Equity in Access to Oncology Biomarker Testing

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Discolsure

- CONSULTING FEES: Roche/Genetech, Novartis, Eli Lilly, Gilead, Puma, Pfizer, AstraZeneca, Biotheranuatics, Daiichi Sankyo, Concerto AI, Sanofi
- FEES FOR NON-CME SERVICES: Eli Lilly, Astrazeneca, Gilead
- CONTRACTED RESEARCH: Roche/Genetech, Puma, Celcuity, Merck, BMS, Eli Lilly, GTx inc, Astrazeneca, Pfizer, Gilead, Tesaro, Halozyme,
- Ownership: Veris Health

Biomarker Approach to Treatment of Cancer

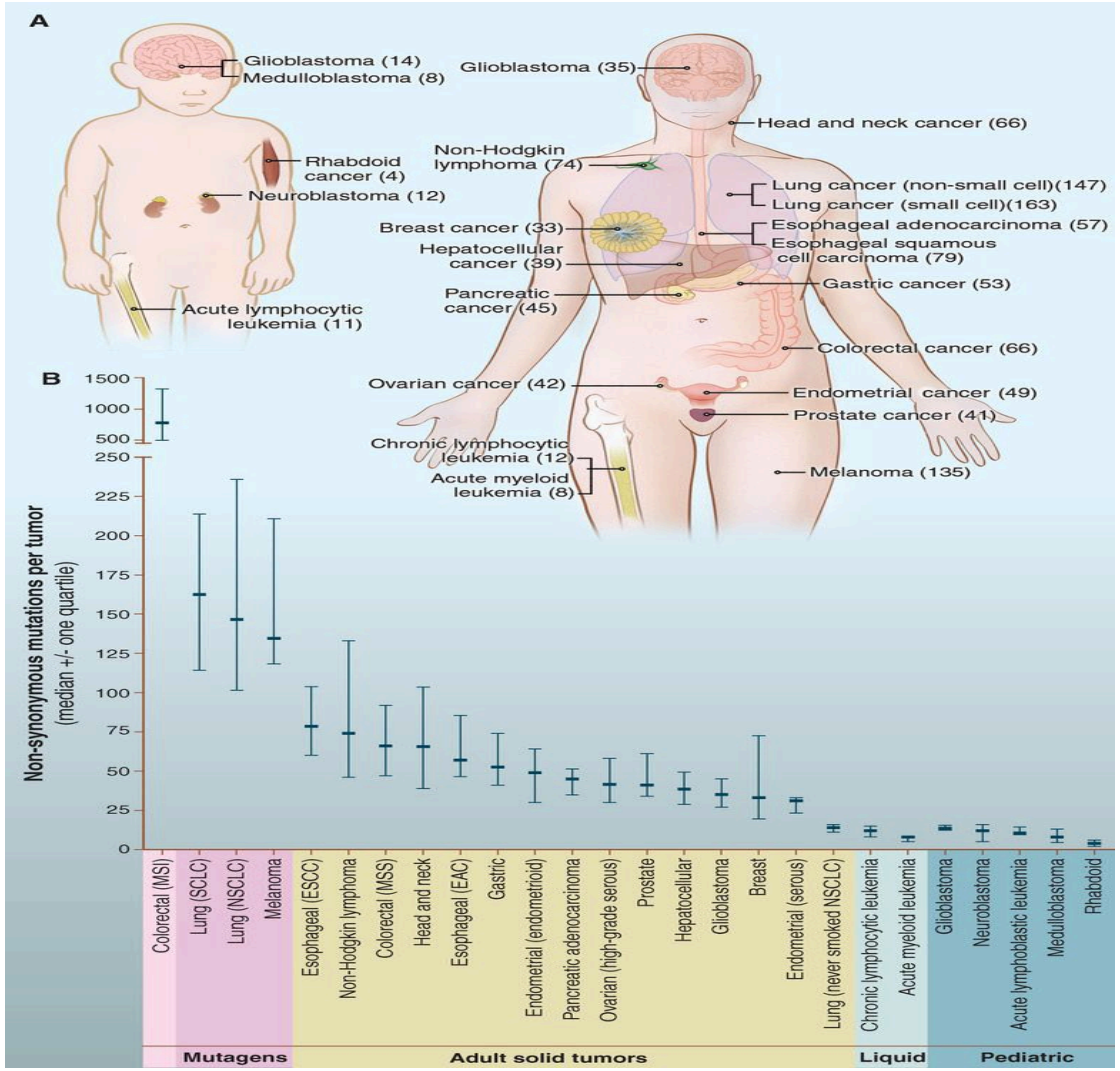
Mo and Renna, JHOP 2021

Biomarker definition: refers to a measurement variable that is associated with disease outcome.

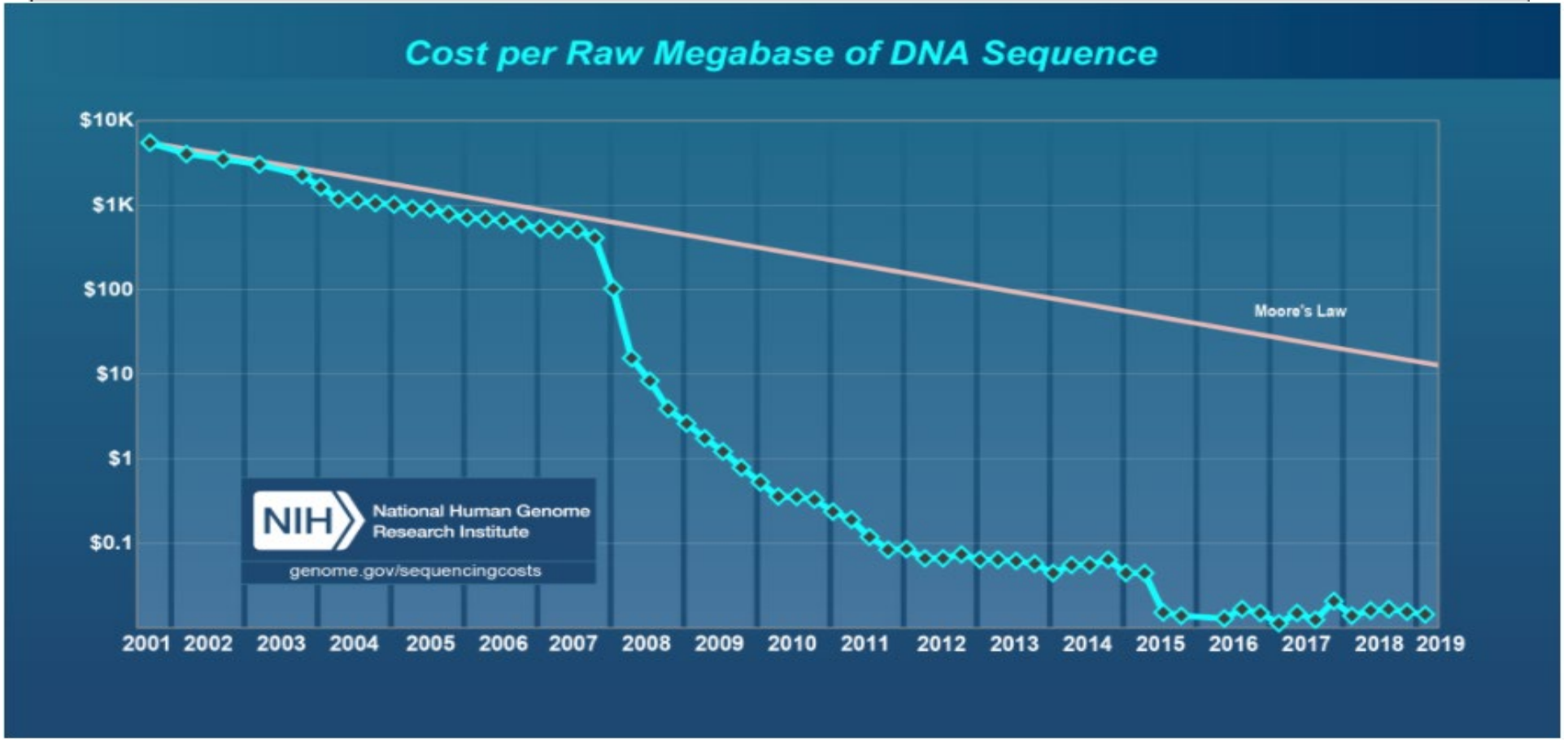
Table Selected Genetic Biomarkers and Targeted Therapies in Solid Tumor Malignancies

