Commentary

# State legislative trends related to biomarker testing

Gelareh Sadigh, MD [1]; Hilary Gee Goeckner, MSW[2]; Ella A. Kazerooni, MD [3,4]; Bruce E. Johnson, MD[5]; Robert A. Smith, PhD [6]; Devon V. Adams, RN, MPH[2]; and Ruth C. Carlos, MD [3]

Comprehensive biomarker testing has become the standard of care for informing the choice of the most appropriate targeted therapy for many patients with advanced cancer. Despite evidence demonstrating the need for comprehensive biomarker testing to enable the selection of appropriate targeted therapies and immunotherapy, the incorporation of biomarker testing into clinical practice lags behind recommendations in National Comprehensive Cancer Network guidelines. Coverage policy differences across insurance health plans have limited the accessibility of comprehensive biomarker testing largely to patients whose insurance covers the recommended testing or those who can pay for the testing, and this has contributed to health disparities. Furthermore, even when insurance coverage exists for recommended biomarker testing, patients may incur burdensome out-of-pocket costs depending on their insurance plan benefits, which may also create barriers to testing. Prior authorization for biomarker testing for some patients can add an administrative burden and may delay testing and thus treatment if it is not done in a timely manner. Recently, three states (Illinois, Louisiana, and California) passed laws designed to improve access to biomarker testing at the state level. However, there is variability among these laws in terms of the population affected, the stage of cancer, and whether the coverage of testing is mandated, or the legislation addresses only prior authorization. Advocacy efforts by patient advocates, health care professionals, and professional societies are imperative at the state level to further improve coverage for and access to appropriate biomarker testing. ***Cancer* 2022;128:2865-2870**. © *2022 American Cancer Society.*

**KEYWORDS:** biomarker testing, coverage, insurance, legislation, prior authorization.

## INTRODUCTION

The knowledge and practice of precision medicine in cancer have been progressing rapidly, with advances in targeted cancer therapies and immunotherapy that can prolong patient survival and quality of life in patients who harbor specific driver mutations or markers predictive of a response to immunotherapy identified through comprehensive biomarker testing (CBT).[1–4] Eligibility for treatment with these novel therapies requires CBT to determine whether a patient is a candidate for a specific treatment. Failure to determine candidacy through CBT can mean a missed opportunity for patients to receive more effective targeted treatment and result in either mistreatment with a less effective therapy (e.g., they never discover actionable mutations that would allow them to receive the most appropriate therapy) or delayed treatment in the case of a failed response to an initial, less effective therapy and a later switch to the more effective targeted therapy. Conversely, immunotherapy may not be effective in patients with lung cancer and an *EGFR* mutation or *ALK* rearrangement. The presence of these two oncogenic drivers has been an exclusion criterion for immunotherapy trials in patients with lung cancer.[5,6] Indeed, consideration of CBT has become the standard of care for many cancers, with more to follow, and today CBT is often required to determine patient eligibility for clinical trials.[7] Furthermore, a large proportion of driver mutations identified by CBT are actionable and can be treated with a US Food and Drug Administration (FDA)–approved agent. For example, 78% of mutations in patients with lung adenocarcinoma who were currently smoking and 47% of mutations in patients with lung adenocarcinoma who had never smoked were actionable.[8] Similarly, 54% of mutations in Korean patients with cancer were actionable.[9] These examples confirm the importance of CBT in appropriate patients before the initiation of therapy.[10]

Currently, there are different approaches to testing for genetic alterations that can potentially guide treatment. Multiple single-gene assays, each of which identifies a single analyte, are needed to select the appropriate targeted agent or immunotherapy; however, if this is done in sequence, it can result in significant delays in initiating either novel or conventional therapies according to the testing outcomes. In contrast, a next-generation sequencing (NGS) panel can identify multiple genetic alterations with a single test that identifies several to hundreds of genetic alterations.[11] There

**Correspondence**Gelareh Sadigh, Department of Radiology and Imaging Sciences, Emory University School of Medicine, 1364 Clifton Rd NE, Ste BG20, Atlanta, GA 30322, USA. Email: gsadigh@emory.edu

