original contributions

Association Between Medicare's National Coverage Determination and Utilization of Next-Generation Sequencing

Daniel M. Sheinson, PhD[1]; William B. Wong, PharmD, MS[1]; Carlos Flores, MPH[2]; Sarika Ogale, PhD[1]; and Cary P. Gross, MD[3]

QUESTION ASKED: Did Medicare's 2018 decision to reimburse next-generation sequencing (NGS) tests for previously untested patients with advanced cancer lead to an increase in NGS testing among Medicare beneficiaries and commercially insured patients?

SUMMARY ANSWER: Across four tumor types (advanced non–small-cell lung cancer [aNSCLC], metastatic colorectal cancer [mCRC], metastatic breast cancer [mBC], and advanced melanoma), NGS testing increased at a higher rate after the Medicare decision (national coverage determination [NCD]) than before the NCD, and this increase was similar for patients enrolled in Medicare or with commercial insurance. However, Medicare beneficiaries received significantly fewer second NGS tests than commercially insured patients.

WHAT WE DID: This was a retrospective analysis of 70,290 patients with advanced cancer using the Flatiron Health electronic health record (EHR)-derived deidentified nationwide longitudinal database. Included patients had aNSCLC, mCRC, mBC, or advanced melanoma with a de novo or recurrent advanced diagnosis from January 1, 2011, through December 30, 2019. Patients were classified as having Medicare or commercial insurance. NGS testing was assessed by receipt of first NGS test result within 60 days of advanced diagnosis. Interrupted time series analysis assessed NGS utilization pre- and post-NCD effective date by insurance type.

WHAT WE FOUND: Among patients with aNSCLC, mCRC, or mBC, NGS testing rates increased post-NCD versus pre-NCD ($P < .05$). There was no statistically significant difference in trends pre- and post-NCD between Medicare beneficiaries and commercially insured patients in any tumor. Rates of repeat NGS testing were similar between Medicare beneficiaries and commercially insured patients before the 2018 NCD (24.8% *v* 28.5%, respectively), but post-NCD Medicare beneficiaries were less likely to have a repeat NGS test (27.7% *v* 36.0%; $P < .01$).

BIAS, CONFOUNDING FACTORS: This study was based on real-world EHR data, which may result in misclassification of data. It is possible some patients received testing at sites outside the Flatiron Health network, which may not have been recorded. Some patients may have switched insurance providers during the course of the study. The study had limited follow-up time post-NCD, and further research will be needed to determine whether trends observed here will hold with longer follow-up.

REAL-LIFE IMPLICATIONS: After the Medicare NCD in 2018, NGS testing increased for both Medicare beneficiaries and commercially insured patients, indicating that private insurers may have considered Medicare guidance in forming their coverage policies. However, post-NCD Medicare beneficiaries had significantly fewer second NGS tests compared with commercially insured patients, suggesting that the NCD policy may be limiting utilization of repeat NGS tests for some patients with advanced or metastatic cancer.

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ASSOCIATED CONTENT
Appendix
Data Supplement
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HEALTH POLICY

original contributions

Association Between Medicare's National Coverage Determination and Utilization of Next-Generation Sequencing

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abstract

PURPOSE In 2018, Medicare issued a national coverage determination (NCD) providing reimbursement for next-generation sequencing (NGS) tests for beneficiaries with advanced or metastatic cancer and no previous NGS testing. We examined the association between NCD implementation and NGS utilization trends in Medicare beneficiaries versus commercially insured patients.

METHODS This was a retrospective study of patients with advanced non–small-cell lung cancer (aNSCLC), metastatic colorectal cancer (mCRC), metastatic breast cancer (mBC), or advanced melanoma with a de novo or recurrent advanced diagnosis from January 1, 2011, through December 30, 2019, using a nationwide US electronic health record–derived deidentified database. Patients were classified by insurance and by advanced diagnosis date. NGS testing was assessed by receipt of first NGS test result ≤ 60 days of advanced diagnosis. Interrupted time series analysis assessed NGS utilization pre- and post-NCD effective date by insurance type.

RESULTS The utilization and repeat NGS testing analysis included 70,290 and 4,295 patients, respectively. Use of NGS rose from < 1% in 2011 to > 45% in Q4 2019 in aNSCLC while remaining < 20% in mBC and advanced melanoma. Among patients with aNSCLC, mCRC, or mBC, NGS testing increased post-NCD versus pre-NCD ($P < .05$). There was no significant difference in trends pre- and post-NCD between Medicare beneficiaries and commercially insured patients in any tumor. Repeat NGS testing was similar before the NCD (Medicare *v* commercial: 24.8% *v* 28.5%). Post-NCD, fewer Medicare beneficiaries had repeat NGS testing (27.7% *v* 36.0%; $P < .01$).

CONCLUSION Trends in NGS utilization significantly changed post-NCD, although the magnitude of change was not significantly different by insurance type, indicating private insurers may also be incorporating NCD guidance. Implementation of the NCD may have limited use of repeat NGS testing in Medicare beneficiaries.

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INTRODUCTION

Advances in precision medicine in oncology have shaped the way cancer care is currently practiced. The number of approved targeted therapies that enable personalized treatment based on the genetic characteristics of a patient's tumor has grown significantly over the years. Most recently, tumor agnostic therapies, which allow treatment of any cancer type that has the molecular alteration targeted by the drug, have been approved. Recent examples of tumor agnostic therapies include entrectinib[1] and larotrectinib,[2] which have been approved for *NTRK*+ solid tumors.