Biomarkers	FDA-approved indications	FDA-approved therapies	Drug class
ALK	NSCLC	Alectinib, crizotinib, ceritinib, brigatinib, lorlatinib	*ALK* inhibitors
BRAF[a]	Melanoma, colorectal, thyroid (anaplastic) cancers	Dabrafenib (trametinib), encorafenib (binimetinib), vemurafenib (cobimetinib)	*BRAF* (with or without *MEK*) inhibitors
BRCA1/BRCA2[a]	Breast, ovarian, pancreatic, prostate cancers	Olaparib, talazoparib, niraparib, rucaparib	*PARP* inhibitors
ER/PR	Breast cancer	*Aromatase inhibitors*: anastrozole, letrozole, exemestane *SERM*: tamoxifen *SERD*: fulvestrant *CDK4/6 inhibitors*: palbociclib, ribociclib, abemaciclib	Aromatase inhibitors SERM SERD CDK4/6 inhibitors
EGFR[a]	NSCLC	Osimertinib, erlotinib (with or without ramucirumab), gefitinib, afatinib, dacomitinib	*EGFR* inhibitors *VEGF* inhibitor (ramucirumab)
FGFR, FGFR2	Bladder cancer	Erdafitinib, pemigatinib	*FGFR* inhibitor
HER2	Breast, colorectal, gastric, esophageal, gastroesophageal junction cancers	Trastuzumab, pertuzumab, lapatinib, ado-trastuzumab emtansine, fam-trastuzumab deruxtecan, neratinib, tucatinib	*HER2* inhibitors
HRD	Ovarian, fallopian tube, peritoneal cancers	Olaparib	*PARP* inhibitor
HRR	Prostate cancer	Olaparib	*PARP* inhibitor
KIT	GIST	Imatinib	*KIT* inhibitor
KRAS (wild-type)	Colorectal cancer	Cetuximab, panitumumab	*EGFR* inhibitors
MET exon 14 skipping	NSCLC	Capmatinib	*MET* inhibitor
NTRK	Tumor agnostic	Larotrectinib, entrectinib	*NTRK* inhibitors
PIK3CA	Breast cancer	Alpelisib	*PI3K* inhibitor
PDGFRA exon 18	GIST	Avapritinib	*PDGFRA* inhibitor
RET	NSCLC, thyroid cancer	Selpercatinib, pralsetinib	*RET* inhibitors
ROS1	NSCLC	Crizotinib, entrectinib	*ROS1* inhibitors

Number of somatic mutations in representative human cancers, detected by genome-wide sequencing studies.



B Vogelstein et al. Science 2013;339:1546-1558



Sanger Sequencing

Massively parallel sequencing

2005
454 pyrosequencing GS-20

2006
Solexa/Illumina sequencer

2007
ABI/SOLiD sequencer

2008
Helicos BioSciences

2009
Illumina GAIIX, SOLiD 3.0

2010
Illumina HiSeq 2000
Oxford Nanopore

2011
Ion Torrent PGM
PacBio RS
Illumina MiSeq

2012
Intelligent BioSystems

Emerging sequencing technologies

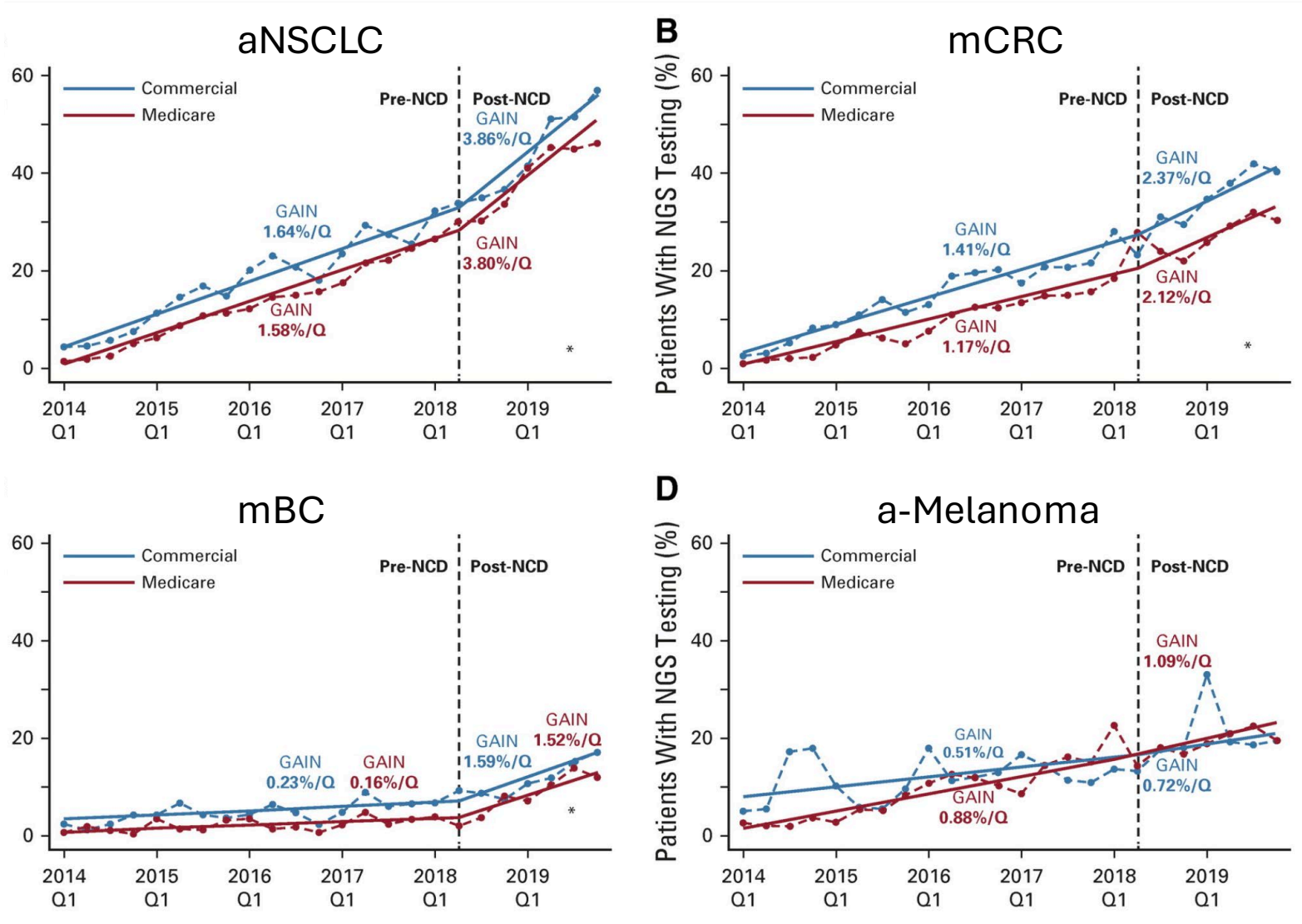
National Human Genome Research Institute, 2020

CMMS NGS- National Coverage Determination(NCD)

- 2018- NCD allowed for somatic/Tumor testing
  - Recurrent, relapsed, refractory, metastatic or advanced stage III/IV
  - Not been previously tested using NGS
  - Decided to seek further treatment
  - Test performed should have FDA approval or clearance and approved indication
  - Results provided to treating physician.
- 2020- Multigene Testing for Hereditary Cancer
  - Ovarian or Breast Cancer
  - Clinical indication and/or risk factor fir germline breast or ovarian cancer
  - Similar lab criteria as 2018.

