Addressing Barriers in Advancing Equitable Biomarker Testing in Community Oncology

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LO #1

Evaluate the latest biomarker testing strategies in prostate, bladder, and lung cancer, including their impact on treatment decision-making

LO #2

Integrate all members of the care team in strategies to provide equitable biomarker testing in community oncology settings

LO #3

Identify the root causes of health inequity in cancer care

LO #4

Incorporate action-oriented strategies to address unconscious bias and patient social determinants of health (SDoH) in cancer care management

To Ask a Question

To submit a question, please go to the *Ask Question* tab at the bottom of the screen.

Cancer Biomarkers

- Types of biomarkers
  - Predictive biomarkers are indicative of therapeutic efficacy because there is an interaction between the biomarker and therapy relative to patient outcome
  - Prognostic biomarkers inform the odds of patient survival independent of the treatment received
  - Genes, proteins, lipids, metabolites, bits of DNA or microRNA
    - DNA biomarkers are most commonly use for treatment decision making
- Biomarker testing to detect actionable targets as part of a diagnostic work up can help personalize care
  - Biomarkers point to more effective, less toxic therapies, while avoiding ineffective therapies and unnecessary toxicities
  - Use of biomarkers reduces the overall costs of cancer care

National Cancer Institute. NCI website. 2021. https://www.cancer.gov/about-cancer/treatment/types/biomarker-testing-cancer-treatment.

Cancer Biomarkers

- National Comprehensive Cancer Network (NCCN) guidelines recommend biomarker testing in most patients with cancer
- Biomarker testing ≠ genetic testing
  - Anyone can have genetic testing to identify inherited mutations that predispose them to cancer
  - Somatic biomarker testing is specific to cancer since cancer has undergone mutations that make it different than the patient
  - However, there can be some overlap (e.g., BRCA mutations, Lynch syndrome)
- Biomarker testing may or may not be necessary prior to using specific targeted therapies — it's complicated and constantly evolving

In almost all cancer types, biomarker analyses are recommended prior to initiating therapy

National Cancer Institute. NCI website. 2021. https://www.cancer.gov/about-cancer/treatment/types/biomarker-testing-cancer-treatment.

Actionable Cancer Biomarkers

Bladder	NSCLC	Prostate
FGFR3	EGFR KRAS ALK ROS1 MET	HRR genes (e.g., BRCA1, BRCA2, ATM, PALB2, FANCA, RAD51D, CHEK2, CDK12, others) PSMA
Tumor-agnostic:	NTRK, PD-L1, MSI-H/dMMR, TMB, BRAF V600E, RET, HER2	

HRR, homologous recombination repair; MSI-H, microsatellite instability high; TMB, tumor mutational burden.

NCCN Guideline. Prostate Cancer. v4.2024. https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf.
NCCN Guideline. Non-Small Cell Lung Cancer. v10.2024. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf.
NCCN Guideline. Bladder Cancer. v4.2024. https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf.
Subbiah V, et al. *CA Cancer J Clin*. 2024;74(5):433–452.

Rising Use of Multi-gene Biomarker Analyses

- Single gene testing is rapidly being abandoned in favor of more comprehensive approaches (e.g., NGS, WGS, WES)
  - Expanding repertoire of biomarker-based therapy options, including tumor-agnostic indications

	SNV/ Indels	Fusions	CNV	TMB	MSI	HRD	Gene Expression	Tissue Need	Cost	TAT	Germline Correlation Needed
Sanger sequencing	✓							+	$	<1 week	No
NGS- targeted panel (20–100 genes)	✓							+	$	1–2 weeks	No
FISH		✓	✓					++	$	<1 week	No
NGS-large panel (hundreds)	✓	✓	✓	✓	✓	✓		++	$$	2+ weeks	Desired
WES	✓		✓	✓	✓	✓		++	$$$	Weeks–months	Yes
WGS	✓	✓	✓	✓	✓	✓		+++	$$$	Weeks–months	Yes
WTS	✓	✓					✓	++	$$$	Weeks–months	N/A

CNV, copy number variant; FISH, florescence in situ hybridization; HRD, homozygous repair deficiency; MSI, microsatellite instability; SNV, single nucleotide variant; TAT, turn-around time; TMB, tumor mutational burden; WES, whole exome sequencing; WGS, whole genome sequencing; WTS, whole transcriptome. sequencing.

Sholl LM, Halmos B. *Brit J Cancer*. 2022;127(7):1177–1179.

Benefits and Limitations of Biomarker Assessment Techniques

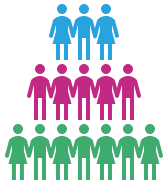
	DNA and RNA				Protein
	NGS	RT-PCR	PCR	FISH	IHC
Benefits	• Large throughput • High accuracy • Rich content information • Multiple types of genetic alterations	• Highly sensitive • Detects fusion transcripts at the RNA level	• Allows for rapid testing	• Knowledge of fusion partner not required • Rearrangements can be discriminated from polysomy/ amplifications	• Sensitive • Familiar • Time saving and easily automatable • Cost-friendly • Many validated antibodies available
Limitations	• Turnaround time • Tissue sample needs • Reports can be hard to interpret • Wide variety of NGS assay platforms	• Poor quality of FFPE RNA samples • Limited number of variants tested at once	• Only test 1 gene at a time • Requires high tumor enrichment	• Not all rearrangements produce an expressed fusion transcript • May miss unknown variants	• May require confirmatory test • Accuracy can vary by fixative and background • Insufficient tumor content of tissue • Skilled pathologist required

IHC, immunohistochemistry; PCR, polymerase chain reaction; RT-PCR, reverse transcriptase PCR

Bruno R, Fontanini G. *Diagnostics (Basel)*. 2020;10(8). Frankel D, et al. *Int J Mol Sci*. 2022;23(18). Pennell NA, et al. *Am Soc Clin Oncol Educ Book*. 2019(39):531–542. Sholl LM, Halmos B. *Brit J Cancer*. 2022;127(7):1177–1179.