[1]Department of Radiology and Imaging Sciences, Emory University School of Medicine, Atlanta, Georgia, USA; [2]American Cancer Society Cancer Action Network, Inc, Washington, District of Columbia, USA; [3]Department of Radiology, University of Michigan, Ann Arbor, Michigan, USA; [4]Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan, USA; [5]Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, Massachusetts, USA; [6]Early Cancer Detection Science, American Cancer Society, Atlanta, Georgia, USA

**DOI:** 10.1002/cncr.34271, **Received:** February 26, 2022; **Revised:** April 13, 2022; **Accepted:** April 25, 2022, **Published online** May 24, 2022 in Wiley Online Library (wileyonlinelibrary.com)

is increased clinical interest in incorporating NGS into clinical practice, with 75% of oncologists nationally reporting the use of NGS testing in 2017 and with 27% reporting incorporating NGS results into their treatment decisions.[12] However, significant variability in CBT rates exists with respect to practice type, setting, and the presence of institutional policy as well as health care provider subspecialization.[10,13] Furthermore, there is significant variation in the coordination of CBT between subspecialty services across institutions.[10]

Despite evidence demonstrating the effectiveness of CBT and targeted therapies or immunotherapy, the incorporation of biomarkers into clinical practice is lagging behind recommendations in clinical guidelines. Currently, challenges to clinical adoption include inadequate or poor-quality tissue specimens, delays in ordering the test, assay variability and inadequate analytic validation, and delays in treatment due to long turnaround times for returning results.[2,7,13] In addition to these testing challenges, financial and logistical factors, including the need for prior authorization, high out-of-pocket costs, and variability in insurance coverage, can all pose significant barriers. In a 2022 landscape study of biomarker testing, the average allowed unit cost per test (i.e., the negotiated rate between payers and providers before member cost sharing) for biomarker testing (single-gene and panel tests) was $224 for commercial payers and $78.80 for Medicaid.[14] Between 2016 and 2019, the average amount allowed for NGS tests varied from $1269 to $2058 per test for all payees.[15] Between 2013 and 2015, the average commercial payer reimbursed amounts for single genes in patients with lung cancer ranged from $406 to $1127.[16] Based on the average reimbursement for individual mutation tests, the total reimbursement for sequential testing comprising KRAS, EGFR, ALK, ROS1, and BRAF tests was $3763, whereas the cost of NGS was $2860.[16] In a 2020 American Cancer Society Cancer Action Network survey of 933 patients with cancer, among the 44% who reported an out-of-pocket cost for biomarker testing, approximately a third paid more than $500.[17] However, for patients whose insurance does not cover NGS, the out-of-pocket costs may exceed $10,000. The uncertainty of coverage policies and differences across insurance health plans can also limit access to CBT for patients.[18–20] In the 2020 American Cancer Society Cancer Action Network survey, 29% of patients who discussed treatment plans with their providers decided to forgo biomarker testing because of its cost.[21] Finally, although biomarker testing for cancer targeted therapy for metastatic colorectal cancer and metastatic non–small cell lung cancer is mostly cost-effective,[22,23] a recent study showed that use of upfront NGS testing in patients with metastatic non–small cell lung cancer was associated with substantial cost savings and shorter time-to-test results in comparison with sequential testing of single analytes for both the Centers for Medicare & Medicaid Services (CMS) and commercial payers.[24]

Studies show that currently only half of patients with cancer in the United States for whom biomarker testing is recommended are receiving the tests.[25] Furthermore, patients who are older, Black, and uninsured or Medicaid-insured are less likely to receive biomarker testing.[26–29] In another study, more than a quarter of patients who did not receive recommended biomarker testing reported that it was because insurance was not covering the test at all and/or they would have incurred high out-of-pocket costs.[30] The existing racial, ethnic, and socioeconomic disparities in access to and utilization of guideline-indicated CBT and appropriate treatment with targeted therapies or immunotherapy contribute to disparities in patient outcomes.[27]

## INSURANCE COVERAGE

Currently, commercial payers and Medicare typically cover the majority of oncology single-analyte companion diagnostic biomarker tests when they meet the criteria for clinical utility by the FDA.[31] For biomarker tests that have not yet received FDA approval, additional materials for payer consideration include clinical practice guidelines from entities such as the National Comprehensive Cancer Network, the American Society of Clinical Oncology, technology assessment organizations, and published peer-reviewed evidence on clinical utility.[31]

