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Article

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The Association Between Medicare Low-Income Subsidy and Anticancer Treatment Uptake in Advanced Lung Cancer

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Abstract

Background: High out-of-pocket costs may impact anticancer treatment uptake. The Low-Income Subsidy (LIS) program can reduce patient out-of-pocket cost for Medicare Part D–covered treatments. We examined whether the LIS increased uptake and reduced time to initiate orally administered anticancer drugs in patients with advanced non–small cell lung cancer (NSCLC).

Methods: Using Surveillance, Epidemiology and End Results (SEER)-Medicare data, we identified older adults (aged 65 years and older) diagnosed with advanced NSCLC from 2007 through 2013 and categorized them as full LIS, partial LIS, or non-LIS. We used propensity-score weighted (IPTW) Cox proportional hazards regression to assess the likelihood of and time to initiate Part D treatments. Part B medication uptake was our negative control because supplemental insurance reduces out-of-pocket costs for those drugs. All statistical tests were two-sided.

Results: Among 19 746 advanced NSCLC patients, approximately 10% initiated Part D treatments. Patients with partial or no LIS were less likely to initiate Part D treatments than were those with full subsidies (partial LIS vs full LIS $HR_{IPTW} = 0.77$, 95% confidence interval = 0.62 to 0.97; non-LIS vs full LIS $HR_{IPTW} = 0.87$, 95% confidence interval = 0.79 to 0.95). Time to initiate Part D treatments was also slightly shorter among full-LIS patients (full LIS mean [SD] = 10.8 [0.04] months; partial LIS mean [SD] = 11.3 [0.08] months; and non-LIS mean [SD] = 11.1 [0.03] months, $P < .001$). Conversely, patients with partial or no LIS had shorter time to initiation of Part B drugs.

Conclusions: Patients receiving the full LIS had higher orally administered anticancer treatment uptake than patients without LIS. Notably, patients with partial LIS had the lowest treatment uptake, likely because of their low incomes combined with high expected out-of-pocket spending. High out-of-pocket costs for Part D medications may be a barrier to treatment use for patients without full LIS.

Lung cancer is the leading cause of death from cancer in the United States (1,2). Non–small cell lung cancer (NSCLC) is the most common type of lung cancer, accounting for about 85% of cases, and more than 80% are diagnosed at late stages (1,3). In recent years, a number of orally administered anticancer drugs have been approved by the US Food and Drug Administration for metastatic NSCLC, improving survival for eligible patients. However, the high cost of these treatments is concerning. On average, the cost of novel oral anticancer drugs now exceeds $14 000 per month of therapy (4–6). In addition, use of combination therapy is common, which increases spending (7) and may contribute to financial toxicity (8–10).

Prior work suggests that many patients with cancer experience delays in filling prescriptions for orally administered anticancer treatments or never fill them at all, with abandonment being more likely for Medicare beneficiaries and those who face high out-of-pocket prescription drug costs (11–15). High rates of abandonment for Medicare beneficiaries is particularly

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concerning because Medicare is the primary health insurance program for people aged 65 years and older in the United States, including coverage of outpatient prescription drugs under the Medicare Part D program. While Medicare Part D is required to cover anticancer therapies, plans do so with very high out-of-pocket costs (16). One key exception is for Medicare Part D enrollees who are eligible and enrolled in the Low-Income Subsidy (LIS) program (or Extra Help) (11,12). This program provides cost-sharing support for Part D prescription drugs for Medicare beneficiaries with limited incomes (≤150% federal poverty level) and resources (≤$12 600 for individuals in 2018) (17). This subsidy reduces patient out-of-pocket costs dramatically. For example, the expected out-of-pocket cost for filling the first month of crizotinib (a targeted NSCLC therapy with a list price of approximately $16 500/month in 2019) would be over $2 300 for a patient with no LIS, $1194 for a patient with a partial LIS, and only $8.50 for a patient with full LIS (Table 1) (17,18). Notably, despite having high out-of-pocket costs when initiating treatment, patients with partial LIS pay $8.50/fill after reaching the catastrophic spending phase (ie, after patients spend $5100 out-of-pocket on branded drugs in 2019), whereas patients without subsidies pay 5% of the drug's list price ($825.00/month) during that same benefit period.