Landscape of Biomarker Testing Coverage

- 15 states have laws mandating biomarker coverage (May 2024)
- >50% of U.S. population may not be covered by legislative mandates governing insurance coverage
- State mandates may not significantly impact those most affected by healthcare disparities (e.g., uninsured or some Medicaid populations)



>2.0 Million

people are estimated to be diagnosed with cancer in 2024 in the United States

>$1,200

upfront costs for broad panel biomarker testing

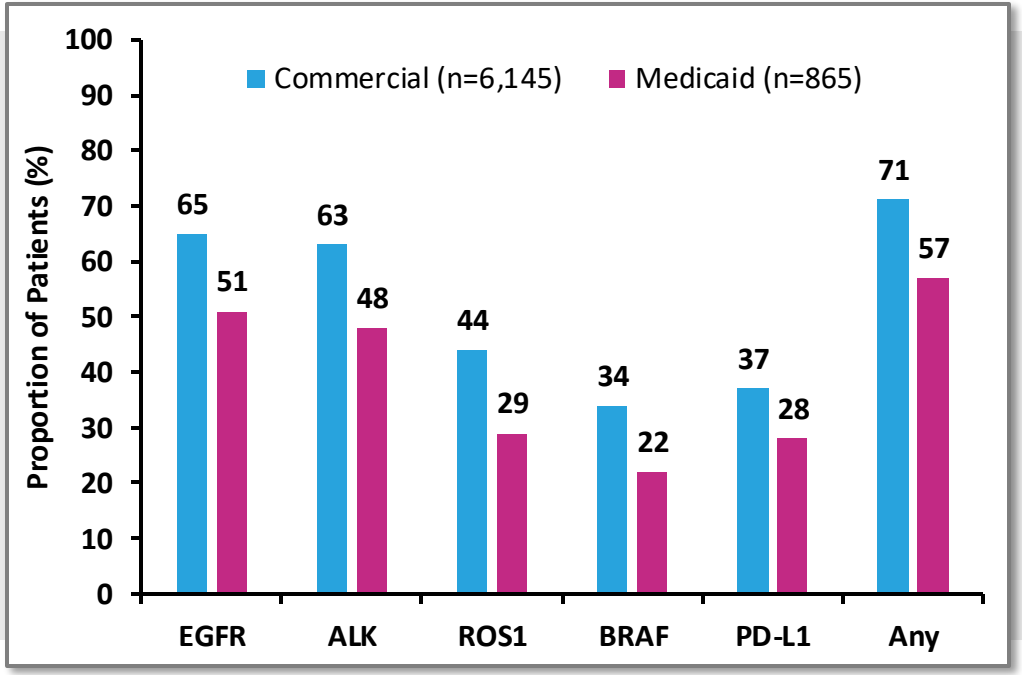
66%

oncology providers reporting lack of biomarker testing coverage as a barrier to care

Siegel RL, et al. *CA Cancer J Clin.* 2024;74(1):12–49. Lin GA, et al. *JAMA.* 2024;331(22):1885–1886.
Dieguez G, Carioto J. Milliman website. 2022. https://www.milliman.com/en/insight/the-landscape-of-biomarker-testing-coverage-in-the-US.
Association of Cancer Care Centers. ACCC website. 2023. https://www.accc-cancer.org/acccbuzz/blog-post-template/accc-buzz/2023/12/12/the-cost-of-biomarker-testing-moving-from-support-based-to-sustainable-solutions.

Biomarker Testing Patterns by Insurance Type

- Coverage issues remain a leading concern of providers
- Disconnect between covering tests vs drugs
- Retrospective analysis of nationwide U.S. healthcare database of patients receiving a diagnosis of advanced NSCLC from 2011–2019
- Receipt of biomarker testing (ALK, EGFR, ROS1, BRAF, and PD-L1) was assessed



Gross CP, et al. *J Natl Compr Canc Netw*. 2022;20(5):479–487.

Which of the following did community oncology clinicians identify as the factor that would make them LEAST likely to order biomarker testing for their patients with NSCLC?

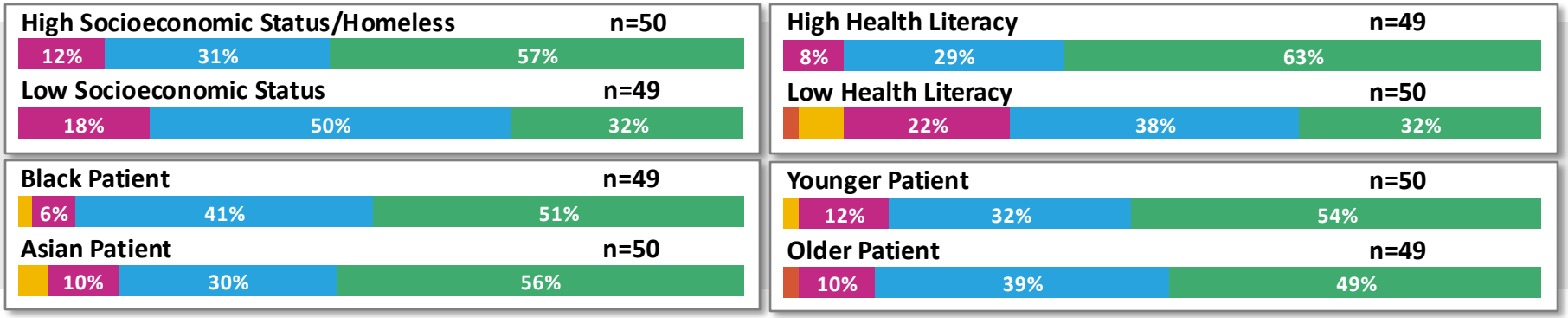
A. Low economic status
B. Low health literacy
C. Black ethnicity
D. Older patient
E. I don’t know

Which of the following did community oncology clinicians identify as the factor that would make them LEAST likely to order biomarker testing for their patients with NSCLC?

A. Low economic status
B. Low health literacy
C. Black ethnicity
D. Older patient
E. I don’t know

Gaps in Biomarker Testing between Community and Academic Oncology Settings

Patient Characteristics Affecting the Likelihood of Ordering Biomarker Testing (all clinicians)



- 99 clinicians (67% community setting) who treat patients with NSCLC responded to an online survey from ACCC (2020)

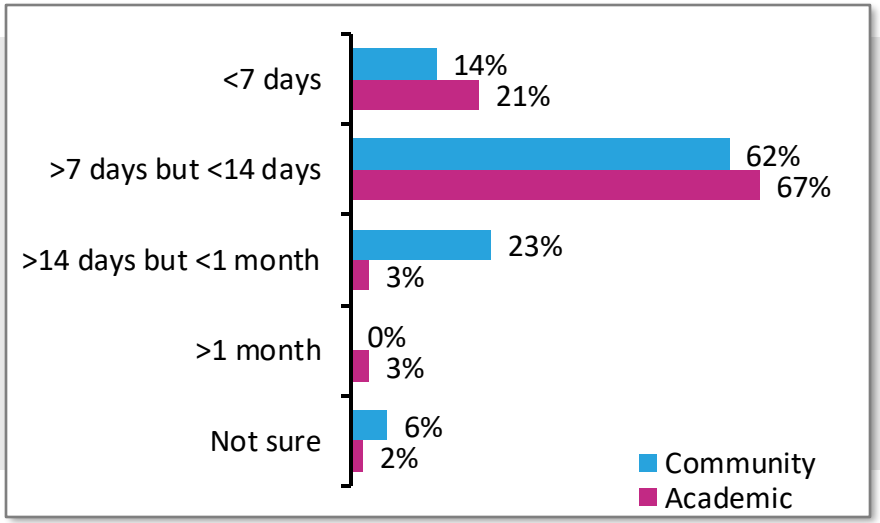
While most clinicians surveyed discuss biomarker testing with their patients with lung cancer, the likelihood of ordering guideline concordant testing decreased for patients with lower socioeconomic status and health literacy.