Recently, there has been an increase in the number of large multigene NGS panels, which are offered by institutions and commercial providers and make more efficient use of tissue samples by providing more information in comparison with single-gene tests. However, insurance coverage policies make it a challenge to cover the costs of the testing. Reimbursement continues to lag substantially for panel testing and may cover only single-gene tests or a combination of multiple single-gene tests that have established clinical utility. A recent analysis has shown that many commercial health plan coverage policies are more restrictive than clinical guidelines for multigene panel tests, with coverage varying among different states.[32] Although multigene panels are also used to identify patients eligible for clinical trials, the mandate to cover the routine costs of clinical trials does not extend this testing to the majority of payers aside from

**TABLE 1.** Characteristics of 2021 State Biomarker Legislation

| Characteristic | California SB 535 | Illinois HB 1779 | Louisiana SB 84 |
|---|---|---|---|
| Requires insurance plans to cover biomarker testing | No | Yes (when supported by medical evidence)[a] | Yes (when it meets the insurers' medical necessity criteria) |
| Applies to all patients with cancer | No | Yes | Yes |
| Disease agnostic | No | Yes | No |
| Addresses prior authorization | Yes (i.e., prohibits prior authorization for Stage III or IV cancer) | No | No |
| Addresses cost sharing | No (i.e., coverage is subject to annual deductible, coinsurance, and copayment provisions of health coverage plan) | | |

Abbreviations: HB, House Bill; SB, Senate Bill.
[a]Food and Drug Administration–approved test or indicated test for a Food and Drug Administration–approved drug, Centers for Medicare & Medicaid Services national coverage determination, nationally recognized clinical practice guidelines, consensus statement, professional society recommendations, or peer-reviewed literature.
The incorporation of comprehensive biomarker testing into clinical practice lags behind guideline recommendations, with coverage policy differences across insurance health plans remaining an important barrier. Although recent legislation in Illinois, Louisiana, and California is aimed at improving access to biomarker testing, there remains variability among these laws in terms of the population affected, the cancer stage, and whether the coverage of testing is mandated, or the legislation addresses only prior authorization.

Medicare.[31] The main justifications for the lack of coverage are high costs and the belief that the panels are for investigational purposes.[31] However, the precision treatments that result from this testing may be less costly and more effective than traditional treatments involving chemotherapy or multiple sequenced rounds of traditional therapeutics before the initiation of the treatment most effective for an individual, which could have been identified on the basis of information from a genomic change on an NGS panel or an assessment of biomarkers associated with the efficacy of immunotherapy. For example, immunotherapy recently has been approved as a first-line treatment for patients with unresectable or metastatic microsatellite instability–high or mismatch repair–deficient colorectal cancer, with studies showing significantly longer progression-free survival in comparison with standard chemotherapy regimens (5-fluorouracil–based therapy with or without bevacizumab or cetuximab).[33–35]

The CMS issued a national coverage determination for NGS[36] effective in March 2018 for patients with recurrent, relapsed, refractory, metastatic, or advanced Stage III or IV somatic (acquired) cancers not previously tested with FDA-approved or -cleared NGS for an FDA-approved or -cleared indication. Subsequently, CMS approved NGS national coverage for patients with germline (inherited) cancers, including breast and ovarian cancers, who have not been tested before with the same germline test using NGS[36] in January 2020. The CMS local coverage determination (LCD) for NGS comprehensive genomic profile testing for solid tumors, updated in April 2022,[37] will improve access to CBT. The LCD is expected to facilitate comprehensive genomic profile testing, an NGS approach that uses a single assay to assess hundreds of genes, including relevant cancer biomarkers, with evidentiary support for clinical utility in guidelines and clinical trials.[37] Although the 2018 and 2020 national coverage determinations subsequently affected private payer decisions to similarly cover NGS testing,[20,38,39] many payers who cover the testing negotiate payment only for those medically necessary biomarkers and not full NGS.[31] In contrast, Medicaid is not bound by either Medicare national coverage determinations or commercial payer policy, with coverage varying significantly from state to state.[40]