Impact of 2018 CMMS- NGS NCD on Testing rates

Sheinson et al; JCO-OP 2021



Disparity in NGS testing aNSCLC, mBC or mCRC (N=14 786).

Bruno et al; JCO precision Oncology 2022

NSCLC Biomarker Testing	White (n = 9,793) No. (%)	Black/AA (n = 1,288) No. (%)	P[a]
Ever tested, any biomarker test	7,477 (76.4)	948 (73.6)	.0300
Any biomarker test before first-line therapy	6,064 (61.9)	784 (60.9)	.4700
Ever NGS tested	4,904 (50.1)	513 (39.8)	< .0001
NGS tested before first-line therapy	3,081 (31.5)	332 (25.8)	< .0001

CRC Biomarker Testing	White (n = 4,803) No. (%)	Black/AA (n = 838) No. (%)	P[a]
Ever tested, any biomarker test	4,031 (83.9)	707 (84.4)	.7500
Any biomarker test before first-line therapy	3,253 (67.7)	601 (71.7)	.0200
Ever NGS tested	2,478 (51.6)	350 (41.8)	< .0001
NGS tested before first-line therapy	876 (18.2)	130 (15.5)	.0600

BC Biomarker Testing	White (n = 3,314) No. (%)	Black/AA (n = 593) No. (%)	P[a]
Ever NGS tested	786 (23.7)	136 (22.9)	.6800
NGS tested before first-line therapy	136 (4.1)	22 (3.7)	.6500

Clinical Trial Participation and NGS testing

Bruno et al; JCO precision Oncology 2022

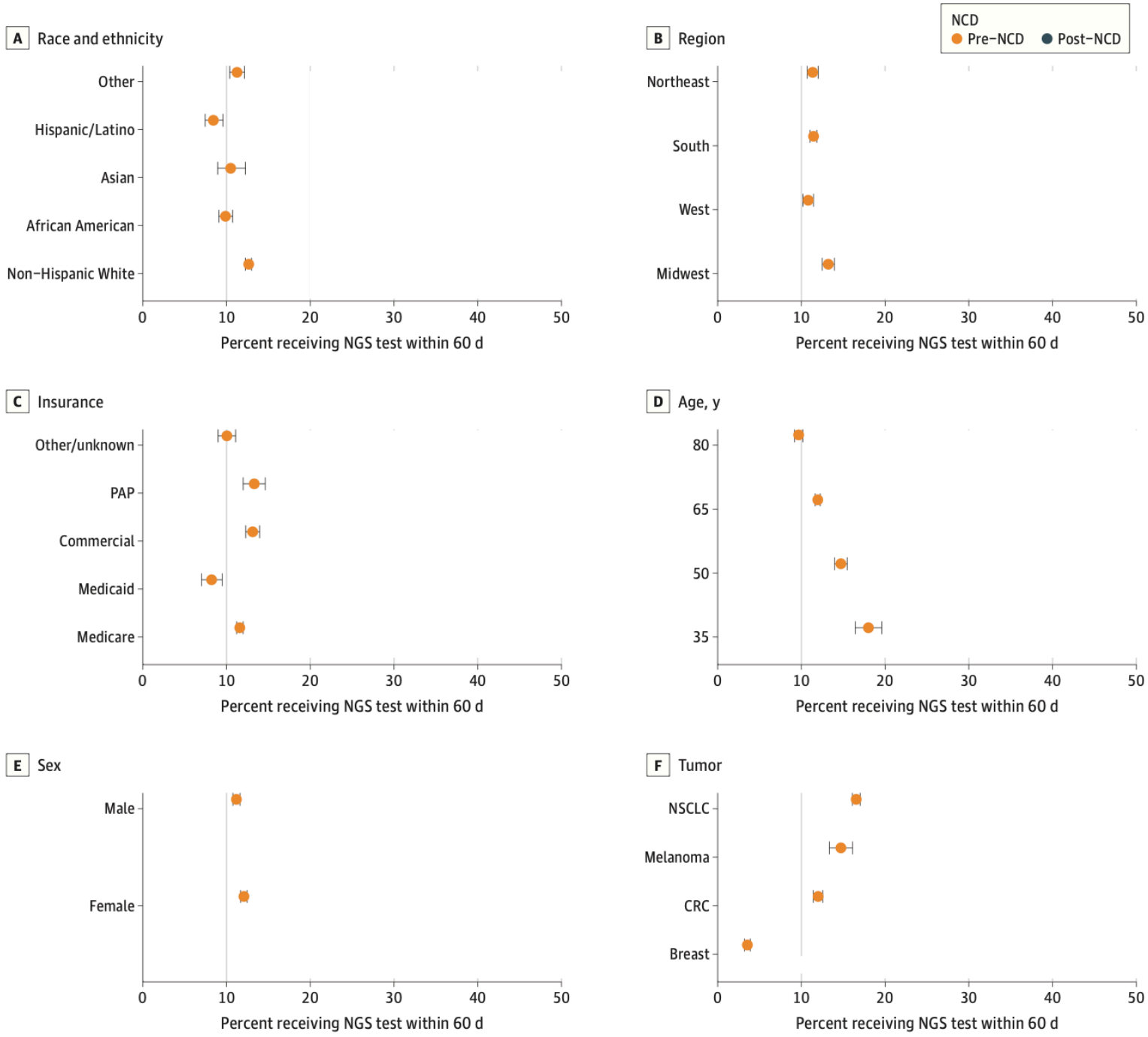
Clinical Trial Participation	White	Black/AA	P[a]
NSCLC	385/9,793 (3.9%)	24/1,288 (1.9%)	.0002
NS NSCLC	261/6,705 (3.9%)	19/922 (2.1%)	.0060
CRC	141/4,803 (2.9%)	24/838 (2.9%)	.9100
BC	193/3,314 (5.8%)	26/593 (4.4%)	.1600

	Any Biomarker Test			Any NGS-Based Testing		
Biomarker Tests at Any Time: NSCLC (n = 14,768)	Yes	No	P[a]	Yes	No	P[a]
Clinical trial enrollment, No. (%)						
Evidence of clinical trial enrollment	424 (3.8)	60 (1.7)	< .0001	318 (4.4)	166 (2.2)	< .0001
No evidence of clinical trial enrollment	10,873 (96.2)	3,411 (98.3)		6,867 (95.6)	7,417 (97.8)	
Targeted therapy, No. (%)						
Ever receiving targeted therapy	2,166 (19.2)	162 (4.7)	< .0001	1,450 (20.2)	878 (11.6)	< .0001
Never receiving targeted therapy	9,131 (80.8)	3,309 (95.3)		5,735 (79.8)	6,705 (88.4)	
Initiated targeted therapy during first line	1,648 (14.6)	136 (3.9)	< .0001	1,077 (15.0)	707 (9.3)	< .0001
Did not initiate targeted therapy during first line	9,649 (85.4)	3,335 (96.1)		6,108 (85.0)	6,876 (90.7)	

	Any Biomarker Test			Any NGS-Based Testing		
Biomarker Tests at Any Time: CRC (n = 7,879)	Yes	No	P[a]	Yes	No	P[a]
Clinical trial enrollment, No. (%)						
Evidence of clinical trial enrollment	182 (2.8)	12 (0.9)	.0001	154 (4.0)	40 (1.0)	< .0001
No evidence of clinical trial enrollment	6,425 (97.2)	1,260 (99.1)		3,720 (96.0)	3,965 (99.0)	
Targeted therapy, No. (%)						
Ever receiving targeted therapy	824 (12.5)	53 (4.2)	< .0001	565 (14.6)	312 (7.8)	< .0001
Never receiving targeted therapy	5,783 (87.5)	1,219 (95.8)		3,309 (85.4)	3,693 (92.2)	
Initiated targeted therapy during first line	305 (4.6)	31 (2.4)	.0004	182 (4.7)	154 (3.8)	.0600
Did not initiate targeted therapy during first line	6,302 (95.4)	1,241 (97.6)		3,692 (95.3)	3,851 (96.2)	

