially for non-academic institutions – most of the patients are there)
- Trial Location Accessibility – patients have to come to the Research Center
 - Lack of trial availability leads to loss of 50% of potential trial participants



Advancing DEI in Cancer Clinical Trials: Workforce

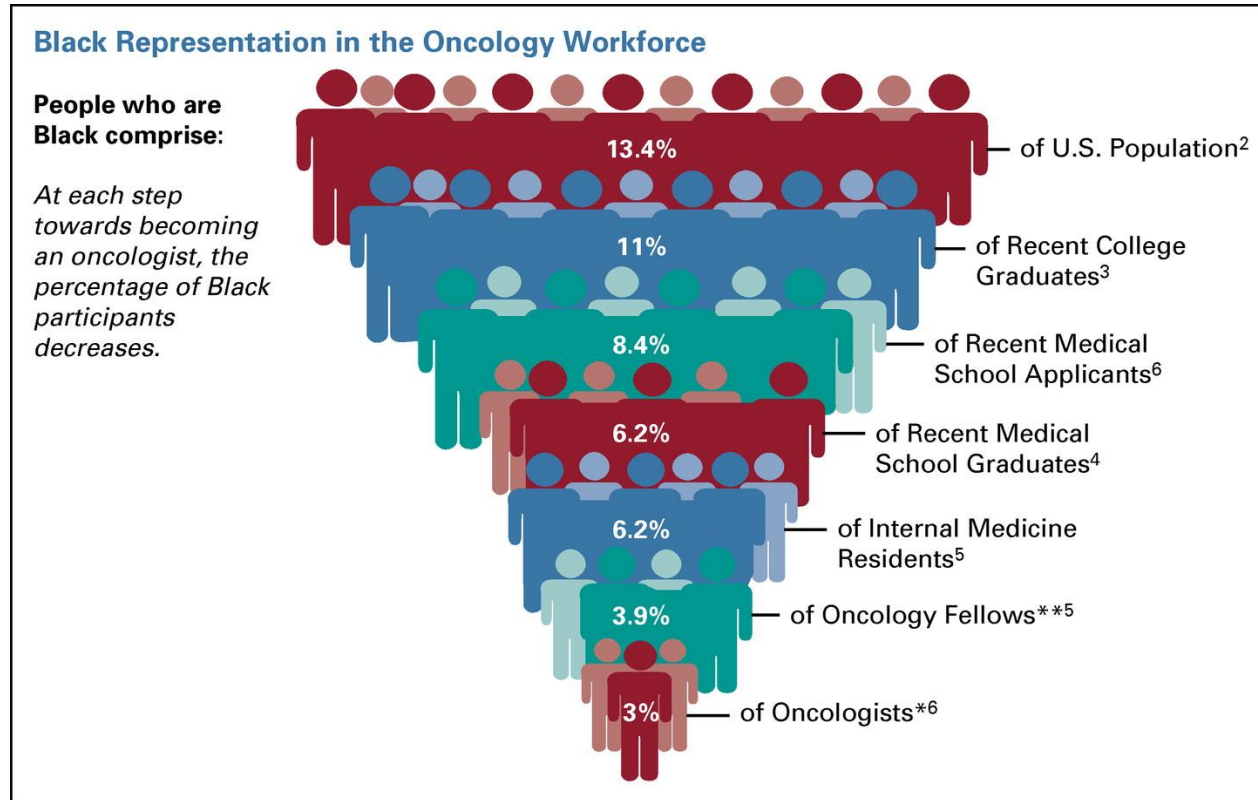


FIG 1. Black representation in the medical oncology workforce pipeline.



Advancing DEI in Cancer Clinical Trials

- Patients can't accept if not offered a trial
- 19-76% of eligible candidates are not offered (Fleury - Proc ASCO 2022)
- Will they accept if offered?