In addition to variable coverage across insurance plans, there is also variability among payers regarding prior authorization specifications. Although prior authorizations are intended to ensure medical necessity, these additional requirements can add an administrative burden and may delay testing if not performed in a timely manner. Additionally, the time required for laboratories to process tests can also delay the initiation of appropriate treatment. A recent survey of oncologists showed that clinical decision-making for non–small cell lung carcinoma is influenced by the range of wait times for biomarker testing from the time of ordering to the receipt of results, with more experienced clinicians being more likely to defer treatment with nontargeted therapies while waiting for results; most oncologists found 2 weeks to be an acceptable wait time, but only 37% were willing to wait longer.[13]

## RECENT STATE BIOMARKER LEGISLATION

In 2021, three states (Illinois, Louisiana, and California) passed laws intended to improve access to CBT, and they vary in design (Table 1). Because these laws take effect in 2022, it is not yet possible to assess their impact on CBT rates. Arizona, California, Massachusetts, New Hampshire, New York, Rhode Island, and Washington are considering additional bills this year that are designed to address barriers to CBT.

### *Coverage of biomarker testing—Illinois House Bill 1779*

Effective January 1, 2022, Illinois House Bill 1779 requires coverage of CBT under state-regulated insurance policies and managed care plans for the purposes of diagnosis, treatment, appropriate management, or ongoing monitoring of an enrollee's disease or condition when the test is supported by medical and scientific evidence (i.e., approved by FDA or recognized by nationally recognized medical guidelines).[41] The new law also improves access to CBT for Medicaid and state employee plans. This law is not limited to patients with cancer and requires coverage of CBT for any medical condition when this is supported by medical and scientific evidence, including FDA-approved or -deemed tests, Medicare coverage determinations, and nationally recognized clinical practice guidelines.[42] The law is silent on the requirement for prior authorization; although testing must be covered, insurers may require prior authorization. Lastly, the law is silent on patients' financial responsibilities for biomarker testing, which therefore remain subject to annual deductibles, coinsurance, and copayment provisions established under the health plan.

### *Coverage of biomarker testing—Louisiana Senate Bill 84*

Effective January 1, 2022, Louisiana Senate Bill 84 requires broad insurance coverage for genetic and molecular testing for patients with cancer including, but not limited to, tumor mutation testing, NGS, hereditary germline mutation testing, pharmacogenomic testing, and CBT. Coverage applies to any state-regulated health plan and is subject to annual deductibles, coinsurance, and copayment provisions established under the health plan. The coverage is also subject to applicable evidence-based medical necessity criteria under the plan[43] and does not specify the sources of evidence to determinate medical necessity. Furthermore, the law remains silent on the requirement for prior authorization.

### *Prior authorization for biomarker testing—California Senate Bill 535*

Effective July 1, 2022, California Senate Bill 535 prohibits state-regulated health insurance plans, including Medi-Cal managed care plans, from requiring prior authorization for CBT for an enrollee or insured individual with advanced or metastatic Stage III or IV cancer (initial diagnosis, progression, or recurrence).[44] This law addresses prior authorization for plans that already cover CBT and does not mandate any other plan to cover CBT. It applies only to CBT for FDA-approved therapies, and this could limit the impact of this legislation because testing is necessary to then select the appropriate therapy. Therefore, if the choice of therapy is not determined at the time that the test is being ordered, the insurance plan can still require prior authorization or deny coverage. The provisions limiting application to patients with advanced or metastatic cancer are also a barrier to widespread impact. Lastly, the law is silent on patients' financial responsibilities for biomarker testing, which therefore remain subject to annual deductibles, coinsurance, and copayment provisions established under the health plan.