Boehmer L, et al. *J Clin Oncol*. 2021;39(suppl 28): 123.

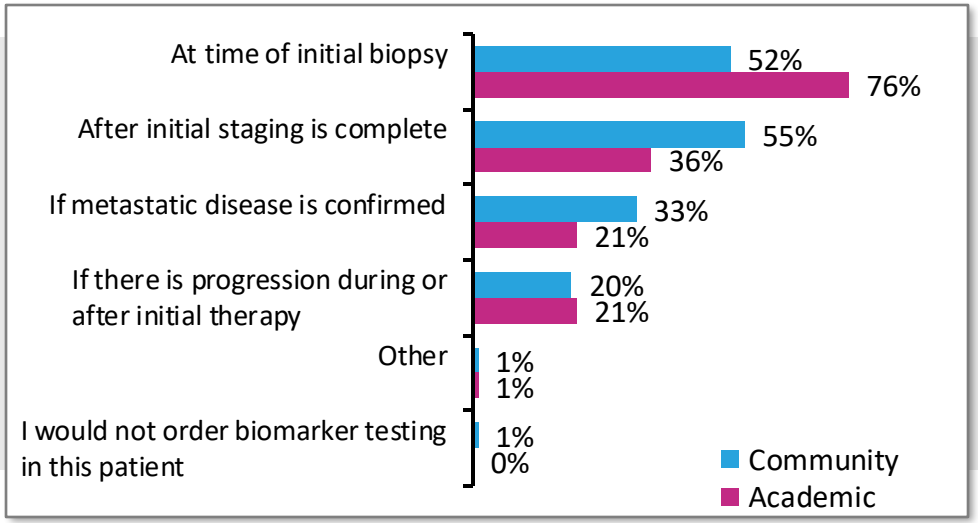
Gaps in Biomarker Testing between Community and Academic Oncology Settings

- 99 clinicians (67% community setting) who treat patients with NSCLC responded to an online survey from ACCC (2020)

Approximate Time to Receipt of Test Results



At What Point in the Course of This Patient's Management Would You Order Biomarker Testing?



ACCC, Association of Cancer Care Centers; NSCLC, non–small cell lung cancer.

Real-world NSCLC Biomarker Testing Rates

Retrospective observational chart review of metastatic NSCLC (mNSCLC) patients initiating first-line therapy between (April 2018–March 2020)

- 90% of patients received ≥1 biomarker test
- 46% received all 5 biomarker tests
- Next-generation sequencing (NGS) testing increased from 33% to 44% (P<0.0001)
- Time from mNSCLC diagnosis to biomarker results: 14–21 days
- Turn around time (TAT) from biomarker testing orders to results: 10–15 days
- Time from mNSCLC diagnosis to first-line therapy: 35 (22, 55) days

	Total Patients	Cohort 1 Biomarker Test Result Received Prior to First Line	Cohort 2 Biomarker Test Result Received During/After First Line	Cohort 3 No Biomarker Test
Overall n (%)[a]	3,474	2,752 (79)	371 (11)	351 (10)
Any biomarker test[b]	3,123	2,752 (88)	371 (12)	NA
5 biomarker tests[b]	1,602	1,230 (77)	372 (23)	NA
Biomarker testing, n (%)[a]				
ALK	2,446	1,986 (57)	460 (13)	1,028 (30)
BRAF	1,912	1,489 (43)	423 (12)	1,562 (45)
EGFR	2,443	1,979 (57)	464 (13)	1,031 (30)
PD-L1	2,882	2,526 (73)	356 (10)	592 (17)
ROS1	2,348	1,897 (55)	451 (13)	1,126 (32)

[a]Row percentage denominator: 3,474

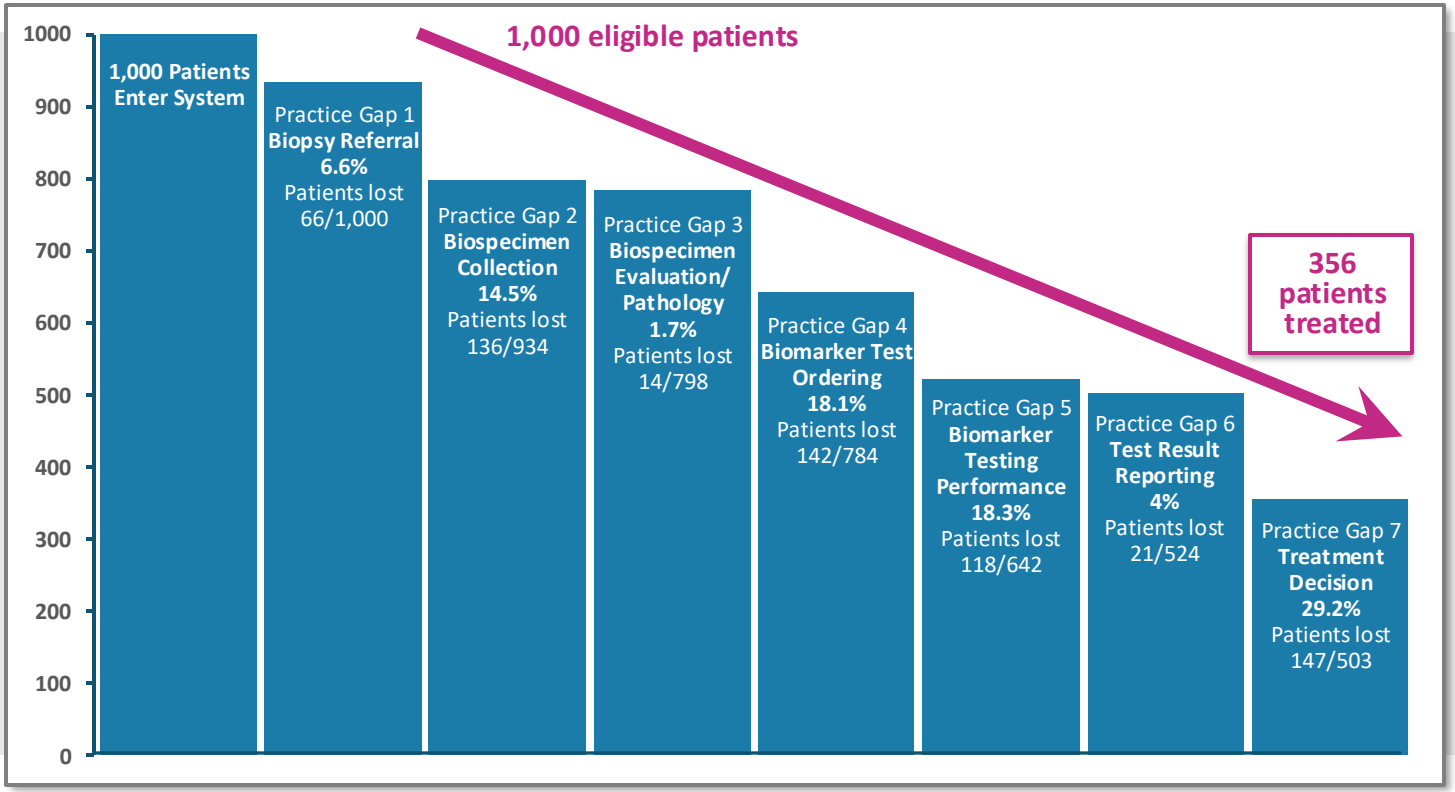
[b]Row percentage denominator: total patients with test

Note: Additional biomarkers have been deployed since this study was undertaken

Robert NJ, et al. *J Clin Oncol*. 2021;39(15_suppl):9004.