With the increase in the development of targeted therapies and their dissemination into clinical practice, there is an increasing interest in identifying patients who have cancers with genetic alterations that can potentially be treated. Next-generation sequencing (NGS) technology can identify multiple genetic alterations within a single test, allowing for a single specimen to be tested for hundreds of genetic alterations. Evidence of the clinical and economic value of NGS is rapidly evolving as more targets are identified and more targeted therapies are approved. Although a real-world study by Presley et al[3] using 2011-2016 electronic medical record data found no mortality benefit of NGS testing compared with *EGFR* and *ALK* testing in patients with advanced non–small-cell lung cancer (aNSCLC), since then several additional targeted

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agents for various genetic alterations (*ALK*, *EGFR*, *ROS1*, *TRK*, *BRAF*, *RET*, and *MET*) have been approved by the US Food and Drug Administration (FDA).

In a recent analysis, Pennell et al[4] found that if all patients identified with specific actionable driver mutations (*EGFR*, *ALK*, *ROS1*, *BRAF*, *RET*, *MET*, and *NTRK*) were assumed to receive matched treatment, it would result in substantial gain in life years at a reduced cost. Yet, these specific mutations—which have targeted therapies—are a notably distinct subset of the numerous genetic alterations that are identified in broad-based genomic sequencing studies. Hence, it is unclear how widespread adoption of NGS testing might influence care patterns and outcomes. On the one hand, there is some uncertainty around the clinical benefits of widespread adoption of NGS testing into clinical practice, as well as difficulty in interpreting NGS results (reported by 51% of oncologists).[5] On the other hand, there is increased interest in incorporating NGS into clinical practice. A 2017 survey of 1,281 oncologists found that more than 75% reported using NGS testing within the previous year and 27% reported that they often incorporated NGS results into their treatment decisions.[5] Despite the uptake by clinicians, financial reimbursement for the NGS test has been cited as a common barrier, with about one third of North American oncologists reporting frequent challenges in a 2016 survey of ASCO members.[6]

Historically, NGS coverage has varied across both Medicare and commercial payers, often restricting coverage to either specific biomarkers or tumor types.[7,8] However, in 2018, Medicare issued an NGS national coverage determination (NCD) memo[9] that classified NGS as a reasonable and necessary diagnostic laboratory test for patients with cancer when performed in a Clinical Laboratory Improvement Amendments–certified laboratory. The resulting NCD facilitated reimbursement for FDA-approved or FDA-cleared NGS tests in patients with advanced or metastatic cancer who had not been previously tested using the same NGS test for the same primary cancer. Although theoretically this could lead to greater use of NGS, previous research examining the effects of national coverage decisions on NGS utilization have been mixed.[10] Some studies have found that the NCD policies may not have an impact on NGS utilization in a Medicare population, whereas others have observed a noticeable impact on utilization and outcomes.[11,12] Furthermore, commercial payers may disagree with Medicare on coverage decisions, which may limit the impact of a Medicare NCD on NGS utilization among commercially insured patients. A study examining the relationship between Medicare NCDs and private insurance coverage for Medicare devices found that equivalent coverage policies were present only 51% of the time, with private insurance coverage being more restrictive 22% of the time.[13] Nonetheless, there is little evidence that points to the influence, or lack thereof, of Medicare NCDs on private insurers' coverage decisions. To our knowledge, there have been no reports of an assessment of the Medicare NGS NCD on real-world NGS utilization and whether any utilization effect may spill over to commercially insured patients. To address these knowledge gaps, we examined the association between the NCD and NGS utilization trends and repeat NGS testing in both commercially insured and Medicare patients.

METHODS

Study Design

This was a retrospective analysis using the Flatiron Health electronic health record (EHR)-derived deidentified nationwide longitudinal database. During the study period, data were collected from approximately 280 cancer clinics (approximately 800 sites of care) representing more than 2.4 million US patients with cancer. The deidentified patient-level data include structured and unstructured data, curated via technology-enabled abstraction.[14] Institutional review board approval of the study protocol was obtained before study conduct and included a waiver of informed consent. Patients with aNSCLC, metastatic colorectal cancer (mCRC), metastatic breast cancer (mBC), or advanced melanoma with an advanced or metastatic diagnosis from January 1, 2011 (January 1, 2013, for mCRC), through December 30, 2019, were included in the study. These tumors were chosen based on the likelihood of NGS use because of the number of targeted therapies available for each cancer type.[15-19] Additional inclusion criteria included evidence of either Medicare or commercial insurance, requirement of a clinic visit within 90 days of advanced or metastatic diagnosis, and ≥ 18 years of age and care in the community practice setting. For the NGS utilization trends analysis, patients were excluded if they had any other cancer or if they had an NGS test before the date of their diagnosis of advanced or metastatic cancer (aNSCLC, mCRC, mBC, and advanced melanoma). For the repeat testing analysis, patients with two or more advanced or metastatic cancer diagnoses at any time were excluded along with patients who did not have at least one biomarker test after the date of their advanced or metastatic cancer diagnosis (Appendix Table A1, online only).