## IMPLICATIONS AND FUTURE DIRECTIONS

The current variability in coverage for CBT contributes to the widening of the insurance disparity gap. Although the CMS national coverage determination increased NGS testing for Medicare patients and subsequently commercially insured patients,[20,39] those covered by Medicaid and patient assistance programs have slower growth rates of NGS testing.[38] There is substantial variability in NGS coverage because Medicaid coverage is determined at the state level. Because of differences in the racial and ethnic compositions of the insured population (Black individuals account for 20% of Medicaid enrollees and approximately 10% of Medicare or commercial enrollees), the variability in coverage contributes to the increasing racial and ethnic disparity gaps among patients with cancer.[38] Finally, even for health plans with current coverage of CBT, patients may incur out-of-pocket costs that are dependent on their insurance benefits, which can be a barrier to testing if the cost-sharing amount is not affordable or may result in sticker shock or surprise bills and a subsequent financial burden if patients are not aware of the cost-sharing until after they receive their bill.

Cancer care is associated with substantial out-of-pocket medical costs, which together with lost productivity and changes in employment, income, and insurance can result in financial hardships that can adversely affect patients' health outcomes.[45–48] Additionally, the direct and indirect costs of navigating a complex health care system can place a disproportionate burden on households with fewer socioeconomic resources, those who are uninsured or underinsured, or racial/ethnic minorities who are at higher risk of financial hardship.[17,49,50] Therefore, inconsistencies in coverage for CBT as well as the amount of cost-sharing are more likely to affect those who already have a higher risk of financial hardship.

The laws recently passed and implemented in Illinois, Louisiana, and California demonstrate momentum and

interest from lawmakers in expanding access to CBT as well as the importance of coordination among stakeholders and policymakers to ensure that legislation does indeed expand access to appropriate testing. However, barriers not addressed by ensuring coverage may also contribute to persistent disparities in NGS testing among different geographic and socioeconomic groups. After the national coverage determination in 2018, there was an increase in NGS testing among all racial and ethnic groups across all insurance types, with estimates of the proportion of patients tested across all covariates increasing from 3.5%–16.6% before national determination coverage to 10.3%–44.6% after it.[38] However, testing rates were lower in the Black and Hispanic/Latino groups than the White group during both pre– and post–national coverage determination periods, regardless of the insurance type; this suggested a persistent racial/ethnic disparity gap.[38]

In summary, the studies thus far have demonstrated that variability in insurance coverage for CBT contributes to the widening of racial and ethnic disparity gaps in testing rates. Public policy measures need to be identified and deployed to bring appropriate biomarker testing for guiding precision therapy to patients with cancer for whom it is medically appropriate and to ameliorate the socioeconomic and ethnic barriers. By increasing NGS testing for Medicare enrollees with subsequent adoption by many commercially insured plans, the Medicare national coverage determination in 2018 was an important first step in this direction. The proposed CMS LCD for comprehensive genomic profile testing, effective since April 1, 2022, is an additional step toward CBT. However, Medicaid and other state-regulated plans remain unaddressed. The examples of the three states that recently passed laws designed to improve access to CBT point out opportunities that may guide other states contemplating legislation to expand access to CBT. Specifically, legislation requiring insurance coverage for all disease types and stages may be most beneficial to the patients. Coordinated advocacy efforts by all stakeholders are needed to further improve coverage across all states and health insurance plans. Providers, patient advocates, and professional societies have a valuable role to play not only in advocating for legislative changes but also in understanding these policy changes and ensuring that their patients benefit from new legislation.

## CONFLICTS OF INTEREST

Gelareh Sadigh declares receiving an honorarium from the *Journal of the American College of Radiology* for her role as associate editor. Devon V. Adams and Hilary Gee Goeckner have worked on projects related to biomarker testing uptake and funded through grants to their employer from Amgen, Bayer, EMD Serono, Foundation Medicine, Inc, Pfizer, Janssen, Genentech, and NeoGenomics. Moreover, Adams' salary is funded through institutional grants to his employer from Amgen, Bayer, Blueprint Medicine, Genentech, Janssen, and Pfizer, and Goeckner reports speaker honoraria given to her employer from the National Comprehensive Cancer Network and the Association of Community Cancer Centers. Bruce E. Johnson receives postmarketing royalties for EGFR mutation testing from the Dana-Farber Cancer Institute; has consulted for Novartis, Boston Pharmaceuticals, Checkpoint Therapeutics, Chugai, Daichi Sankyo, AstraZeneca, Foundation Medicine, G1 Therapeutics, Genentech, GSK, Hengrui Therapeutics, Janssen, Jazz Pharma, Hummingbird, and Bluedot; has received support for attending meetings and/or travel from the American Society of Clinical Oncology and the American Cancer Society; and has received research support from Cannon Medical Imaging and Novartis. Robert A. Smith reports that the American Cancer Society receives grants from private and corporate foundations, including foundations associated with companies in the health sector; his salary is solely funded through American Cancer Society funds. Ruth C. Carlos receives salary support from the *Journal of the American College of Radiology* for her role as editor-in-chief. The other author made no disclosures.