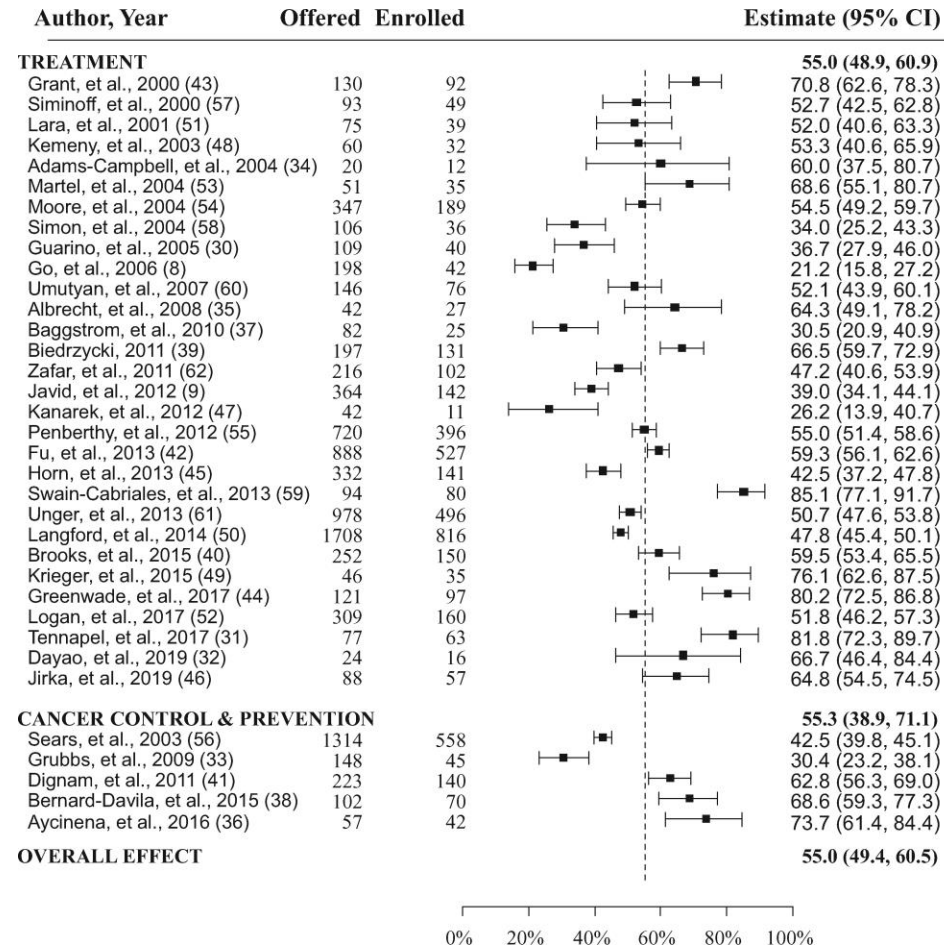


Advancing DEI in Cancer Clinical Trials

- *Unger et al* , JNCI 2021
- Evaluated studies that evaluated the participation of cancer patients in clinical trials – computerized literature search for 2000-2020
- Treatment or cancer control studies – total of 35 appropriate studies
- Almost 10,000 patients
- 71% Academic setting, 23% Community, 6% both



Figure 2. Forest plots of the study-level and summary estimates for each domain. The boxes show the study-level ...



Advancing DEI in Cancer Clinical Trials

- Unger et al , JNCI 2021 - Results
- Overall rate of trial acceptance / participation was 55%
- 58% at academic sites, 45% at Community sites
- 15 out of 35 studies provided data to estimate rates of participation based on race
- Black patient participation (58%) was higher than white patient participation (55%)
- So – Most patients will participate if offered!



Advancing DEI in Cancer Clinical Trials

What can be done to correct the problem?



ASCO-ACCC Research Statement

Oyer RA, Hurley P, Boehmer L, Bruinooge SS, Levit K, Barrett N, Benson A, Bernick LA, Byatt L, Charlot M, Crews J, DeLeon K, Fashoyin-Aje L, Garrett-Mayer E, Gralow JR, Green S, Guerra CE, Hamroun L, Hardy CM, Hempstead B, James S, Mann M, Matin K, McCaskill-Stevens W, Merrill J, Nowakowski GS, Patel MI, Pressman A, Ramirez AG, Segura J, Segarra-Vasquez B, Hanley Williams J, Williams JE, Winkfield KM, Yang ES, Zwicker V, Pierce LJ. **Increasing Racial and Ethnic Diversity in Cancer Clinical Trials: An American Society of Clinical Oncology and Association of Community Cancer Centers Joint Research Statement.** *Journal of Clinical Oncology*. 2022. DOI: 10.1200/JCO.22.00754.

asco.org/asco-accc



Advancing DEI in Cancer Clinical Trials: ASCO & ACCC: Joint Statement 2022

1. Clinical Trials are integral to quality cancer care and all patients should have an opportunity to participate
2. Sponsors and Investigators should design trials that reduce barriers and enhance DEI
3. Sponsors, investigators and sites should partner with patients, advocacy groups and the community to inform trial development
4. Trial designers should have formal training to decrease bias and develop cultural understanding
5. Research stakeholders (pharma, institutions) should invest in programs to increase DEI in clinical trials
6. Research Stakeholders should collect and publish data racial and ethnic diversity when reporting results