Outcomes and Definitions

We defined NGS tests as any use of NGS technology, regardless of the number of genes in the panel. NGS testing was identified by the biomarker testing variables derived by Flatiron Health, which are based on abstracted data from EHRs. Evidence of NGS testing in EHRs included identification of tests via terminology (ie, next-generation sequencing), use of NGS technology platforms (ie, Illumina HiSeq), or use of specific NGS tests (ie, Foundation Medicine), but RNA sequencing NGS tests and germline or hereditary NGS tests are excluded. This definition was consistent with the objective of this study of examining NGS use for the purpose of guiding therapy decisions in the

advanced or metastatic cancers studied, for which somatic mutations are most relevant. Furthermore, the NGS NCD considered RNA NGS tests to be out of scope.[9]

Patients were categorized into year-quarters (eg, 2016 Q1) based on the date of their advanced or metastatic cancer diagnosis, which could occur at initial diagnosis (de novo) or at a later date for those patients who were diagnosed initially with an early-stage disease and later progressed (recurrent). Among patients who had evidence of Medicare or commercial insurance, patients who were < 65 years old as of their advanced cancer diagnosis were classified as commercially insured unless Medicare was reported at any time before the end of the quarter of their advanced cancer diagnosis, whereas those ≥ 65 years old as of their advanced cancer diagnosis were classified as Medicare. The Medicare category included patients with supplemental commercial coverage (ie, Medicare Advantage) because the NCD would apply similarly to these beneficiaries as to those with traditional Medicare. Patients with other types of insurance or missing insurance were excluded unless they also had evidence of Medicare or commercial insurance. We calculated the proportion of patients who received NGS testing each quarter by dividing the number of patients diagnosed in that quarter who had an NGS test within 60 days after their advanced or metastatic cancer diagnosis by the total number of patients diagnosed during the quarter. To assess the association of the NCD with NGS testing utilization, we designated the quarters after the policy effect date (starting the second quarter of 2018 given the policy effect date of March 16, 2018) as the post-NCD period and the quarters before that as the pre-NCD period, and we assessed NGS utilization changes before and after policy.

Repeat testing outcomes included frequency of repeat NGS testing (ie, among patients who had received one NGS test, the proportion of patients who subsequently received an additional NGS test within 60 days of the first NGS test). To further understand whether the same NGS test was repeated, we also report the proportion of repeated tests at the same laboratory as the first NGS test for a subset of patients with aNSCLC with laboratory name data available.

Statistical Analysis

Descriptive statistics, including means and percentages, were calculated to compare differences in baseline patient

TABLE 1. Baseline Demographics of Study Sample According to NGS Use

Characteristic	Medicare Insurance (n = 47,885)	Commercial Insurance (n = 22,405)	*P*
Median age (Q1-Q3), years	72 (67-77)	55 (49-60)	
Sex, No. (%)			< .01
Female	25,835 (54)	13,312 (59)	
Male	22,047 (46)	9,091 (41)	
Missing	3 (< 0.1)	2 (< 0.1)	
Race or ethnicity, No. (%)			< .01
Asian	923 (1.9)	608 (2.7)	
Black or African American	3,805 (7.9)	2,407 (10.7)	
Hispanic or Latino	286 (0.6)	214 (1.0)	
White	33,409 (69.8)	14,808 (66.1)	
Other	4,630 (9.7)	2,411 (10.8)	
Missing	4,832 (10.1)	1,957 (8.7)	
Region, No. (%)			< .01
Midwest	7,406 (15.5)	3,794 (16.9)	
Northeast	10,336 (21.6)	4,198 (18.7)	
South	20,991 (43.8)	10,149 (45.3)	
West	8,856 (18.5)	4,137 (18.5)	
Missing	296 (0.6)	127 (0.6)	
Tumor type, No. (%)			< .01
aNSCLC	27,992 (58.5)	9,009 (40.2)	
mBC	7,518 (15.7)	5,520 (24.6)	
mCRC	9,177 (19.2)	6,120 (27.3)	
Advanced melanoma	3,198 (6.7)	1,756 (7.8)	

Abbreviations: aNSCLC, advanced non–small-cell lung cancer; mBC, metastatic breast cancer; mCRC, metastatic colorectal cancer; NGS, next-generation sequencing.

characteristics between Medicare and commercially insured populations.

We used an interrupted time series model to assess (1) changes in the level and trend (ie, slope) of NGS testing pre- and post-NCD at the population level and (2) differences between the Medicare and commercially insured populations in terms of the change in trend of NGS testing between pre- and post-NCD (ie, three-way interaction) (Data Supplement, online only). For each tumor type, a full model that included the three-way interaction term was fit to the data. If the three-way interaction term was not statistically significant at $P < .05$, remaining model parameters were interrupted using a reduced model that omitted the three-way interaction term. Repeat NGS testing was examined by calculating the proportion of patients among those with an NGS test who had a second NGS test within 60 days of the first test. Trends in repeat testing over time were explored by categorizing patients into one of the three time blocks of equal duration (2014 Q3-2016 Q2, 2016 Q3-2018 Q1, and 2018 Q2-2019 Q4) based on the date of their first NGS test. We used two periods in the pre-NCD period to observe any trends over time. Two sample proportion z tests were used to test for differences in proportions using repeat NGS tests within each period.