Clinical Process Gaps Result in Lung Cancer Patients Missing the Opportunity to Benefit from Personalized Medicine

"The data was normalized to a patient population of **1,000** to easily demonstrate the number of eligible patients that may be lost to receiving targeted therapies due to each clinical practice gap."

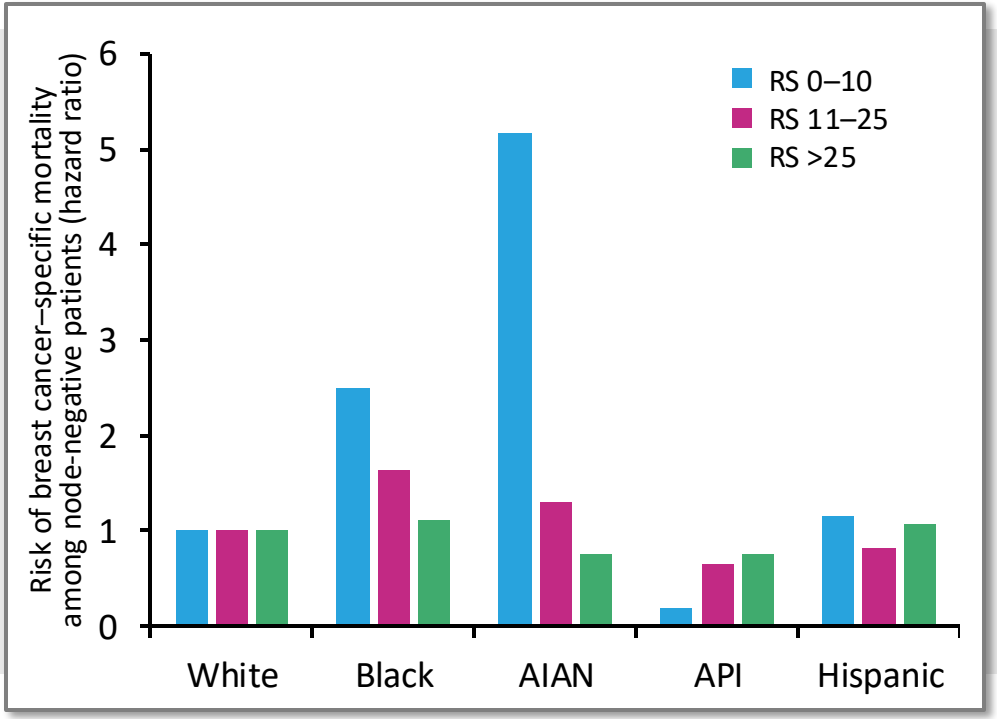


Sadik H, et al. *JCO Precis Oncol*. 2022;6:e2200246.

Underrepresentation of Ethnic Groups in Biomarker Development

- 21-gene Oncotype DX Breast Recurrence Score (RS) test is used for risk-adapted treatment decisions among patients with early breast cancer
- The landmark trial validating the RS included only 5% Black women
- This study examined the prognostic accuracy of the RS in ethnic minority groups

Multivariant analysis adjusted for age, year of diagnosis, tumor size, progesterone receptor status, type of surgery, and administration of radiotherapy and chemotherapy

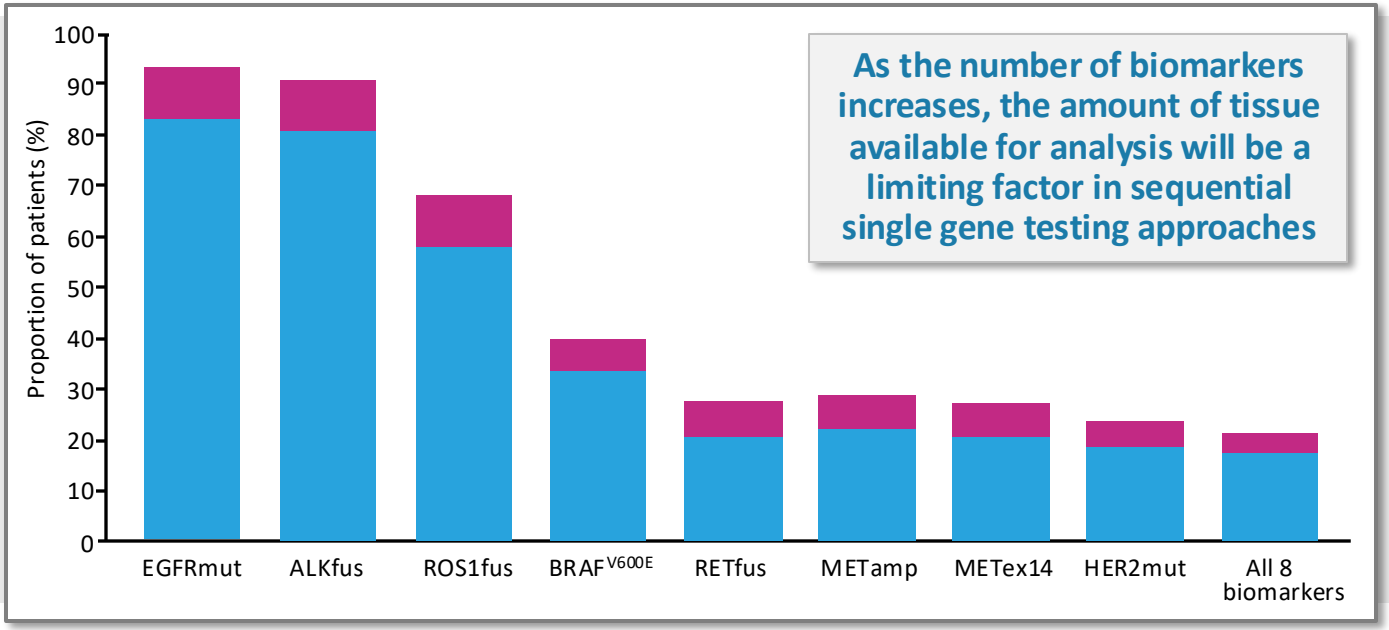


AIAN, American Indians and Alaska Natives; API, Asian and Pacific Islanders.
Paik S, et al. *N Engl J Med.* 2004;351(27):2817–2826.