Few studies have evaluated the impact of high up-front cost-sharing on patient access to drugs offered on Medicare Part D. Further, evidence of Part D treatment uptake for people with full, partial, or no subsidies under Medicare Part D has not been explored for high-priced anticancer treatments. Given the rapid advances in treatment options for patients with NSCLC and the growing number of orally administered drugs available, it is important to understand whether there are barriers to timely treatment uptake for seniors enrolled in Medicare Part D. Our objectives are to compare orally administered anticancer drug uptake among patients with advanced NSCLC by LIS level.

Methods

Data Source and Sample Selection

We used Surveillance, Epidemiology and End Results (SEER)-Medicare data for this study (19). The SEER-Medicare data represent a linkage of two population-based data sources—the SEER cancer registry and fee-for-service Medicare claims—that provides detailed health information about Medicare beneficiaries with cancer. The SEER program collects cancer-related characteristics on incident cancer cases from 18 population-based cancer registries in diverse geographic areas, covering approximately 30% of the US population. Medicare is the primary insurer for 97% of adults aged 65 years and older in the United States, with 70% of the Medicare enrollees in traditional fee-for-service Medicare. We identified a cohort of patients aged 65 and older and diagnosed with locally advanced or metastatic NSCLC, stages IIIB/IV (using the derived American Joint Committee on Cancer Stage Group from the SEER registry data) between July 1, 2007, and December 31, 2013. We required patients to have continuous enrollment in Medicare Parts A and B for 6 months before NSCLC diagnosis and Parts A, B, and D from the month of NSCLC diagnosis through death, disenrollment, or 12 months post diagnosis, whichever occurred first. We excluded patients enrolled in Medicare Advantage plans because their claims would not be fully observed, as well as those whose diagnosis was made by death certificate or autopsy or who died within 30 days after diagnosis (Figure 1).

Table 1. Summary of eligibility and cost-sharing for Medicare Part D benefit for LIS groups* (17, 18)

Subsidy group	LIS eligibility requirement	Maximum monthly premium	Maximum annual deductible	Cost-sharing for plan's formulary drugs	
				Up to out-of-pocket/catastrophic limit	Above out-of-pocket/catastrophic limit
Full LIS	Full-benefit dual eligibles† Medicare Savings Program‡ SSI recipients§ Income ≤135% FPL with resources not exceeding $9 230 ($14 600 if married)	$0	$0	Copay: $3.40 generics, $8.50 brand-name drugs	$0
Partial LIS	Income ≤150% FPL with resources between $9 230 – $14 390 ($14 600 – $28 720 if married)	25–100%	$85	Coinsurance: 15%	Copay: $3.40 generics, $8.50 brand-name drugs
Non-LIS	Does not meet eligibility for LIS	Base at $33.19 varied by plan and adjusted by income	$415	Coinsurance: 25–37% depending on coverage phase	Coinsurance: 5% or $3.40 for generics/ $8.50 for brand-name drugs, whichever is greater

*Data Source: Centers for Medicare & Medicaid Services (CMS): full & partial LIS: 2019 Resource and Cost-Sharing Limits for Low-Income Subsidy (17); Non-LIS: Medicare 2019 Costs at a Glance, 2019 (18). FPL = federal poverty level; LIS = low-income subsidy; SSA = Social Security Administration; SSI = Supplemental Security Income.
†People eligible for both Medicare and full Medicaid benefits.
‡Medicare beneficiaries who are participants in the Medicare Saving Programs, which are Qualified Medicare Beneficiary Program, Specified Low-Income Medicare Beneficiary Program, and Qualified Individual Program.
§SSI recipients, including SSI recipients who do not qualify for Medicaid, and individuals deemed to be SSI recipients.