Advancing DEI in Cancer Clinical Trials: Institutional and Investigator Approaches

- Implicit Bias Training
- Prioritize Increasing Diversity in the Workforce
- Provide patient education
- Utilize Telemedicine to reach rural/underserved areas - GulfSouth Minority NCORP is piloting this approach
- Open trials likely to accrue minority patients
- **Offer Trials to All Patients**



Advancing DEI in Cancer Clinical Trials: Institutional and Investigator Approaches

- Monitor Institutional progress across time and sites for
 - 1) trial availability
 - 2) screening of minority patients
 - 3) enrollment of minority patients
 - 4) workforce diversity



Advancing DEI in Cancer Clinical Trials

- **Two main clinical trial site-self assessments:**
 - **The NCI Clinical Trials Assessment of Infrastructure Matrix (CT-AIM)**
 - Developed by NCI's Community Cancer Centers Program (NCCCP) in 2011 “to facilitate research program improvements through annual self-assessments and benchmarking...move [sites] beyond minimum standards set by Good Clinical Practice to exemplary attributes.”
 - Diamond et al. Clinical Trial Assessment of Infrastructure Matrix Tool to Improve the Quality of Research Conduct in the Community. J Ocol Pract. 2016.
 - **The Society for Clinical Research Sites (SCRS) Diversity Site Assessment Tool (DSAT)**
 - “for implementation of the best practices for recruiting and meeting the needs of diverse patient populations in clinical trials”
 - Foster, D. The Diversity Site Assessment Tool (DSAT), Reliability and Validity of the Industry Gold Standard for Establishing Investigator Site Ranking Integr J Med Sci. 2020.



Advancing DEI in Cancer Clinical Trials: Patient Directed Strategies

- Provide education on clinical trial participation
- Be aware of cultural barriers
- Optimize communication strategies – language, communication preferences / watch for digital barriers
- Ensure informed consent language is accessible to all patients
- Provide financial support when appropriate and possible
- Bring trials to patients whenever possible (outreach)



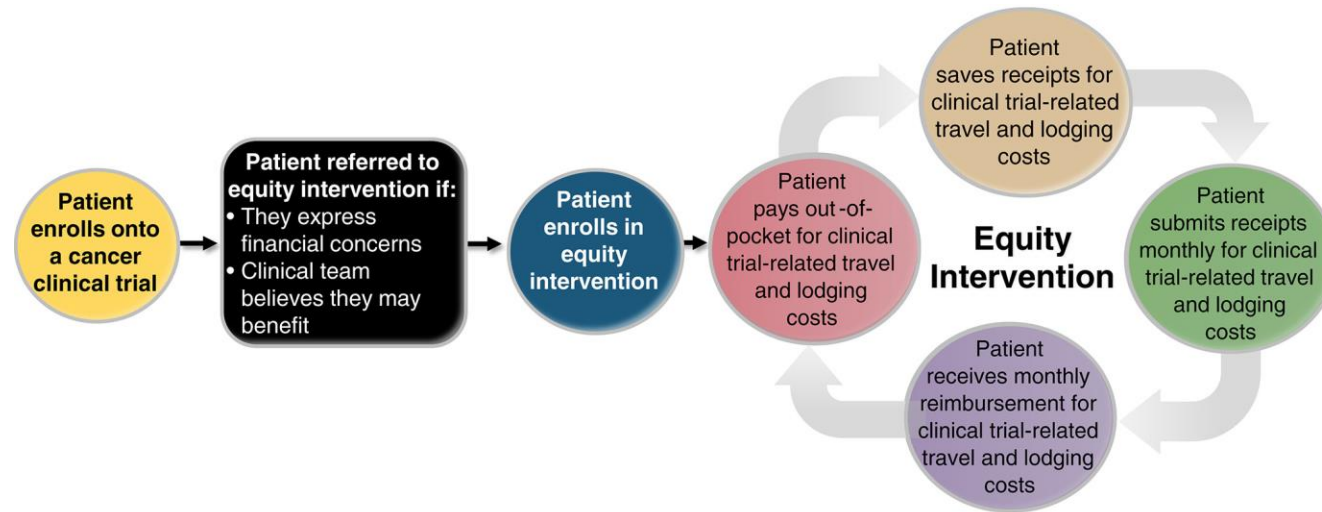
Advancing DEI in Cancer Clinical Trials: Patient Education