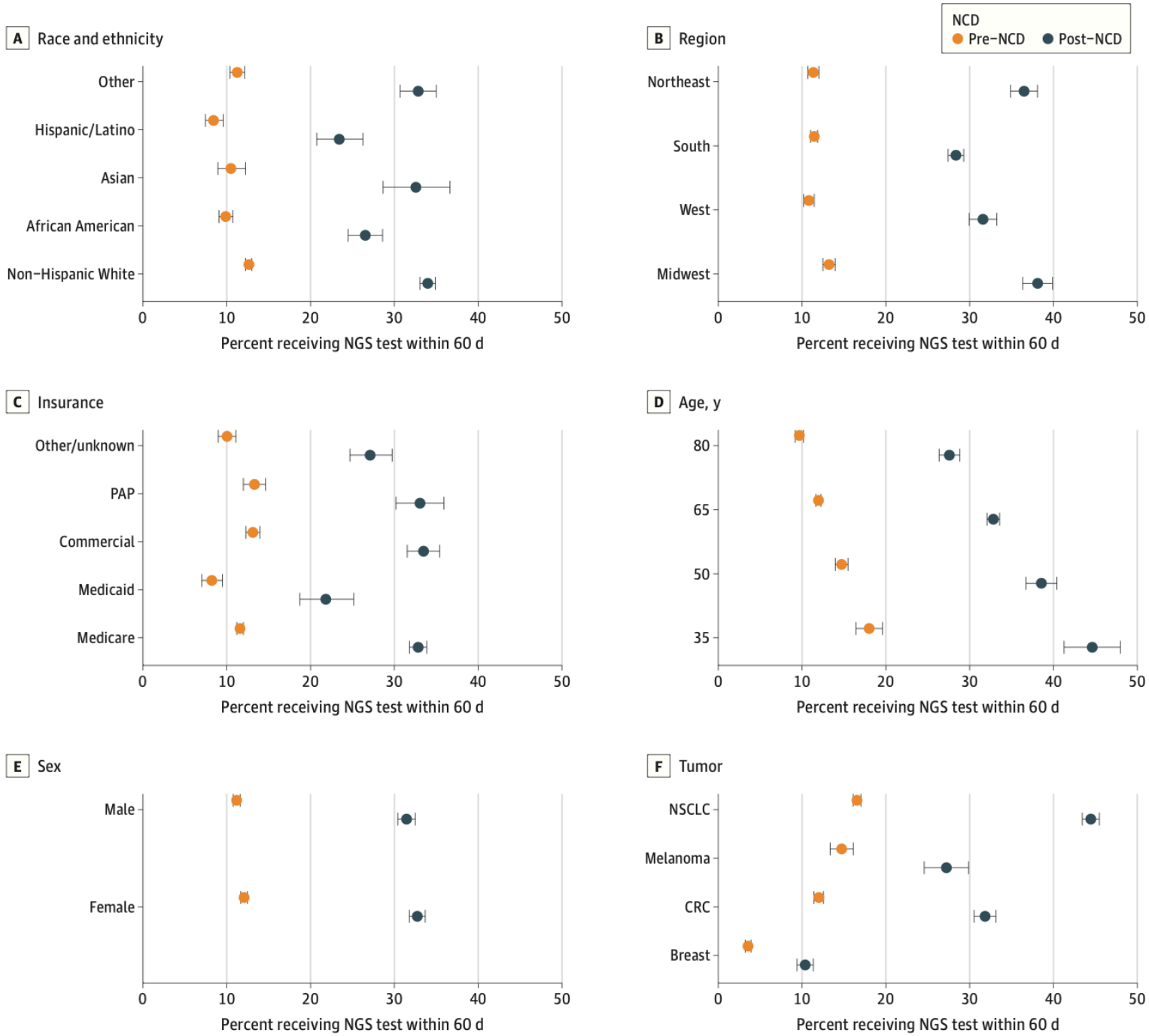
	Any NGS-Based BRCA Test		
Biomarker Tests at Any Time: BC (n = 5,276)	Yes	No	P[a]
Clinical trial enrollment, No. (%)			
Evidence of clinical trial enrollment	107 (8.9)	156 (3.8)	< .0001
No evidence of clinical trial enrollment	1,089 (91.1)	3,924 (96.2)	
Targeted therapy, No. (%)			
Ever receiving targeted therapy	241 (20.2)	705 (17.3)	.0200
Never receiving targeted therapy	955 (79.8)	3,375 (82.7)	
Initiated targeted therapy at start of first line	95 (7.9)	549 (13.5)	< .0001
Did not initiate targeted therapy at start of first line	1,101 (92.1)	3,531 (86.5)	

Demographic Difference in Next –Generation Sequencing (NGS) Testing Stratified by Pre NCD Periods



Sheinson et al, JAMA Network Open, 2021

Demographic Difference in Next –Generation Sequencing (NGS) Testing Stratified by Pre and Post National Coverage Determination Periods



Sheinson et al, JAMA Network Open, 2021

Factors Contributing to the Disparity Gaps in NGS Testing by Race/Ethnicity

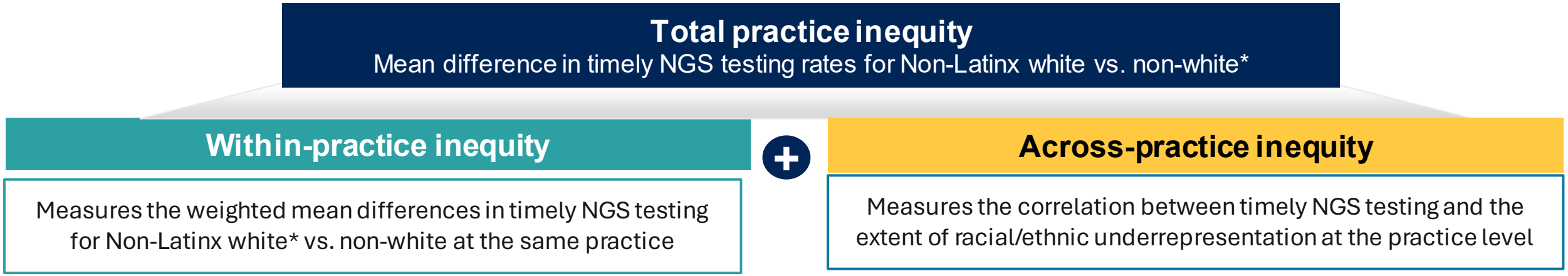
Potential Contributors
- Age
- Sex
- Region
- Insurance type