RESULTS

Association of the Medicare NCD Implementation and NGS Testing

A total of 70,290 patients were included in the NGS utilization analysis. Most of the sample was composed of aNSCLC cases (52.6%), followed by mCRC (21.8%), mBC (18.5%), and advanced melanoma (7.0%). Although sex, race, and regional differences between Medicare beneficiaries and commercially insured patients were minimal, Medicare beneficiaries were older and had a higher proportion of aNSCLC cases (Table 1). Across the four tumors combined, the proportion using NGS rose from < 1% in 2011 (in both patients with Medicare and commercial insurance) to 37% in Medicare patients and 41% in commercially insured patients in Q4 2019 (Fig 1). In patients within each tumor type, NGS utilization was < 6% in Q1 2014; however, the rate of increase in NGS utilization varied by tumor (Fig 2). NGS utilization rose the highest in patients with aNSCLC, increasing to 48% in Medicare patients and 58% in commercially insured patients in Q4 2019, followed by mCRC with 30% in Medicare patients and 40% in commercially insured patients in Q4 2019. NGS utilization was substantially lower in patients with mBC and advanced melanoma, with the proportion receiving NGS remaining < 20% in Q4 2019.

At the time of the NCD (Q2 2018) in aNSCLC, mCRC, and mBC, the proportion using NGS was significantly higher in the commercial cohort than in the Medicare cohort ($P \leq .01$), with the trends pre-NCD not being significantly different between cohorts ($P > .05$) (Table 2). The difference in NGS utilization trends pre- and post-NCD was not significantly different between Medicare beneficiaries and commercially insured patients in any of the tumors ($P > .05$ within each cancer type) (Table 2). Using the reduced model, in patients with aNSCLC, mCRC, or mBC, the quarterly rate of increase in NGS testing was higher post-NCD than pre-NCD ($P < .05$ for pre-post difference in rate of NGS increase within each cancer type) (Fig 2).

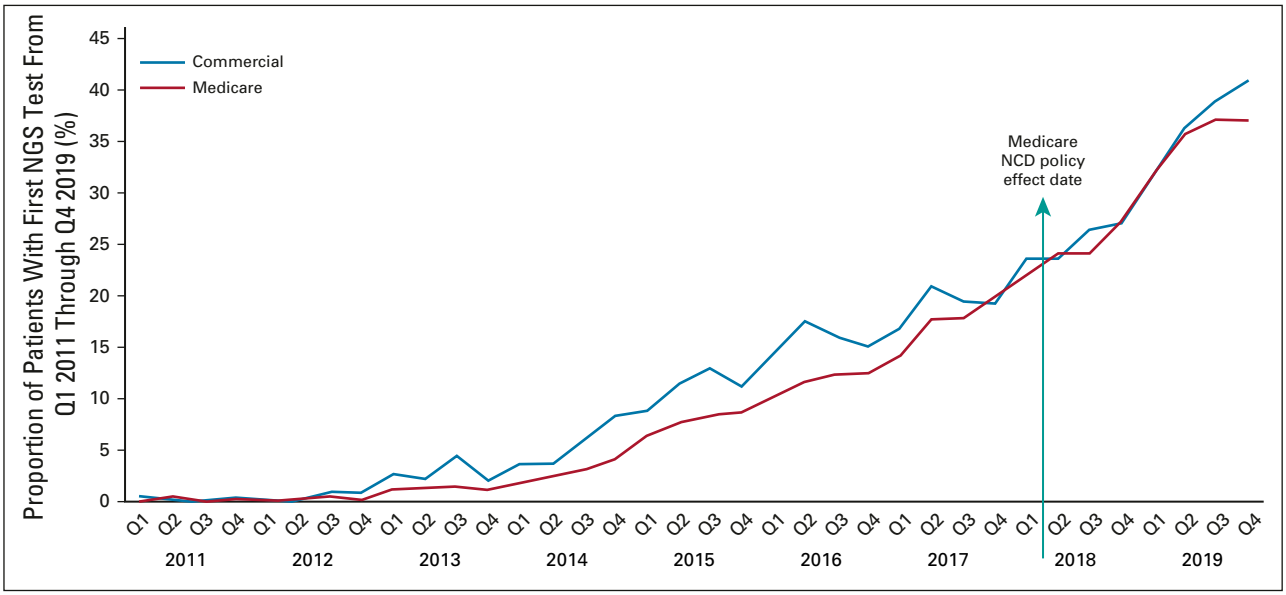

FIG 1. Proportion of patients with NGS testing across four tumors combined: aNSCLC, mCRC, mBC, and advanced melanoma. aNSCLC, advanced non–small-cell lung cancer; mBC, metastatic breast cancer; mCRC, metastatic colorectal cancer; NCD, national coverage determination; NGS, next-generation sequencing.