Barriers to NSCLC Biomarker Testing
Tissue Limitations

Prospectively enrolled patients with previously untreated mNSCLC undergoing physician discretion SoC tissue genotyping submitted a pretreatment blood sample for comprehensive cell-free DNA analysis

- 68.1% of patients were under genotyped*
  - Only ~18% of patients were tested for all eight recommended biomarkers by tissue biopsy



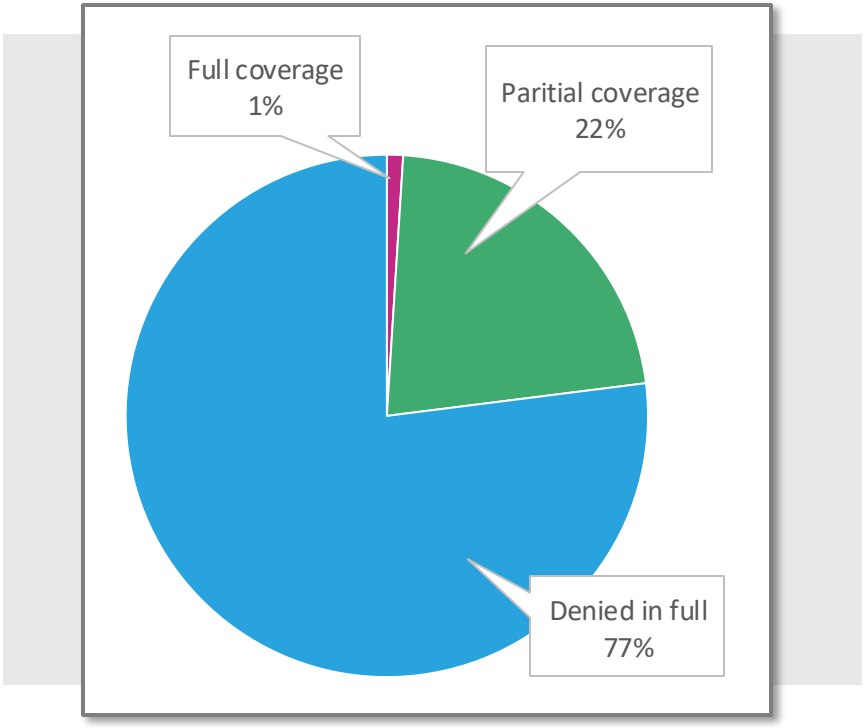
SoC, standard of care.

*Did not have a guideline recommended biomarker identified and were not assessed for all guideline recommended biomarkers

Leighl NB, et al. *Clin Cancer Res*. 2019;25(15):4691–4700.

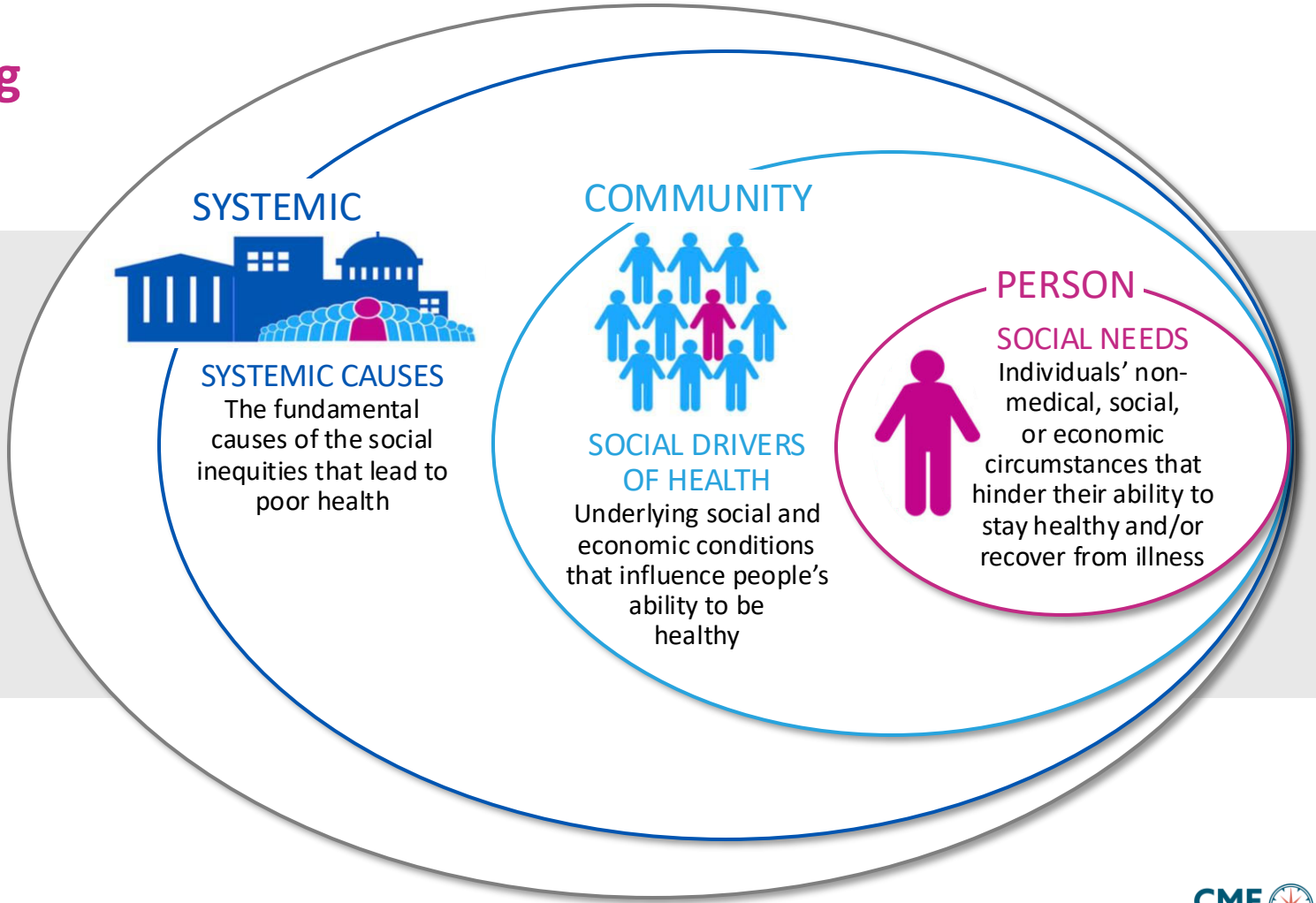
Barriers to NSCLC Biomarker Testing
Payer Coverage

- In 2020, a study among 246 cases (January 2017–March 2018) in New York showed majority of tests denied payer coverage and only 10.75% of the total NGS service charge was reimbursed
- Coverage through private payers may be variable



Leighl NB, et al. *Clin Cancer Res*. 2019;25(15):4691–4700.