Race/ethnicity	Model	Pre-NCD OR (95% CI)	Pre-NCD *P* value	Post-NCD OR (95% CI)	Post-NCD *P* value
African American	No adjustment	0.72 (0.65-0.79)	<.01	0.63 (0.56-0.70)	<.001
	Adjusted for age and sex	0.70 (0.63-0.77)	<.01	0.63 (0.56-0.69)	<.001
	Adjusted for age, sex, and tumor	0.73 (0.66-0.80)	<.01	0.63 (0.56-0.70)	<.001
	Adjusted for age, sex, tumor, and region	0.74 (0.67-0.81)	<.01	0.69 (0.61-0.76)	<.001
	Adjusted for age, sex, tumor, and insurance type	0.75 (0.68-0.82)	<.01	0.64 (0.57-0.72)	<.001
	Adjusted for age, sex, tumor, insurance type, and region	0.76 (0.68-0.84)	<.01	0.70 (0.62-0.78)	<.001
Asian	No adjustment	0.79 (0.65-0.93)	.03	0.96 (0.79-1.13)	.96
	Adjusted for age and sex	0.77 (0.63-0.90)	.01	0.95 (0.78-1.12)	.93
	Adjusted for age, sex, and tumor	0.77 (0.52-0.70)	.02	0.93 (0.76-1.11)	.86
	Adjusted for age, sex, tumor, and region	0.81 (0.66-0.95)	.08	0.92 (0.75-1.10)	.83
	Adjusted for age, sex, tumor, and insurance type	0.77 (0.63-0.91)	.02	0.94 (0.76-1.11)	.89
	Adjusted for age, sex, tumor, insurance type, and region	0.81 (0.66-0.96)	.09	0.94 (0.76-1.11)	.89
Hispanic/Latino	No adjustment	0.55 (0.47-0.62)	<.01	0.50 (0.42-0.57)	<.001
	Adjusted for age and sex	0.53 (0.45-0.60)	<.01	0.49 (0.41-0.57)	<.001
	Adjusted for age, sex, and tumor	0.61 (0.52-0.70)	<.01	0.55 (0.46-0.64)	<.001
	Adjusted for age, sex, tumor, and region	0.63 (0.54-0.72)	<.01	0.58 (0.48-0.68)	<.001
	Adjusted for age, sex, tumor, and insurance type	0.62 (0.53-0.71)	<.01	0.56 (0.47-0.65)	<.001
	Adjusted for age, sex, tumor, insurance type, and region	0.64 (0.55-0.73)	<.01	0.59 (0.50-0.69)	<.001
Non-Hispanic White		1 [Reference]		1 [Reference]	
Other[a]	No adjustment	0.84 (0.76-0.91)	<.01	0.94 (0.85-1.04)	.62
	Adjusted for age and sex	0.83 (0.76-0.91)	<.01	0.94 (0.84-1.03)	.54
	Adjusted for age, sex, and tumor	0.85 (0.77-0.93)	<.01	0.93 (0.84-1.03)	.50
	Adjusted for age, sex, tumor, and region	0.87 (0.79-0.95)	.02	0.93 (0.83-1.03)	.56
	Adjusted for age, sex, tumor, and insurance type	0.85 (0.77-0.93)	<.01	0.94 (0.84-1.04)	.64
	Adjusted for age, sex, tumor, insurance type, and region	0.88 (0.79-0.96)	.02	0.95 (0.85-1.05)	.75

Sheinson et al, JAMA Network Open, 2021

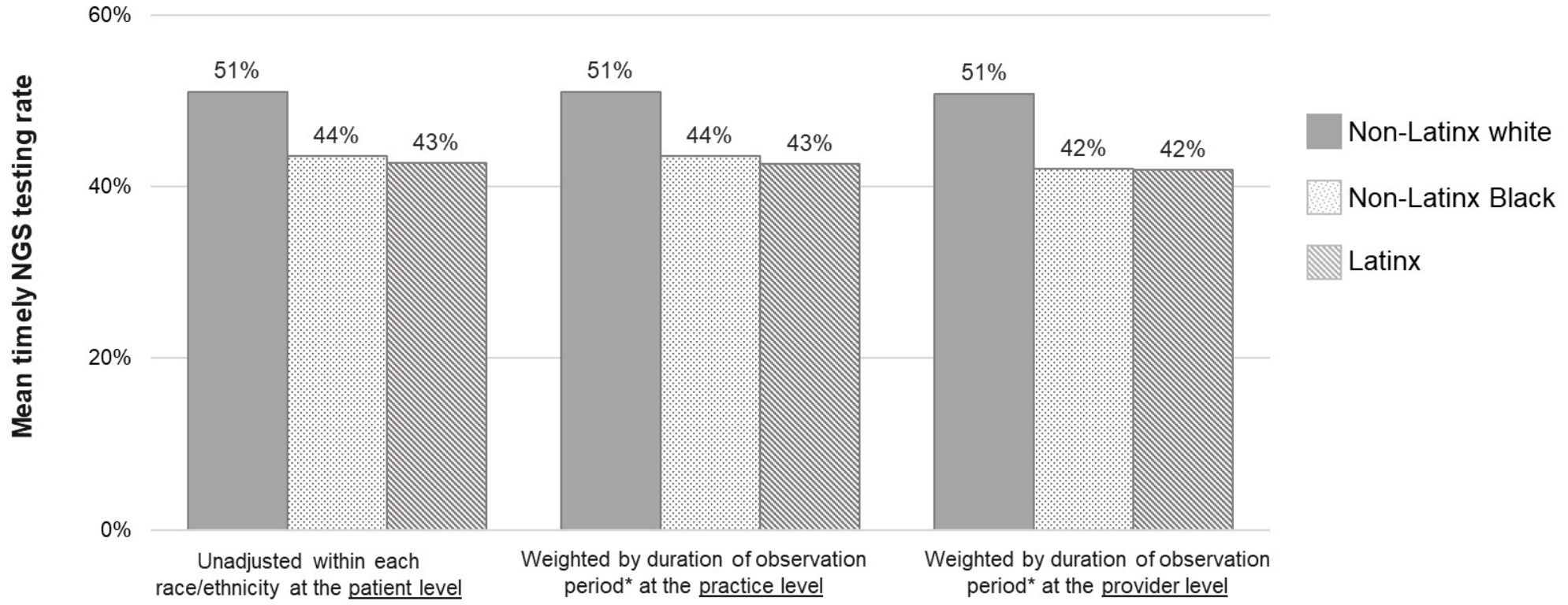
Title: Practice and provider- level inequities in next-generation sequencing (NGS) testing by race/ethnicity for patients with advanced non-small cell lung cancer (aNSCLC) treated in the community setting

OBJECTIVE: To better understand the extent to which racial/ethnic inequity in timely NGS testing for community treated patients with aNSCLC is driven by differences in care within and across practices and providers



Timely NGS Testing Rate

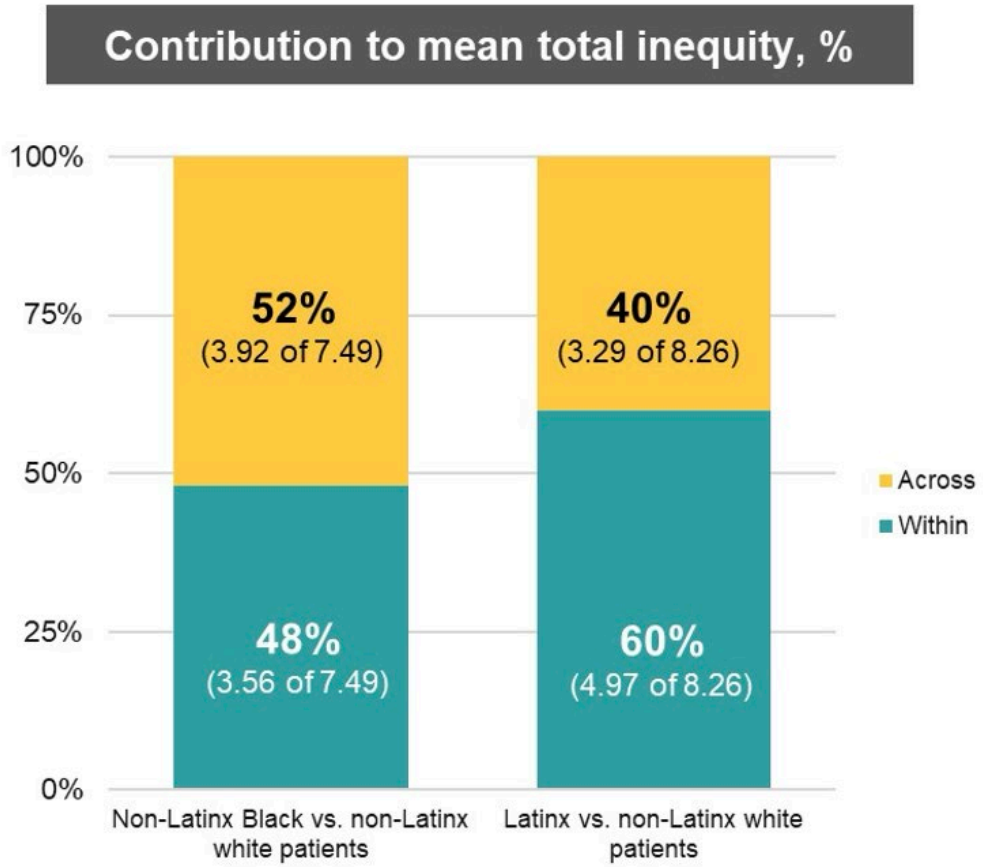
- Non-Latinx white patients had higher timely NGS testing rates than non-Latinx Black and Latinx at the patient, provider and practice levels