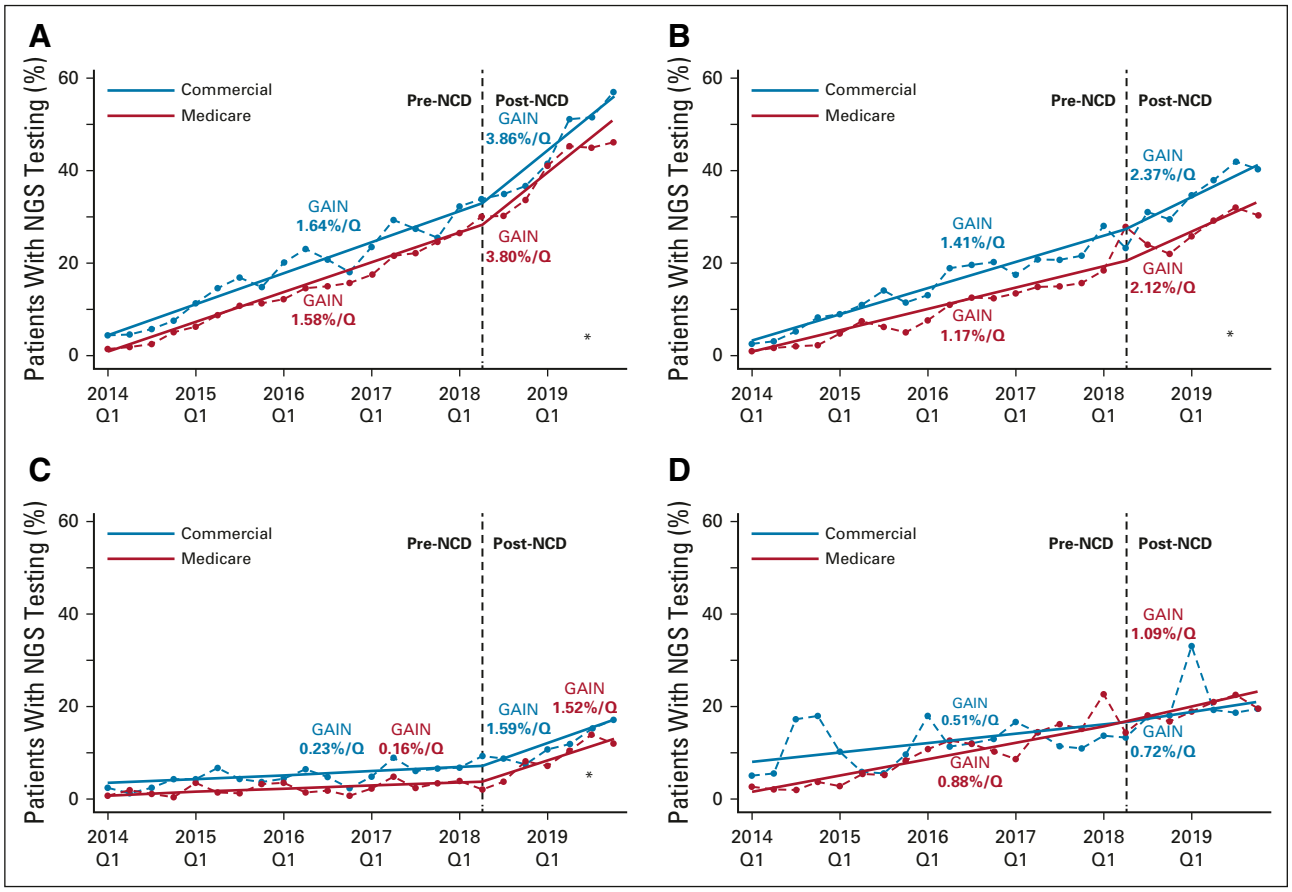

FIG 2. NGS utilization trends by tumor with model fits. (A) aNSCLC, (B) mCRC, (C) mBC, and (D) advanced melanoma. *$P < .05$ for pre-post difference in rate of NGS increase. aNSCLC, advanced non–small-cell lung cancer; mBC, metastatic breast cancer; mCRC, metastatic colorectal cancer; NCD, national coverage determination; NGS, next-generation sequencing.

Relationship Between the Medicare NCD and Repeat Testing

The repeat NGS testing analysis consisted of 4,198 patients who met the inclusion criteria. Among patients who used NGS as their first test type, 28.4% of patients received a second NGS test. The proportion of patients with repeat NGS testing increased over time, but the increase differed between Medicare beneficiaries and commercially insured patients. In the pre-NCD period, there were similar proportions of patients with repeat NGS tests (Q3 2014-Q2 2016: 18.2% *v* 17%, $P = .62$; Q3 2016-Q1 2018: 24.8% *v* 28.5%, $P = .17$). In the post-NCD period, a significantly fewer proportion of Medicare beneficiaries than commercially insured patients had a repeat NGS test (Q2 2018-Q4 2019: 27.7% *v* 36%, $P < .01$) (Fig 3). Among a subset of patients with aNSCLC with laboratory information available, most repeated tests identified were from the same laboratory as the first NGS test (ranging from 54% to 71%), with the exception of one laboratory (11%) (Appendix Fig A1, online only).

DISCUSSION

Using a large national oncology EHR-derived deidentified database, we found that NGS utilization increased at a higher rate in the post-NCD period than in the pre-NCD period. In addition, the increase in rate of NGS use post-NCD was not significantly different between Medicare beneficiaries and the commercially insured population. This suggests that commercial payers may be following, to some degree, the Medicare NCD in their coverage and reimbursement policies. To our knowledge, this is the first study examining NGS utilization rates in relation to the NCD policy. These findings are in line with a recent study of NGS coverage, which found that private payers implemented coverage policies at a higher pace after the Medicare NCD than before the NCD.[8] Although other studies have shown that private payers may not always follow a Medicare NCD,[13] payers have stated their intent to at least consider the contents for the Medicare NGS NCD, along with other criteria, for their own policy decisions.[20]

The repeat testing component of the Medicare NCD was a point of concern with the implementation of the NCD. Many individuals who responded to the open comment period for the proposed NCD were concerned that restricting repeat utilization of NGS would affect the care of patients.[21] In this study, we found that repeat testing was a frequent part of clinical practice patterns; approximately 28% of patients