Factors Contributing to Health Disparities



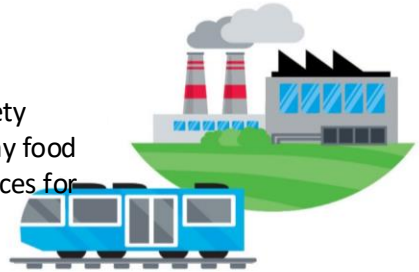
American Hospital Association (AHA). AHA website. 2022. https://www.aha.org/societalfactors.

U.S. Cancer Disparities

Complex and interrelated factors contribute to cancer health disparities in the United States. Adverse differences in many, if not all, of these factors are directly influenced by structural and systemic racism. The factors may include, but are not limited to, differences or inequalities in:

Environmental Factors

- Air and water quality
- Radon
- Transportation
- Housing
- Community safety
- Access to healthy food sources and spaces for physical activity



Behavioral Factors

- Tobacco use
- Diet
- Excess body weight
- Physical inactivity
- Adherence to cancer screening and vaccination recommendations

Social Factors

- Education
- Income
- Employment
- Health literacy

Clinical Factors

- Access to health care
- Quality of health care

Cultural Factors

- Cultural beliefs
- Cultural health benefits

Psychological Factors

- Stress
- Mental health

Biological and Genetic Factors

Mitchell E, et al. *J Natl Med Assoc*. 2022;114(3):236–250.
National Cancer Institute. NCI website. Updated 2024. https://www.cancer.gov/about-cancer/understanding/disparities.

Biomarker Testing in Underserved Patient Populations

- Insurer coverage important for provider uptake and patient access to biomarker testing
  - Coverage differs greatly across the multiple public and private U.S. payers
  - Clinical utility often required—"experimental" biomarkers often used in clinical trials may not be covered

All Patients with NSCLC				
	NSCLC Overall N=14,768	White n=9,793	Black/AA n=1,288	*P*-value White vs Black/AA
Ever tested	11,297 (76.5%)	7,477 (76.4%)	948 (73.6%)	0.03
Tested prior to first-line therapy		6,064 (61.9%)	784 (60.9%)	0.47
Ever NGS tested	7,185 (48.7%)	4,904 (50.1%)	513 (39.8%)	<0.0001
NGS tested prior to first-line therapy		3,081 (31.5%)	332 (25.8%)	<0.0001
Patients with Non-squamous NSCLC				
	Non-squamous N=10,333	White n=6,705	Black/AA n=922	*P*-value White vs Black/AA
Ever tested	8,786 (85%)	5,699 (85%)	764 (82.9%)	0.09
Tested prior to first-line therapy		4,881 (72.8%)	662 (71.8%)	0.52
Ever NGS tested	5,494 (53.2%)	3,668 (54.7%)	404 (43.8%)	<0.0001
NGS tested prior to first-line therapy		2,452 (36.6%)	274 (29.7%)	<0.0001

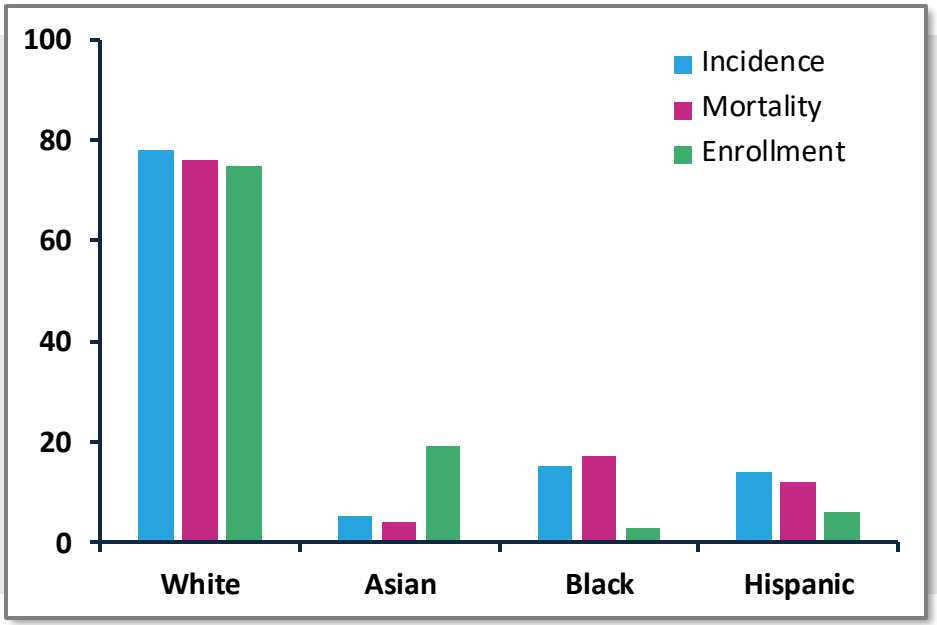
AA, African American.

American Cancer Society (ACS). ACS Action Network website. 2022. https://www.fightcancer.org/policy-resources/improving-access-biomarker-testing.
Bruno DS, et al. *J Clin Oncol*. 2021;39(15_suppl):9005.

Black Patient Representation in Clinical Trials

- Trial participation is lowest among Black patients
- Patient-cited barriers to clinical trial enrollment
  - Mistrust of clinical research
  - Perceived harms
  - Costs
  - Transportation
  - Unclear about goals of trials
  - Time
  - Fear
  - Family

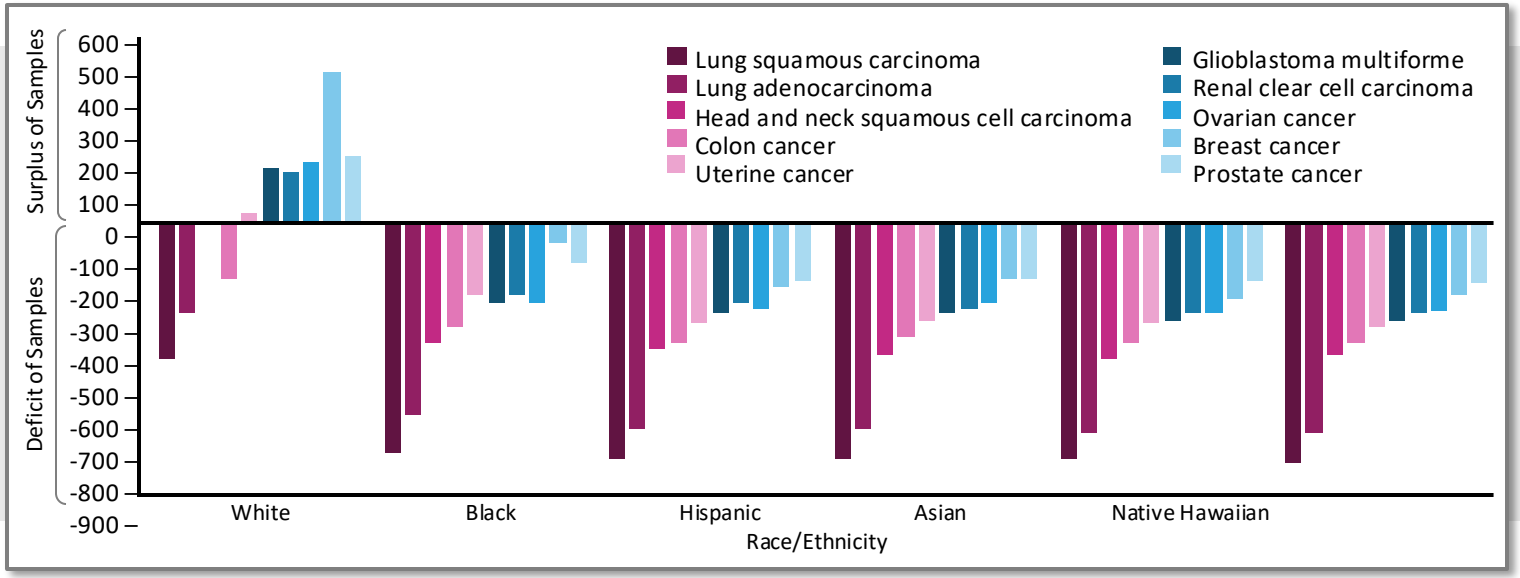
Relative proportion among U.S. patients with cancer compared with trial participants in FDA-approval trials between July 2008 and June 2018.