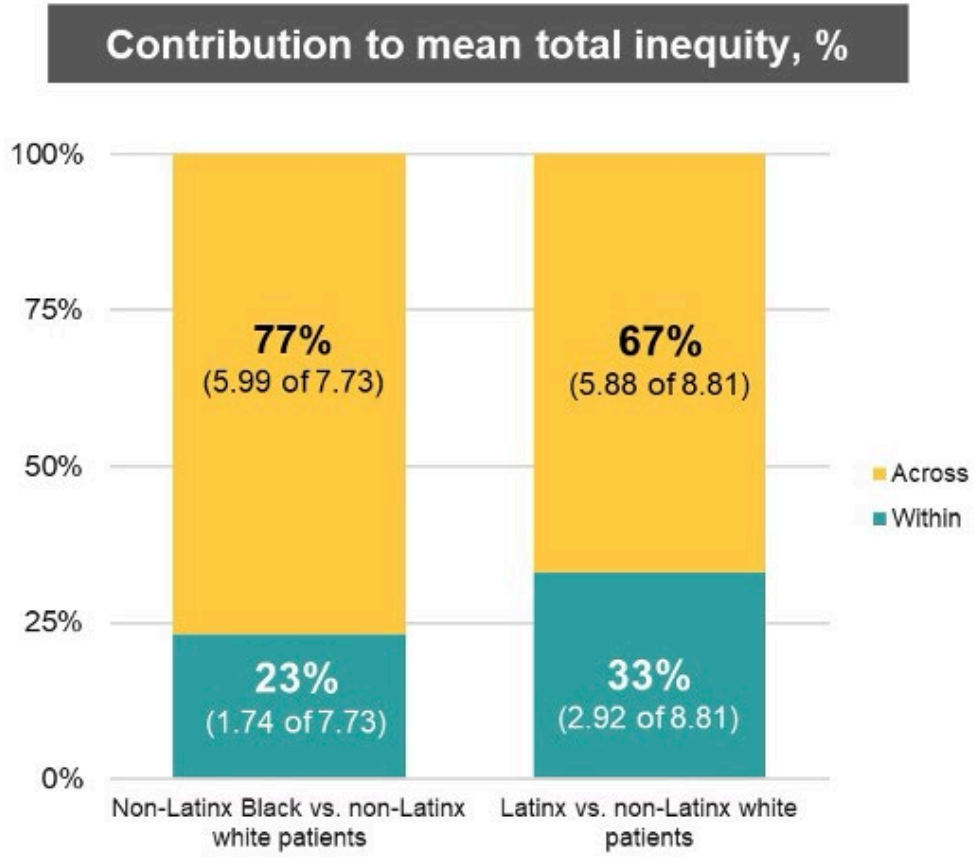
aNSCLC, advanced non-small cell lung cancer; NGS, next-generation sequencing. *Duration of observed period = aNSCLC patient count per year of observation.