## REFERENCES


1. Arbour KC, Riely GJ. Systemic therapy for locally advanced and metastatic non–small cell lung cancer: a review. *JAMA*. 2019;322:764-774.
2. Febbo PG, Ladanyi M, Aldape KD, et al. NCCN task force report: evaluating the clinical utility of tumor markers in oncology. *J Natl Compr Canc Netw*. 2011;9(suppl 5):S1-S32. quiz S33.
3. Mok T, Camidge DR, Gadgeel SM, et al. Updated overall survival and final progression-free survival data for patients with treatment-naive advanced ALK-positive non–small-cell lung cancer in the ALEX study. *Ann Oncol*. 2020;31:1056-1064.
4. John A, Yang B, Shah R. Clinical impact of adherence to NCCN guidelines for biomarker testing and first-line treatment in advanced non–small cell lung cancer (aNSCLC) using real-world electronic health record data. *Adv Ther*. 2021;38:1552-1566.
5. Gandhi L, Rodriguez-Abreu D, Gadgeel S, et al. Pembrolizumab plus chemotherapy in metastatic non–small-cell lung cancer. *N Engl J Med*. 2018;378:2078-2092.
6. Carbone DP, Reck M, Paz-Ares L, et al. First-line nivolumab in stage IV or recurrent non–small-cell lung cancer. *N Engl J Med*. 2017;376:2415-2426.
7. Survey findings summary: understanding provider utilization of cancer biomarker testing across cancers. American Cancer Society Cancer Action Network. Published December 2021. Accessed December 12, 2021. https://www.fightcancer.org/sites/default/files/national_documents/provider_utilization_of_biomarker_testing_polling_memo_dec_2021.pdf
8. Mack PC, Klein MI, Ayers KL, Zhou X, Guin S, Fink M, Rossi M, Ai-Kateb H, O'Connell T, Hantash FM, Oh WK, Newman S, Schadt EE, Chen R, Hirsch FR Targeted next-generation sequencing reveals exceptionally high rates of molecular driver mutations in never-smokers with lung adenocarcinoma. *Oncologist*. 2022; oyac035.
9. Lee SH, Lee B, Shim JH, et al. Landscape of actionable genetic alterations profiled from 1,071 tumor samples in Korean cancer patients. *Cancer Res Treat*. 2019;51:211-222.
10. Fox AH, Jett JR, Roy UB, et al. Knowledge and practice patterns among pulmonologists for molecular biomarker testing in advanced non–small cell lung cancer. *Chest*. 2021;160:2293-2303.
11. Mehta A, Vasudevan S, Sharma SK, et al. Biomarker testing for advanced lung cancer by next-generation sequencing; a valid method to achieve a comprehensive glimpse at mutational landscape. *Appl Cancer Res*. 2020;40:4. doi:10.1186/s41241-020-00089-8
12. Freedman AN, Klabunde CN, Wiant K, et al. Use of next-generation sequencing tests to guide cancer treatment: results from a nationally representative survey of oncologists in the United States. *JCO Precis Oncol*. 2018;2:1-13.
13. Mileham KF, Schenkel C, Bruinooge SS, et al. Defining comprehensive biomarker-related testing and treatment practices for advanced