TABLE 2. Full and Reduced Models for Determining NGS Utilization Trends

		Reduced Model			Full Model		
Tumor Type	**Variable**	**Estimate**	**SE**	***P***	**Estimate**	**SE**	***P***
aNSCLC	Intercept	27.80	0.64	< .01	28.11	0.68	> .99
	Time	1.58	0.06	< .01	1.61	0.06	> .99
	Payer	5.00	0.93	< .01	4.37	1.21	> .99
	Time × payer	0.06	0.09	.48	0.00	0.10	> .99
	Time × policy	2.22	0.29	< .01	2.05	0.43	< .01
	Time × payer × policy				0.34	0.57	.56
mCRC	Intercept	20.37	1.16	< .01	21.08	1.49	< .01
	Time	1.17	0.10	< .01	1.24	0.13	< .01
	Payer	6.76	1.05	< .01	5.34	1.86	.01
	Time × payer	0.24	0.09	.01	0.11	0.16	.52
	Time × policy	0.95	0.38	.02	0.57	0.55	.31
	Time × payer × policy				0.76	0.77	.33
mBC	Intercept	3.72	0.46	< .01	3.22	0.50	< .01
	Time	0.16	0.04	< .01	0.11	0.05	.02
	Payer	3.41	0.60	< .01	4.43	0.87	< .01
	Time × payer	0.07	0.06	.28	0.17	0.08	.05
	Time × policy	1.36	0.18	< .01	1.63	0.33	< .01
	Time × payer × policy				−0.55	0.44	.22
Advanced melanoma	Intercept	16.59	1.14	< .01	17.84	1.39	< .01
	Time	0.88	0.10	< .01	1.00	0.12	< .01
	Payer	0.13	1.66	.94	−2.36	2.04	.25
	Time × payer	−0.37	0.19	.06	−0.61	0.24	.02
	Time × policy	0.21	0.43	.62	−0.46	0.52	.38
	Time × payer × policy				1.34	0.95	.17

Abbreviations: aNSCLC, advanced non–small-cell lung cancer; mBC, metastatic breast cancer; mCRC, metastatic colorectal cancer; NGS, next-generation sequencing.

who received an NGS test received a second NGS test. Invalid NGS test results have been reported in the range of 6.4%[22]-33.8%,[22-24] potentially indicating other clinically driven factors that may drive repeat testing. Additionally, post-NCD, we found that significantly fewer Medicare beneficiaries received a second NGS test compared with

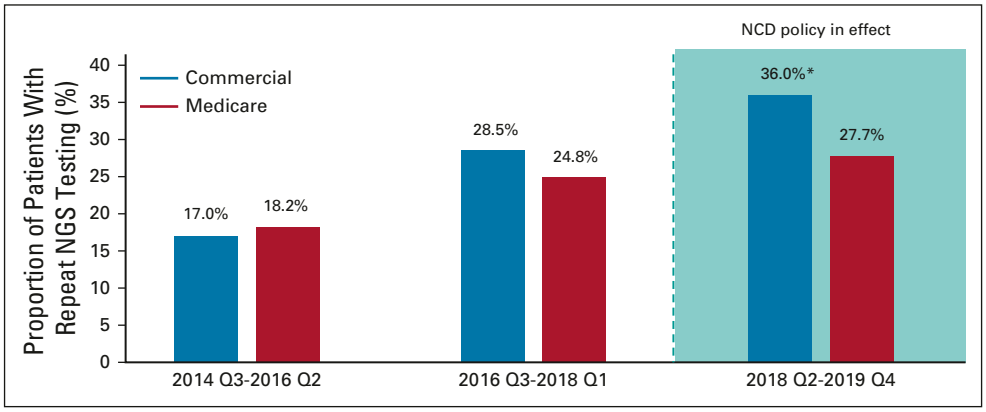

FIG 3. Frequency of repeat NGS testing over time. *$P < .01$. NCD, national coverage determination; NGS, next-generation sequencing.

commercially insured patients, indicating that the repeat testing component of the NCD may be limiting utilization of repeat NGS tests. Given the substantial cost of NGS testing, further research is needed to understand whether repeat testing is associated with improved clinical decision making or, more importantly, clinical outcomes.

Finally, we found that NGS utilization rates have increased over time across all four tumors examined, but the greatest increase was observed in aNSCLC, potentially reflecting the increasing use of NGS to inform treatment decisions and the rate of innovation in targeted therapies available for aNSCLC relative to the other tumors. A recent study found that the use of targeted therapy or immunotherapy in first-line NSCLC has increased from $<$ 15% in 2015 to $>$ 50% in 2018.[25] Furthermore, the availability of recommended targeted therapies may also drive NGS coverage policy decisions specific to cancer types. An examination of public and private payer coverage policies pre-NCD found that multigene panel testing most commonly covered for NSCLC, consistent with recommendations from the National Comprehensive Cancer Network.[7] The use of NGS in patients with aNSCLC is consistent with previous research that has shown utilization to be the highest in aNSCLC, with the greatest potential for growth in utilization for other tumor types.[26]