Ford JG, et al. *Cancer.* 2008;112(2):228–242. Unger JM, et al. *JNCI Cancer Spectr.* 2020;4(4):pkaa034.

Importance of Diversity in Precision Medicine

- Number of samples needed to detect a 5% mutational frequency rate



- Despite the advances gained from genomic sequencing, dedicated efforts beyond TCGA are needed to avoid widening the cancer health disparities gap
- Ethnic diversity in genomic sequencing efforts is important to the generalizability and availability of genomic-based treatments

Spratt DE, et al. *JAMA Oncol*. 2016;2(8):1070–1074.

Factors That Influence Access to Cancer Care

- Patient level
- Provider level
- Systemic level
- Societal level

- Comorbid conditions, overall health status
- Patient health literacy
- Health care beliefs and participation in decision-making
- Personal support system
- Affluency

Recognize the patient is not the "problem," but that the broader society and health care organizations and providers are additional sources of barriers

Osarogiagbon RU, et al. *Am Soc Clin Oncol Educ Book*. 2021(41):66–78.

Factors That Influence Access to Cancer Care

- Patient level
- Provider level
- Systemic level
- Societal level

- Failure to provide guideline-recommended care
  - Biomarker testing
  - Cancer treatments
  - Clinical trials
- Provider knowledge, training, skillsets, years of practice, specialty
- Beliefs and attitudes (e.g., conscious and unconscious biases)

Osarogiagbon RU, et al. *Am Soc Clin Oncol Educ Book*. 2021(41):66–78.

Factors That Influence Access to Cancer Care

- Patient level
- Provider level
- Systemic level
- Societal level

- Geographic location
- Availability of culturally competent services
  - Inadequate medical interpretation services
- Health care worker diversity
- Affiliation with research or academic health care systems
- Inequities of physical infrastructure and technology
- Processes (e.g., reimbursement contracts, scheduling and referrals, hours of operation, and availability of language options)
- Inadequate staffing (burnout and workload)

Osarogiagbon RU, et al. *Am Soc Clin Oncol Educ Book*. 2021(41):66–78.

Factors That Influence Access to Cancer Care

- Patient level
- Provider level
- Systemic level
- Societal level

- Social "drivers" of health
- Socioeconomic and health care policies
- A high proportion of uninsured or underinsured individuals in a population adversely affects access to care and overall quality of care in the whole population
  - Inadequate medical insurance
  - Unequal/disparate job opportunities
  - Unequal/disparate educational opportunities
  - Inadequate public transportation infrastructure

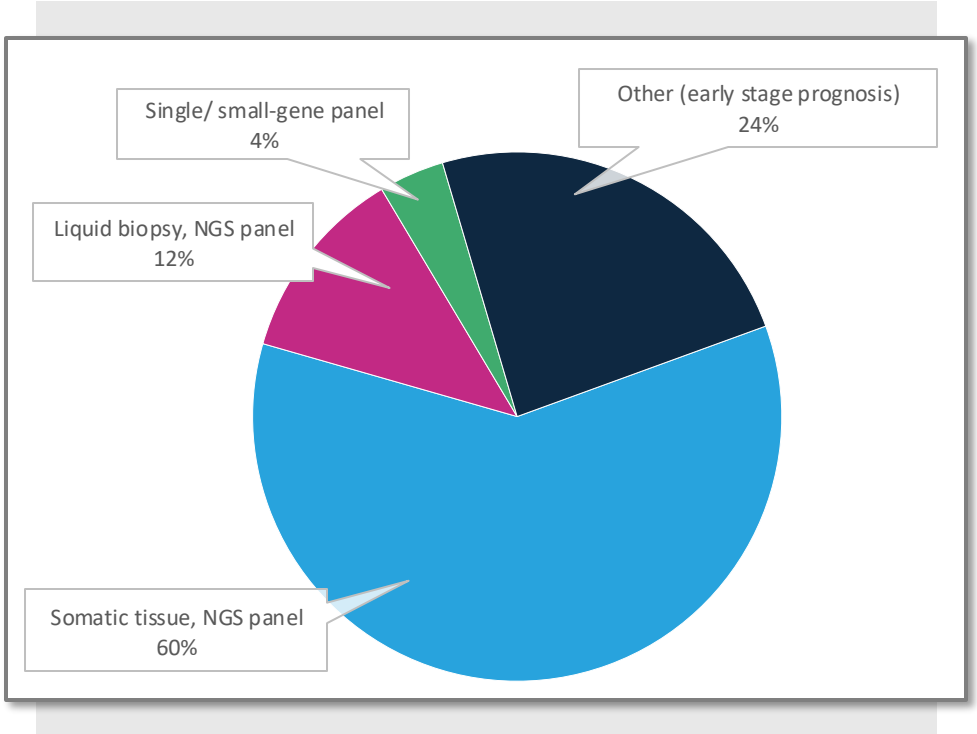
Osarogiagbon RU, et al. *Am Soc Clin Oncol Educ Book*. 2021(41):66–78.