non–small-cell lung cancer: results of a survey of U.S. oncologists. *Cancer Med*. 2022;11:530-538.
14. Dieguez G, Carioto J. The landscape of biomarker testing coverage in the United States. Milliman, Inc. Published February 15, 2022. Accessed April 8, 2022. https://www.milliman.com/en/insight/the-landscape-of-biomarker-testing-coverage-in-the-US
15. Desai K, Hooker G, Gilbert K, Cropper C, Metcalf R, Kachroo S. Real-world trends in costs of next generation sequencing (NGS) testing in U.S. setting. *J Clin Oncol*. 2021;39:e18824.
16. Dalal AA, Guerin A, Mutebi A, Culver KW. Economic analysis of BRAF gene mutation testing in real world practice using claims data: costs of single gene versus panel tests in patients with lung cancer. *J Med Econ*. 2018;21:649-655.
17. Pisu M, Azuero A, Meneses K, Burkhardt J, McNees P. Out of pocket cost comparison between Caucasian and minority breast cancer survivors in the Breast Cancer Education Intervention (BCEI). *Breast Cancer Res Treat*. 2011;127:521-529.
18. Messner DA, Al Naber J, Koay P, et al. Barriers to clinical adoption of next generation sequencing: perspectives of a policy Delphi panel. *Appl Transl Genom*. 2016;10:19-24.
19. Lu CY, Loomer S, Ceccarelli R, et al. Insurance coverage policies for pharmacogenomic and multi-gene testing for cancer. *J Pers Med*. 2018;8:10.
20. Trosman JR, Douglas MP, Liang SY, et al. Insights from a temporal assessment of increases in US private payer coverage of tumor sequencing from 2015 to 2019. *Value Health*. 2020;23:551-558.
21. Survivor views: biomarker testing. American Cancer Society Cancer Action Network. Published September 28, 2020. Accessed April 7, 2022. https://www.fightcancer.org/sites/default/files/Survivor%20Views%20Biomarker%20Testing%20Polling%20Memo.pdf
22. Seo MK, Cairns J. Do cancer biomarkers make targeted therapies cost-effective? A systematic review in metastatic colorectal cancer. *PLoS One*. 2018;13:e0204496.
23. Henderson R, Keeling P, French D, Smart D, Sullivan R, Lawler M. Cost-effectiveness of precision diagnostic testing for precision medicine approaches against non–small-cell lung cancer: a systematic review. *Mol Oncol*. 2021;15:2672-2687.
24. Pennell NA, Mutebi A, Zhou Z-Y, et al. Economic impact of next-generation sequencing versus single-gene testing to detect genomic alterations in metastatic non–small-cell lung cancer using a decision analytic model. *JCO Precis Oncol*. 2019;3:1-9.
25. Chawla A, Peeples M, Li N, Anhorn R, Ryan J, Signorovitch J. Real-world utilization of molecular diagnostic testing and matched drug therapies in the treatment of metastatic cancers. *J Med Econ*. 2018;21:543-552.
26. Kehl KL, Lathan CS, Johnson BE, Schrag D. Race, poverty, and initial implementation of precision medicine for lung cancer. *J Natl Cancer Inst*. 2019;111:431-434.
27. Health equity in biomarker testing and targeted therapy. American Cancer Society Cancer Action Network. Published May 2021. Accessed December 3, 2021. https://www.fightcancer.org/sites/default/files/FS%20Health%20Equity%20in%20BMT%20and%20Targeted%20Therapy_FINAL.pdf
28. Presley C, Soulos P, Chiang A, et al. Disparities in next generation sequencing in a population-based community cohort of patients with advanced non–small cell lung cancer. *J Clin Oncol* 2017;35(15)(suppl):6563.
29. Norris RP, Dew R, Sharp L, et al. Are there socio-economic inequalities in utilization of predictive biomarker tests and biological and precision therapies for cancer? A systematic review and meta-analysis. *BMC Med*. 2020;18:282.
30. Improving access to biomarker testing. American Cancer Society Cancer Action Network. Published September 28, 2020. Accessed December 6, 2021. https://www.fightcancer.org/policy-resources/improving-access-biomarker-testing