This study has several limitations. First, this study was based on real-world EHR data, which may result in misclassification of data. Although a lack of evidence of NGS testing in the EHR may not necessarily indicate a lack of testing, and while we mitigated this risk by requiring patients to have an office visit after their advanced diagnosis, it is possible that a patient received care at sites outside of the Flatiron Health network. In examining the insurance of those excluded because of lack of follow-up, we found that commercially insured patients may be slightly more likely to have been excluded (41% of those excluded had commercial coverage *v* 32% excluded in the final cohort). However, given the higher commercial testing rates and lack of differential impact of NCD on testing by insurance type, our conclusions may be considered robust in that any additional NGS tests that are missing from the commercial population would enhance the spillover effect in the commercial cohort further. Additionally, the insurance information used to classify patients was based on the information available at the time of the advanced cancer diagnosis and thus may not have captured situations where patients switch insurance. However, because we measured the use of NGS within 60 days of a patient's advanced cancer diagnosis, and only 3% of patients turned 65 years old during the year of their advanced diagnosis, the risk of switching insurance within that time frame may be low and thus the impact would be minimal. Third, this study had limited follow-up time post-NCD. Further research would be needed to determine whether the trends observed here would hold with longer follow-up. For repeat NGS tests, we were unable to determine whether the repeat test was reimbursed under the respective commercial or Medicare policy, and further research using EHR-linked claims data would be needed to determine the frequency of reimbursed versus paid out-of-pocket repeat tests. Additionally, we did not examine repeat NGS testing $>$ 60 days after the initial NGS test. Although patients may have received repeat NGS testing at later dates, commercially insured patients may also have switched over to Medicare, making it difficult to disentangle the effect of the NCD policy.

In conclusion, NGS utilization trends significantly changed post-NCD, although the rate of change was not significantly different by type of insurance, indicating that private insurer policies may reflect some of the changes in Medicare policies. Medicare beneficiaries had significantly fewer second NGS tests compared with commercially insured patients post-NCD, suggesting that the NCD policy may be limiting utilization of repeat NGS tests.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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REFERENCES

1. Paz-Ares L, Doebele RC, Farago AF, et al: Entrectinib in NTRK fusion-positive non-small cell lung cancer (NSCLC): Integrated analysis of patients (pts) enrolled in STARTRK-2, STARTRK-1 and ALKA-372-001 [abstract]. Ann Oncol. 30:ii38-ii68, 2019 (suppl 2)
2. Hong DS, DuBois SG, Kummar S, et al: Larotrectinib in patients with TRK fusion-positive solid tumours: A pooled analysis of three phase 1/2 clinical trials. Lancet Oncol 21:531-540, 2020
3. Presley CJ, Tang D, Soulos PR, et al: Association of broad-based genomic sequencing with survival among patients with advanced non-small cell lung cancer in the community oncology setting. JAMA 320:469-477, 2018
4. Pennell N, Zhou J, Hobbs B: A model comparing the value of broad next-gen sequencing (NGS)-based testing to single gene testing (SGT) in patients with nonsquamous non-small cell lung cancer (NSCLC) in the United States. J Clin Oncol 38, 2020 (suppl; abstr 9529)
5. 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 2:1-13, 2018
6. Barroso-Sousa R, Guo H, Srivastava P, et al: Utilization of tumor genomics in clinical practice: An international survey among ASCO members. Future Oncol 15: 2463-2470, 2019
7. Lu CY, Loomer S, Ceccarelli R, et al: Insurance coverage policies for pharmacogenomic and multi-gene testing for cancer. J Pers Med 8:19, 2018
8. 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 23:551-558, 2020
9. Centers for Medicare & Medicaid Services: National Coverage Determination (NCD) for Next Generation Sequencing (NGS) (90.2). 2020. https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=372
10. Foote SB, Virnig BA, Town RJ, et al: The impact of Medicare coverage policies on health care utilization. Health Serv Res 43:1285-1301, 2008
11. Flum DR, Kwon S, MacLeod K, et al: The use, safety and cost of bariatric surgery before and after Medicare's national coverage decision. Ann Surg 254: 860-865, 2011
12. O'Neill BP, O'Neill WW, Williams D, et al: Impact of CMS coverage decision on access to transcatheter aortic valve replacement. Catheter Cardiovasc Interv 84: 114-121, 2014
13. Chambers JD, Chenoweth M, Thorat T, et al: Private payers disagree with Medicare over medical device coverage about half the time. Health Aff (Millwood) 34: 1376-1382, 2015
14. Birnbaum B, Nussbaum N, Seidl-Rathkopf K, et al: Model-assisted cohort selection with bias analysis for generating large-scale cohorts from the EHR for oncology research. arXiv, 2020. https://arxiv.org/abs/2001.09765
15. Targeted Cancer Therapies. National Institutes of Health. National Cancer Institute. https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies/targeted-therapies-fact-sheet
16. Breast Cancer, NCCN Evidence Blocks, version 1.2021–January 15, 2021. National Comprehensive Cancer Network. https://www.nccn.org/professionals/physician_gls/pdf/breast_blocks.pdf
17. Non-Small Cell Lung Cancer, NCCN Evidence Blocks, version 4.2021–March 3, 2021. National Comprehensive Cancer Network. https://www.nccn.org/professionals/physician_gls/pdf/nscl_blocks.pdf
18. Melanoma: Cutaneous, NCCN Evidence Blocks, version 2.2021–February 19, 2021. National Comprehensive Cancer Network. https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma_blocks.pdf
19. Colon Cancer, NCCN Evidence Blocks, version 2.2021–February 9, 2021. National Comprehensive Cancer Network. https://www.nccn.org/professionals/physician_gls/pdf/colon_blocks.pdf
20. Phillips KA, Trosman JR, Weldon CB, et al: New Medicare coverage policy for next-generation tumor sequencing: A key shift in coverage criteria with broad implications beyond Medicare. JCO Precis Oncol 2:PO.18.00206, 2018
21. Centers for Medicare & Medicaid Services. View Public Comments for Next Generation Sequencing (NGS) for Medicare Beneficiaries With Advanced Cancer. 2019. https://www.cms.gov/medicare-coverage-database/details/nca-view-public-comments.aspx?NCAId=296
22. Hagemann IS, Devarakonda S, Lockwood CM, et al: Clinical next-generation sequencing in patients with non-small cell lung cancer. Cancer 121:631-639, 2015
23. Morris SM, Subramanian J, Gel ES, et al: Performance of next-generation sequencing on small tumor specimens and/or low tumor content samples using a commercially available platform. PLoS One 13:e0196556, 2018
24. Mantripragada KC, Olszewski AJ, Schumacher A, et al: Clinical trial accrual targeting genomic alterations after next-generation sequencing at a non-National Cancer Institute-designated cancer program. J Oncol Pract 12:e396-e404, 2016
25. Nadler E, Arondekar B, Aguilar KM, et al: Treatment patterns and clinical outcomes in patients with advanced non-small cell lung cancer initiating first-line treatment in the US community oncology setting: A real-world retrospective observational study. J Cancer Res Clin Oncol 147:671-690, 2021
26. Caplan E, Wong W, Ferries E, et al: Utilization and trends of multi gene panel testing in oncology. J Manag Care Spec Pharm 26:S1-S96, 2020 (4-a suppl)