Inequities in NGS testing at Provider and Practice Level

Practice Level



Provider Level

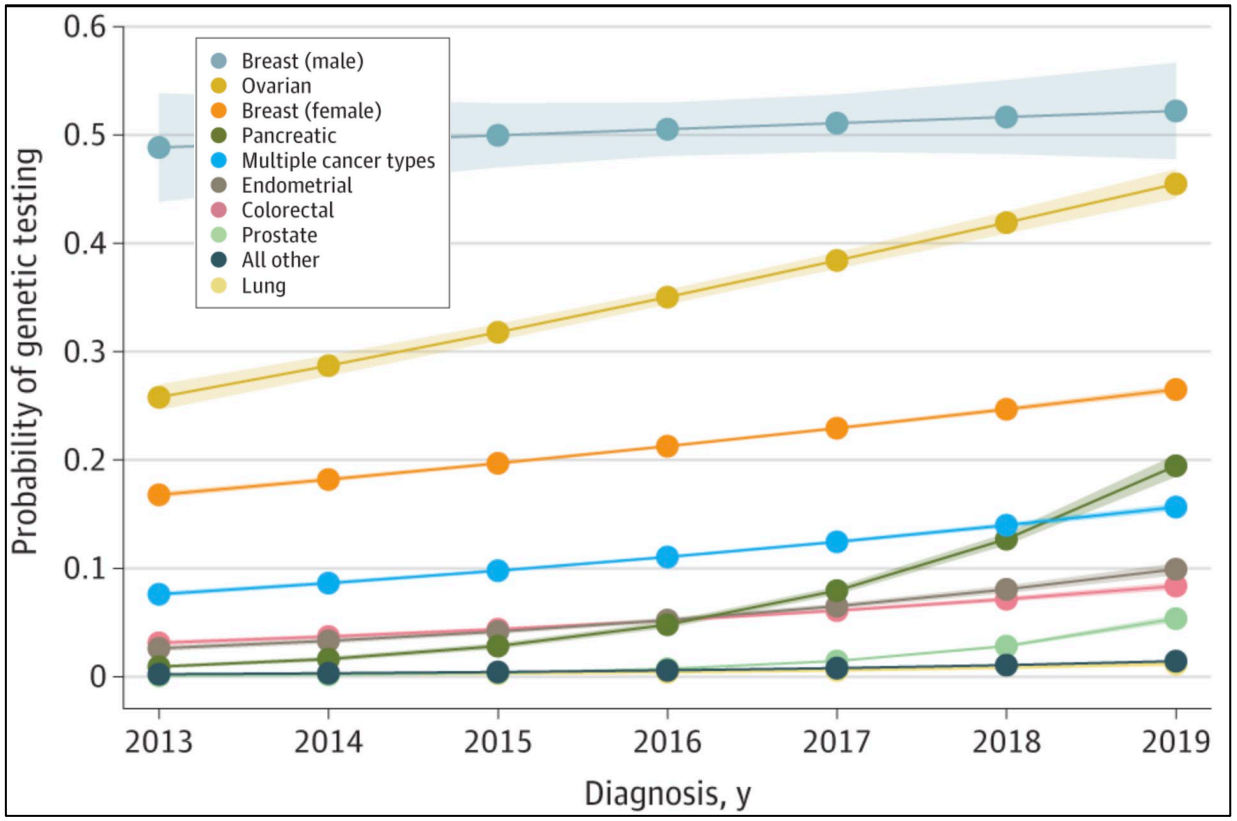


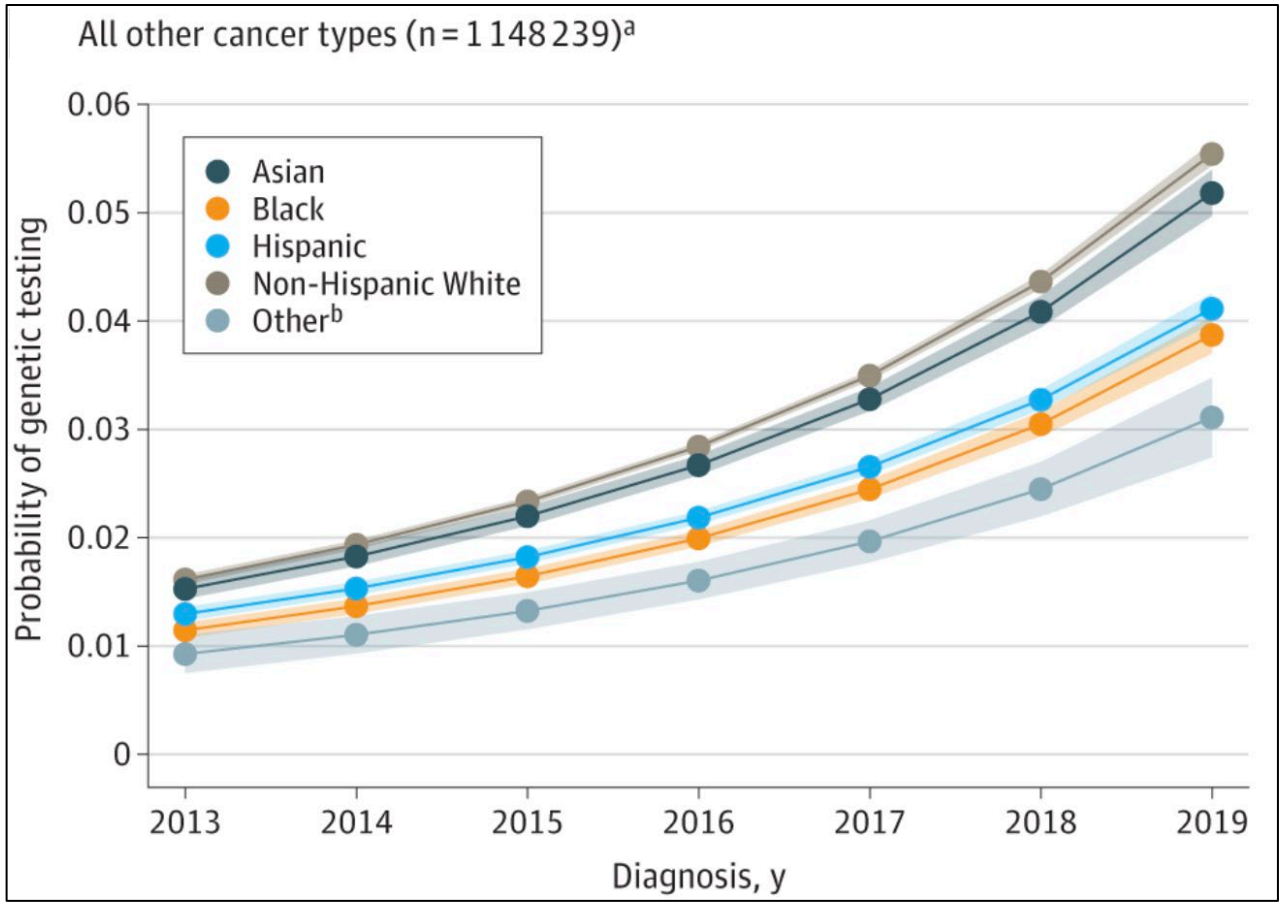
Vidal et al; JCO-OP 2024

Disparity in Germline Testing in California and Georgia

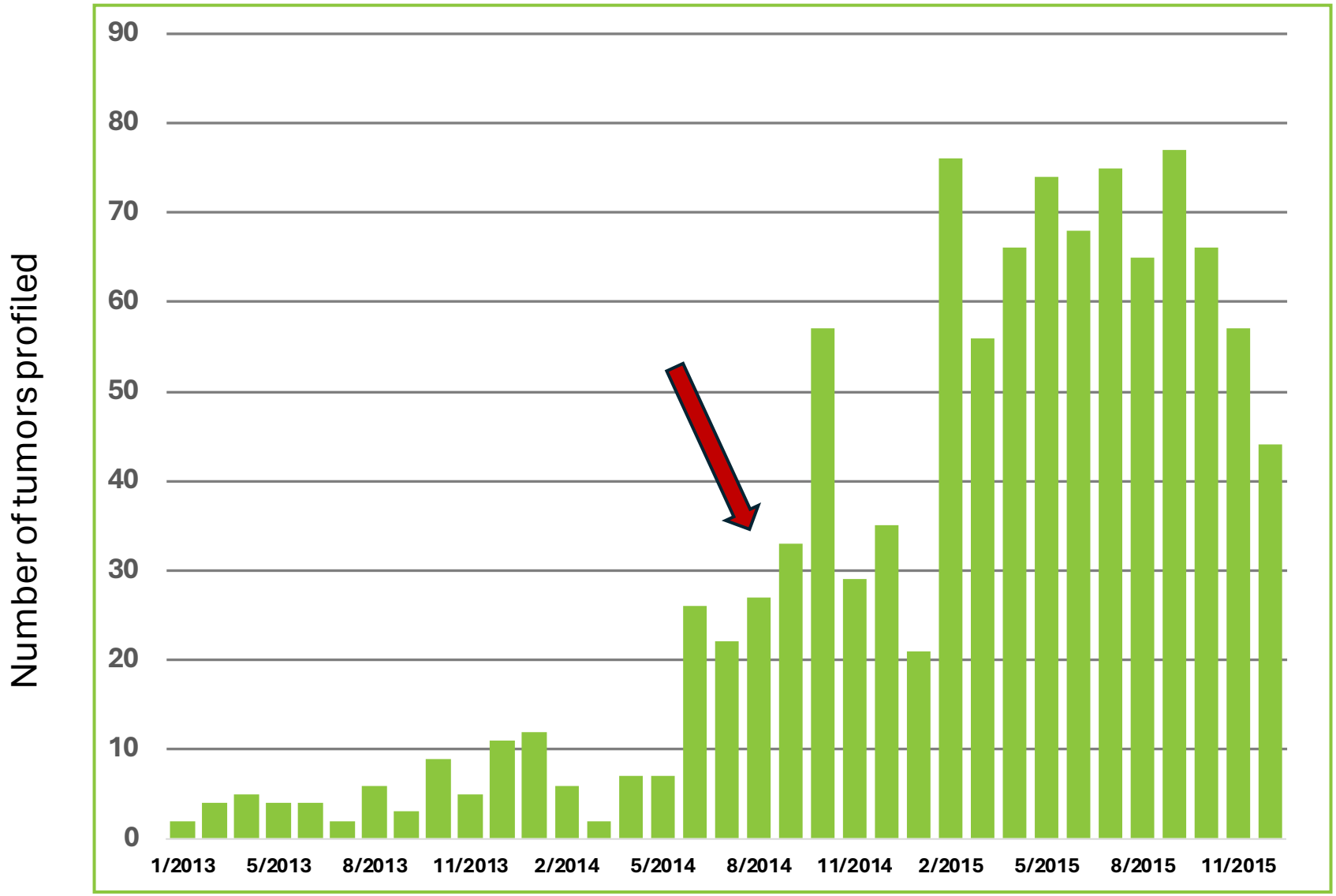
Kurian et al: JAMA 2023

Total pt:	N= 1369603
Pts tested:	N= 93052 (6.8%)