<https://youtu.be/RU7CXQ6ppD4>



Advancing DEI in Cancer Clinical Trials: Addressing the Financial Burden of Cancer Clinical



Nipp et al, *The Oncologist*, Volume: 24, Issue: 8, Pages: 1048-1055, First published: 15 April 2019,
DOI: (10.1634/theoncologist.2019-0146)



Advancing DEI in Cancer Clinical Trials: Trial Design Approaches

- Lack of patient-trial matches/availability is the biggest factor in low enrollment overall and in under-represented groups
- Increasing possible matches - screening
 - Optimize screening to ensure systematic and equitable eligibility screening processes
 - Maximize possible trials against which patients are screened
- **Offering participation to all who match !**



Advancing DEI in Cancer Clinical Trials: Trial Design Approaches

- Require appropriate minority participation in trial design
- Decrease unnecessary trial complexity
- Design trials to meet the disease states of specific groups – work with sponsors to highlight needs
- Optimize eligibility requirements to enhance the ability of patients to qualify -work with sponsors
- Incorporate costs of participation into trial design (travel , lodging etc) to decrease financial toxicity

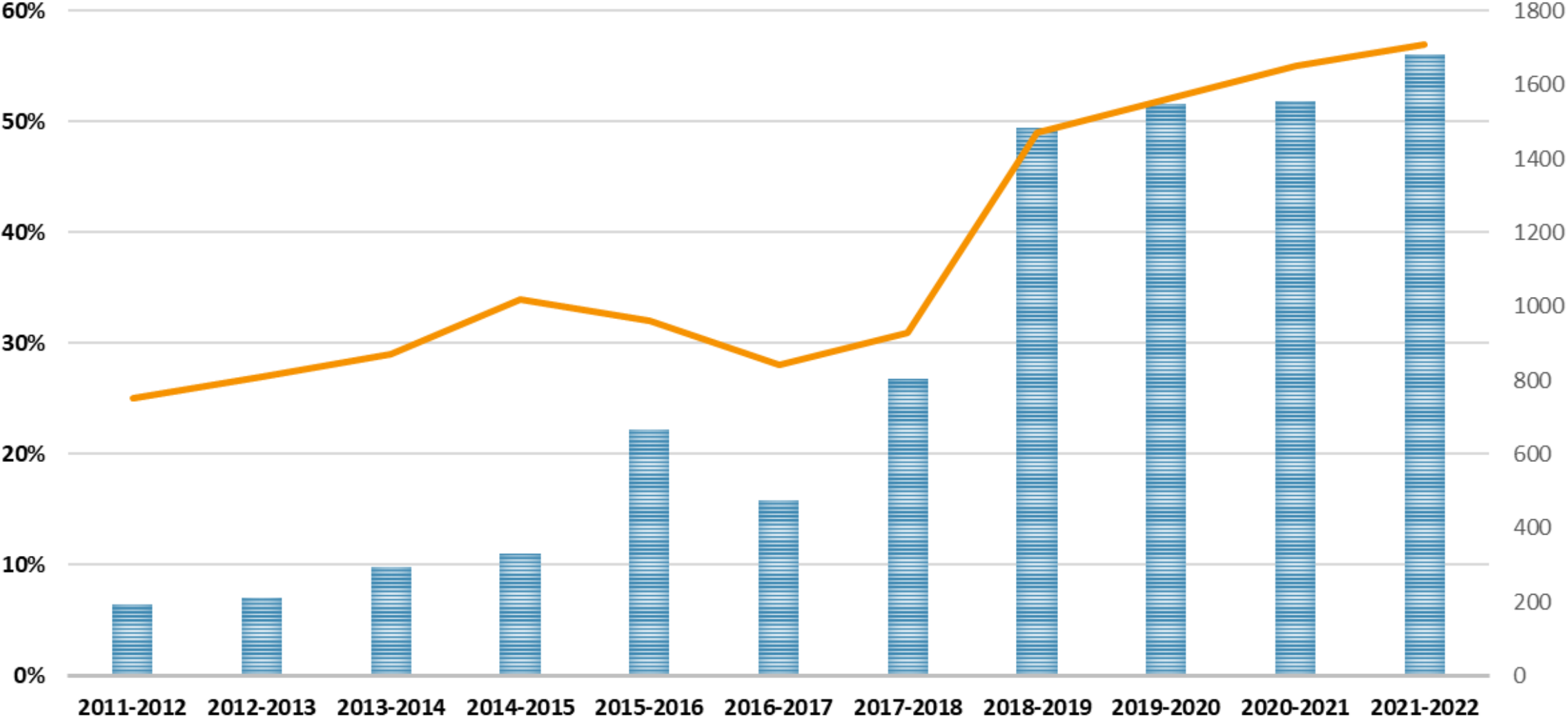


Advancing DEI in Cancer Clinical Trials:

Minority participation can be accomplished!