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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APPENDIX

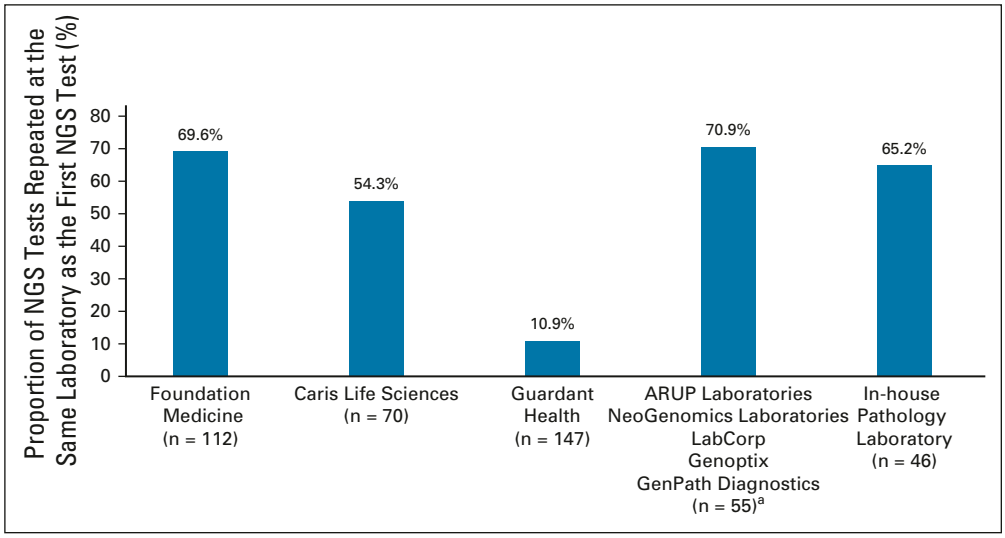

FIG A1. Proportion of repeat NGS tests at same laboratory as first NGS among patients with aNSCLC. [a]Second test at same laboratory as first test. aNSCLC, advanced non–small-cell lung cancer; NGS, next-generation sequencing.

TABLE A1. Attrition Table

Inclusion/Exclusion Criteria	No.	Percentage of Previous Step
No. of patients across all available data sets of interest (aNSCLC, mCRC, mBC, and advanced melanoma)	116,908	
Adult patients ≥ 18 years on date of advanced or metastatic cancer diagnosis	116,630	99.8
Patients from the community practice setting	106,188	91.0
Patients with metastatic or advanced disease on or after 2011	106,188	100
Patients with any type of visit in the Flatiron Health network within 90 days of date of advanced or metastatic cancer diagnosis	93,837	88.4
Patients with evidence of Medicare or commercial insurance	72,264	77.0

Utilization Trends Analysis			Repeat Testing Analysis		
	No.	Percentage of Previous Step		No.	Percentage of Previous Step
Patients with the earliest diagnosis of metastatic or advanced cancer (aNSCLC, mCRC, mBC, and advanced melanoma). If a patient had a previous diagnosis of any other cancer (prostate, bladder, ovarian, HCC, head and neck, CLL, DLBCL, or FL), they were excluded	71,999	99.6	Patients with only one metastatic or advanced cancer diagnosis documented in the EHR	71,771	99.3
Patients without documented evidence of an NGS test before date of metastatic cancer diagnosis	70,931	98.5	Patients with at least one biomarker test on or after date of metastatic or advanced cancer diagnosis	51,385	71.6
Patients with date of metastatic cancer diagnosis on or before 2019	70,290	99.1	Patients with at least one NGS test	4,295	8.4

Abbreviations: aNSCLC, advanced non–small-cell lung cancer; CLL, chronic lymphocytic leukemia; DLBCL, diffuse large B-cell lymphoma; EHR, electronic health record; FL, follicular lymphoma; HCC, hepatocellular carcinoma; mBC, metastatic breast cancer; mCRC, metastatic colorectal cancer; NGS, next-generation sequencing.