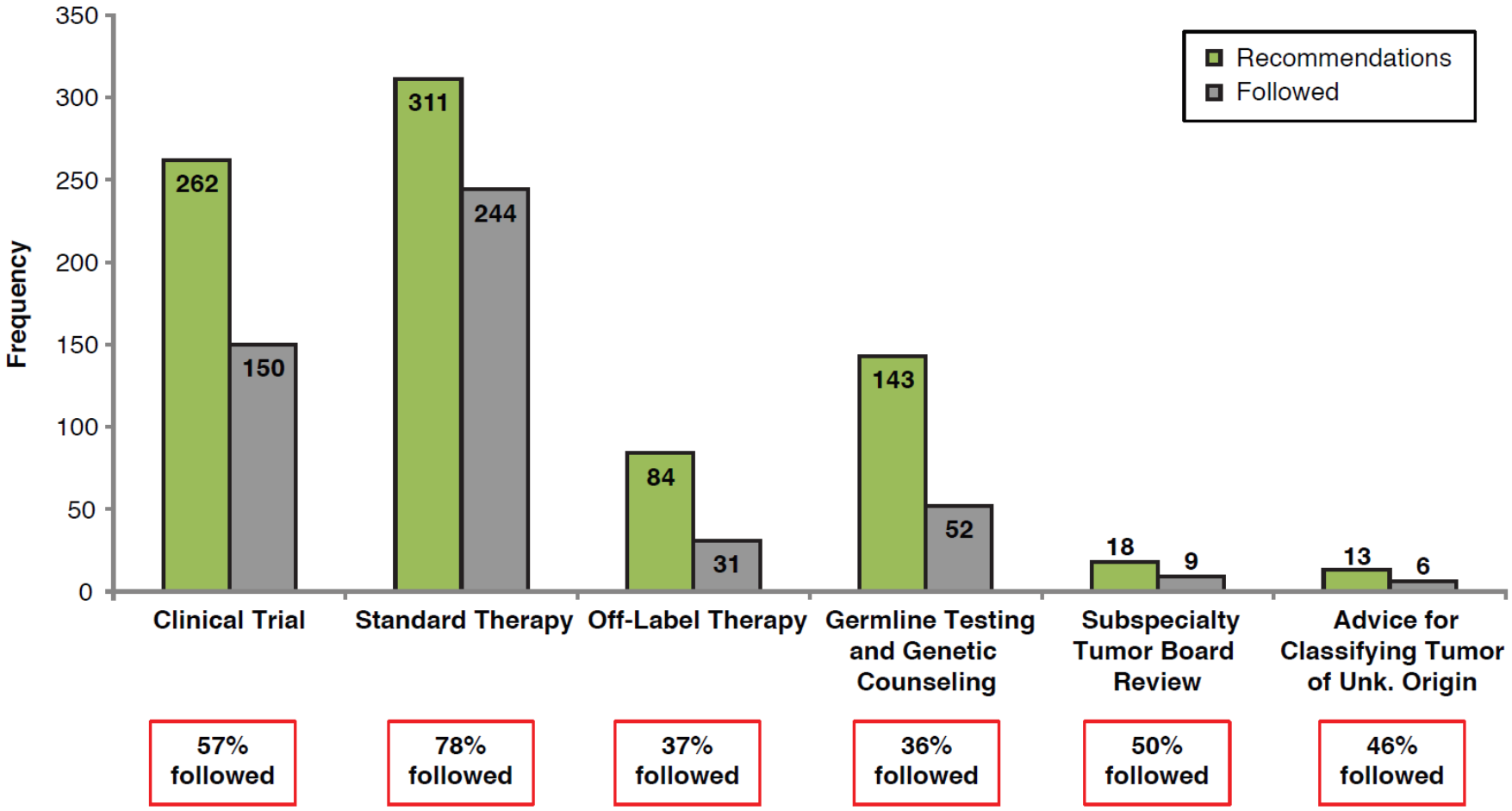


WCCRI- Rate of Uptake of Molecular Profiling



Chandler, WOC 2016

MTB recommendations and subsequent actions by treating physician



Vanderwalde.. A, Vidal...Schwartzberg L; Journal of Precision Medicine 2020

MTB Recommendations and Actions by Race

MTB Recommendation	African-American	Caucasian
Clinical Trial	31%	32%
Standard Therapy	40%	36%
Off-Label Therapy	12%	10%
Germline Testing	15%	18%

Action on Recommendation	African-American	Caucasian
Clinical Trial	52%	60%
Standard Therapy	75%	80%
Off Label Therapy	32%	39%
Germline Testing	27%	38%

Vanderwalde.. A, Vidal...Schwartzberg L; Journal of Precision Medicine 2020

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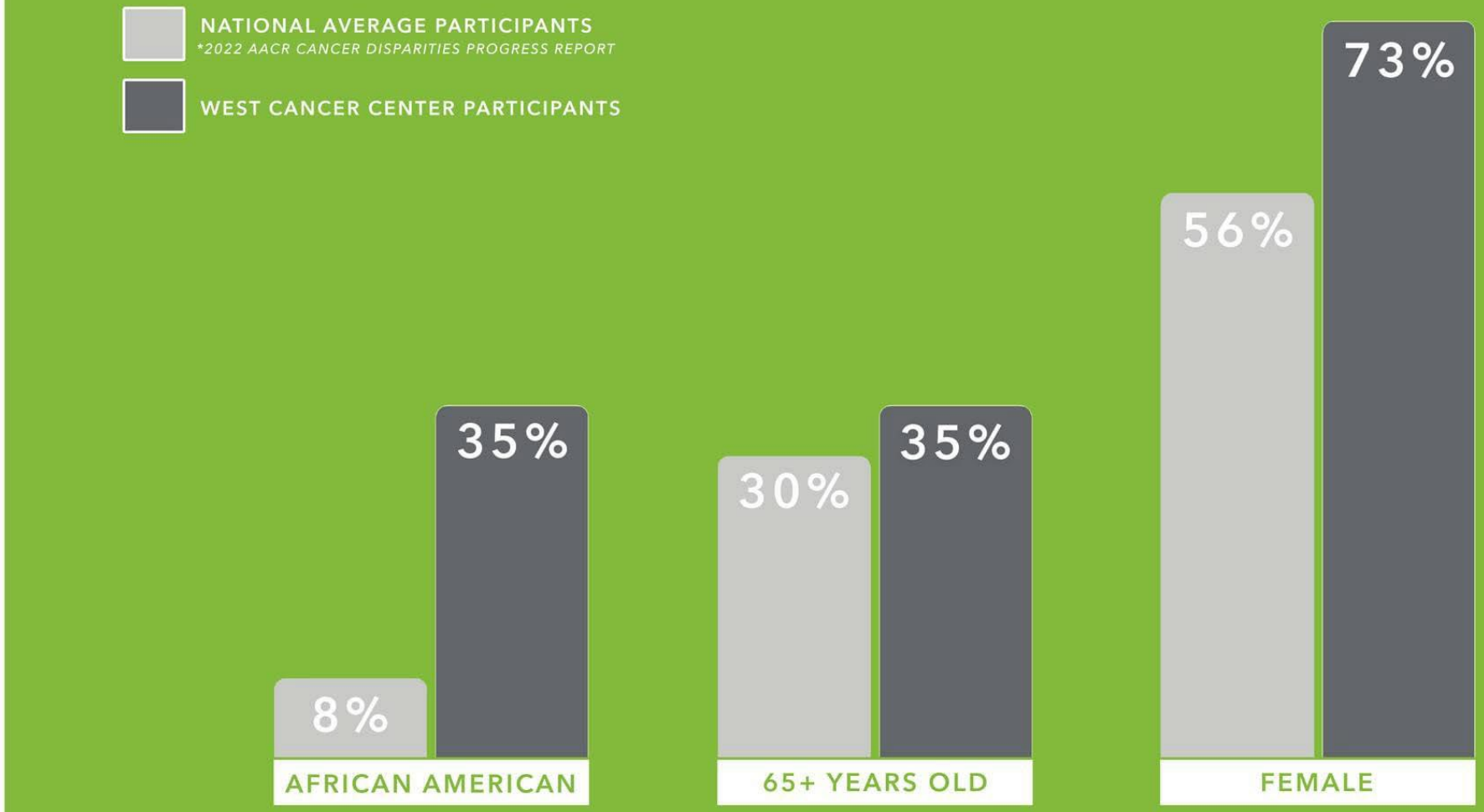
CLINICAL RESEARCH DATA: 2023



Solutions

- Systematic plan for NGS testing
  - Payers Mandating NGS testing prior to approval of oncology drug
  - Universal Germline and somatic testing- (Subbiah and Kurzrock JCO 2016 and 2023)
- Educational programs
  - Mandating CME NGS specific training –similar to pain
  - Strongly/ Encouraging Molecular TB participation for Oncologist
  - Allowing for compensation for participation in activities that directly impact patient care (ex tumor boards).
- Increase representation of underrepresented groups in Clinical Trials and in board rooms where trials ae designed
  - FDA mandate appropriate representation on clinical trial for drug approval

Thank You

- The West Cancer Center and Lee S. Schwartzberg Research Institute