GULF SOUTH NCORP ANNUAL ENROLLMENTS



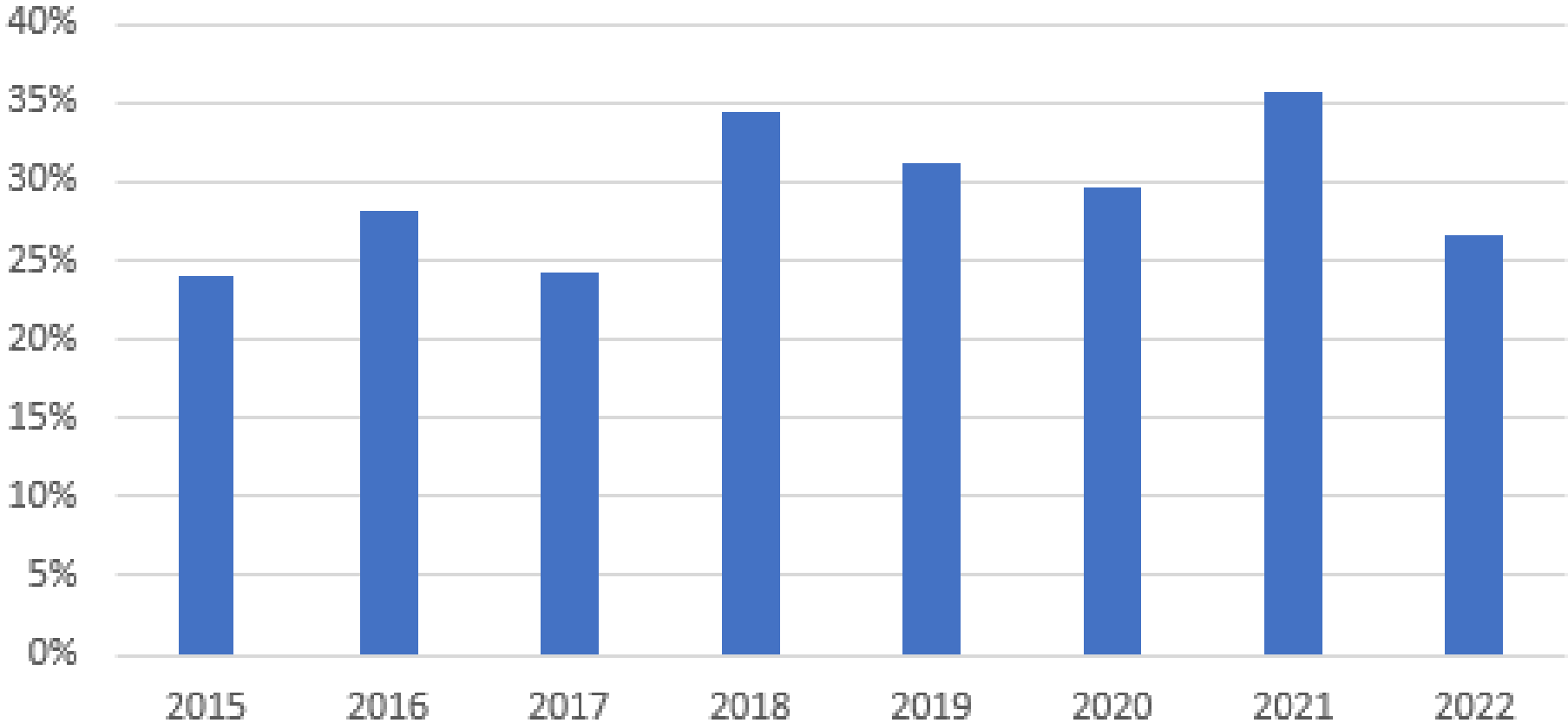
Courtesy of A Ochoa

Accruals % African American



Advancing DEI in Cancer Clinical Trials: Ochsner Data

Minority participation in oncology research protocols



Advancing DEI in Cancer Clinical Trials: Summary

- Many potential barriers exist to minority/underserved participation in clinical trials – we need to understand what they are for our specific patient populations
- Solutions may be generalizable or site specific
- Tools are available to help us in this endeavor
- Trials need to be inclusive and plentiful
- Patients are more likely to say yes to a trial – but this cannot happen unless they get the offer!



THANK YOU