31. Payer Coverage Policies of Tumor Biomarker Testing. American Cancer Society Cancer Action Network and LUNGevity Foundation. Published September 2020. Accessed December 6, 2021. https://www.fightcancer.org/sites/default/files/ACS%20CAN%20and%20LUNGevity_Payer%20Coverage%20Policies%20of%20Tumor%20Biomarker%20Testing.pdf
32. Wong WB, Anina D, Lin CW, Adams DV. Alignment of health plan coverage policies for somatic multigene panel testing with clinical guidelines in select solid tumors. *Per Med*. 2022;19:171-180.
33. Ganesh K, Stadler ZK, Cercek A, et al. Immunotherapy in colorectal cancer: rationale, challenges and potential. *Nat Rev Gastroenterol Hepatol*. 2019;16:361-375.
34. Andre T, Shiu KK, Kim TW, et al. Pembrolizumab in microsatellite-instability-high advanced colorectal cancer. *N Engl J Med*. 2020;383:2207-2218.
35. Casak SJ, Marcus L, Fashoyin-Aje L, et al. FDA approval summary: pembrolizumab for the first-line treatment of patients with MSI-H/dMMR advanced unresectable or metastatic colorectal carcinoma. *Clin Cancer Res*. 2021;27:4680-4684.
36. Next generation sequencing (NGS) (90.2). Centers for Medicare & Medicaid Services. Published January 27, 2020. https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=372
37. Genomic sequence analysis panels in the treatment of solid organ neoplasms. Centers for Medicare & Medicaid Services. Revised May 1, 2022. Accessed April 12, 2022. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=37810&ver=17
38. Sheinson DM, Wong WB, Meyer CS, et al. Trends in use of next-generation sequencing in patients with solid tumors by race and ethnicity after implementation of the Medicare national coverage determination. *JAMA Netw Open*. 2021;4:e2138219.
39. Sheinson DM, Wong WB, Flores C, Ogale S, Gross CP. Association between Medicare's national coverage determination and utilization of next-generation sequencing. *JCO Oncol Pract*. 2021;17:e1774-e1784.
40. State Scorecard: State Medicaid Coverage Policy and Impact on Lung Cancer Outcomes. LUNGevity Foundation. Published March 2020. Accessed December 12, 2021. https://www.lungevity.org/sites/default/files/state-scorecards/LUNGevity-scorecard-030920.pdf
41. Flowers ME. Flowers passes landmark legislation making biomarker testing accessible for Illinoisans. Illinois House Democratic Caucus Published September 27, 2021. Accessed December 17, 2021. https://ilhousedems.com/2021/09/27/flowers-passes-landmark-legislation-making-biomarker-testing-accessible-for-illinoisans/
42. Bill status of HB1779. Illinois General Assembly. Accessed December 17, 2021. https://www.ilga.gov/legislation/BillStatus.asp?DocNum=1779&GAID=16&DocTypeID=HB&SessionID=110&GA=102
43. Senate Bill No. 84. Louisiana State Legislature. Accessed December 17, 2021. http://www.legis.la.gov/Legis/ViewDocument.aspx?d=1227189
44. Senate Bill No. 535. California Legislative Information. Accessed December 17, 2021. https://leginfo.legislature.ca.gov/faces/billNavClient.xhtml?bill_id=202120220SB535
45. Brown ML, Riley GF, Schussler N, Etzioni R. Estimating health care costs related to cancer treatment from SEER-Medicare data. *Med Care* 2002;40(suppl 8):IV-104-17.
46. Short PF, Moran JR, Punekar R. Medical expenditures of adult cancer survivors aged <65 years in the United States. *Cancer*. 2011;117:2791-2800.
47. Finkelstein EA, Tangka FK, Trogdon JG, Sabatino SA, Richardson LC. The personal financial burden of cancer for the working-aged population. *Am J Manag Care*. 2009;15:801-806.
48. The Costs of Cancer. American Cancer Society Cancer Action Network. Published October 2020. Accessed February 8, 2022. https://www.fightcancer.org/sites/default/files/National%20Documents/Costs-of-Cancer-2020-10222020.pdf
49. Yabroff KR, Zhao J, Han X, Zheng Z. Prevalence and correlates of medical financial hardship in the USA. *J Gen Intern Med*. 2019;34:1494-1502.
50. Pisu M, Kenzik KM, Oster RA, et al. Economic hardship of minority and non-minority cancer survivors 1 year after diagnosis: another long-term effect of cancer? *Cancer*. 2015;121:1257-1264.