Texas Oncology PMQI Program

Goal: To improve testing rates and provide patients access to targeted therapies/clinical trials

Methods

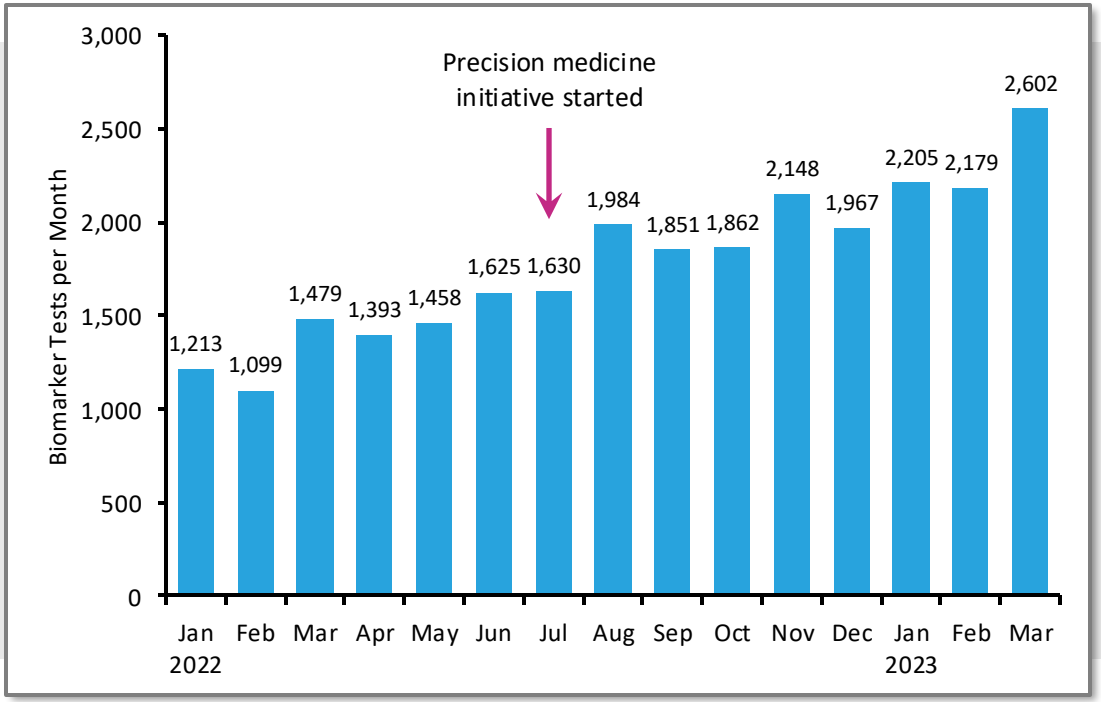
- Patients with eligible solid tumors
- PMQI recommended testing utilizing a broad panel NGS test
- Somatic tissue or liquid biopsy
- Testing ordered through clinical support tool
- Testing order tracked through EHR and tracking tools
- Retrospective analysis January 2022–March 2023



PMQI, Precision Medicine Quality Initiative.

Brisbin L, et al. *JCO Oncol Pract*. 2023;19(11_suppl):385.

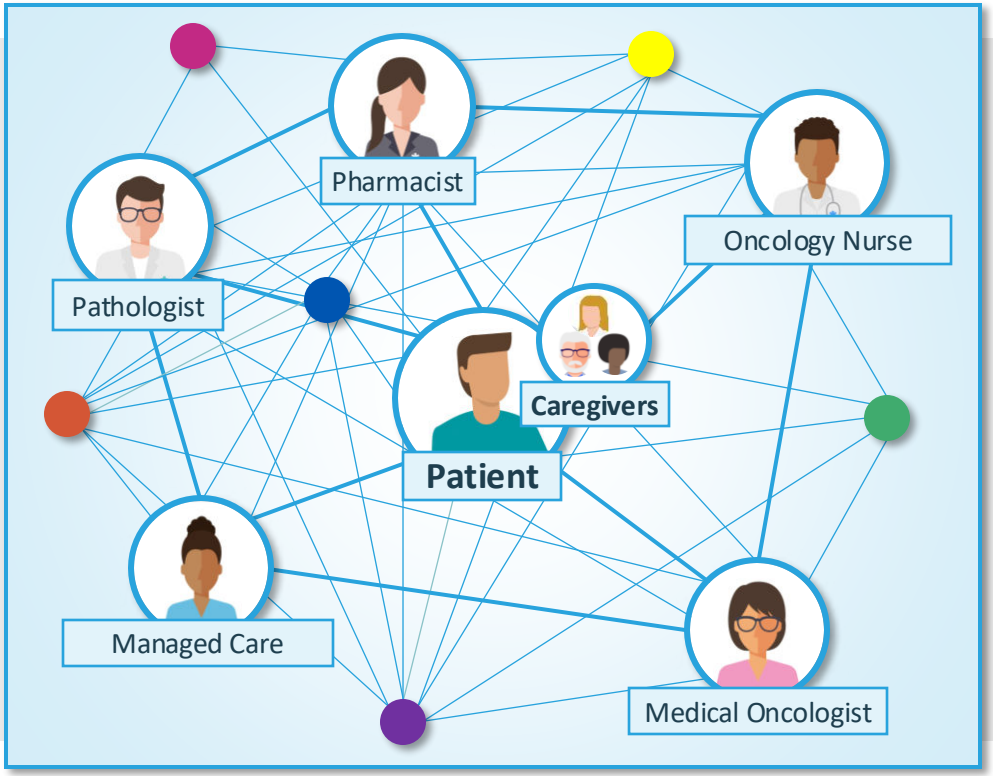
Texas Oncology PMQI Program



- Biomarker testing increased across all tumor types
- Broad-panel NGS tests were ordered increasingly over single gene or small-panel tests
- Liquid biopsies more than doubled
- Testing increased in rural/underserved regions

Brisbin L, et al. *JCO Oncol Pract*. 2023;19(11_suppl):385. Mirsalehi A, et al. *JCO Oncol Pract*. 2023;19(11_suppl):513.

Team-based Approach for the Management of Patients with Cancer



In general, treatment recommendations should be made by a multidisciplinary team (MDT).

MDTs increase treatment personalization, improve outcomes, preserve quality of life, and increase overall patient satisfaction.

Each person on the care team should:

- Verify timely use of biomarker analyses
- Encourage use of multi-gene assays over single-gene assays

Cornelius LA, et al. *Oncologist*. 2021;26(9):e1644–e1651. Daly ME, et al. *J Clin Oncol*. 2022:40(12).
NCCN Guideline. Non–small Cell Lung Cancer. v10.2024. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf.

Questions & Answers

Summary

- Biomarker testing is a critical step in assuring compliance with evidence-based treatment guidelines
- Structural racism, SDoH, and unconscious bias contribute to cancer care disparities, including screening and treatment
- Eliminating cancer care disparities will require a multiprong approach that engages the patient, provider, healthcare system, and society
- Addressing barriers to care requires culturally-appropriate, linguistically-aligned shared decision making and coordinating coverage through community oncology and managed care providers

Put information into action!

Takeaways from this program can be implemented into your practice to improve patient care.

- Ensure that each patient with cancer receives comprehensive biomarker screening through documentation in the EHR system, and if documentation is not present, follow up with request for comprehensive testing and documentation in the EHR of outcome from the request
- Alert supervisors if you see intentional or unintentional biases by your coworkers that affects cancer care
- Engage in thoughtful self reflection on your own biases and preconceived ideas about patients
- Encourage use of a navigator to assist with all the issues of coverage and affordability, working with specialty pharmacy to address these issues, patient support from manufacturers, etc.
- Work with supervisors and team members to revise processes that impede patients from receiving guideline-concordant biomarker screening

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