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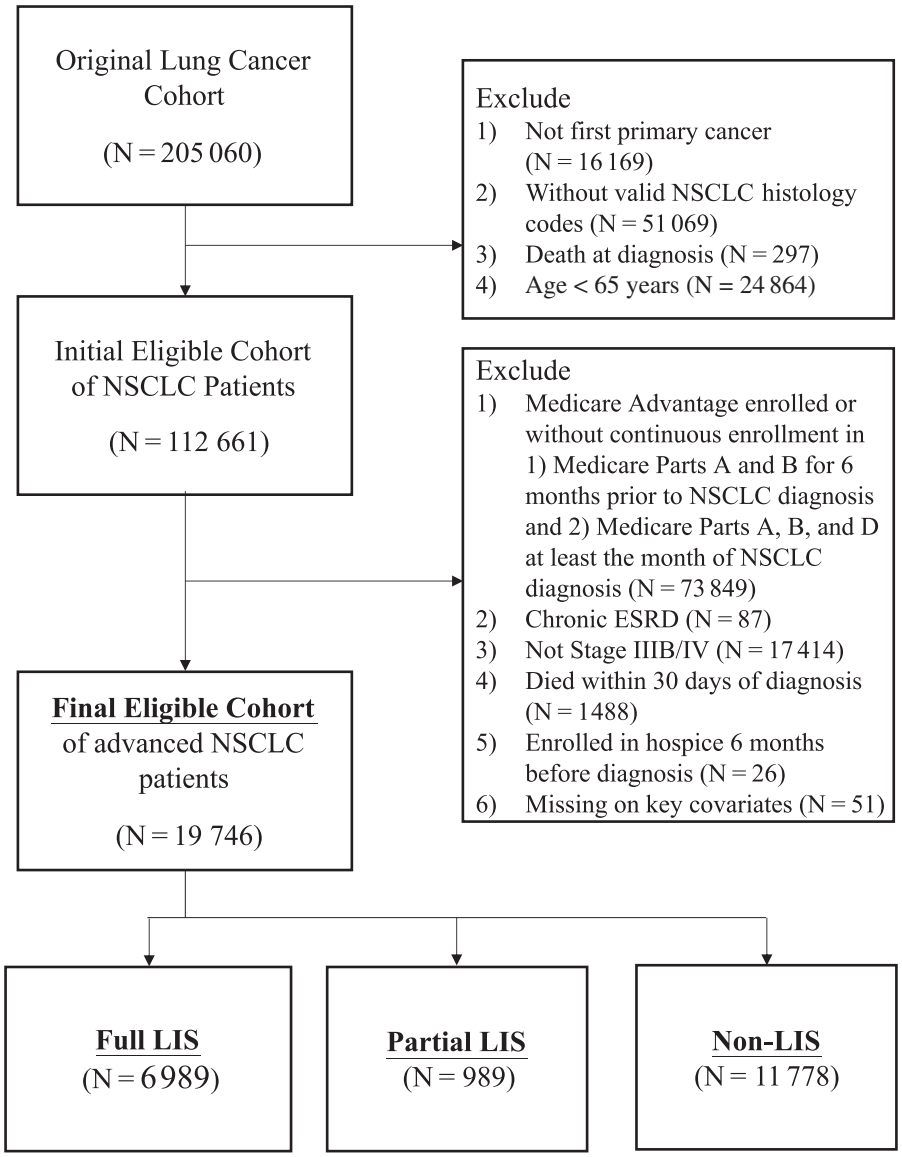

Figure 1. CONSORT diagram of populations included in analyses. ESRD = end-stage renal disease; LIS = low-income subsidy; NSCLC = non–small cell lung cancer.

Exposure Measurement

The primary exposure was patients' LIS status at the month of their advanced NSCLC diagnosis. Patients were defined as having a LIS if they received a full or partial subsidy for their drug costs or if they were dually eligible for both Medicare and Medicaid. We created three categories of subsidy status based on patients' cost-sharing and dual eligible status using previously established definitions (20,21), including full LIS (deemed eligible and automatically enrolled in the LIS program), partial LIS (self-enrolled in LIS with a high copayment or 15% coinsurance), and non-LIS (no cost-sharing subsidy) (Table 1).

Outcome Measure

The primary outcomes of interest were the likelihood of initiating orally administered anticancer drugs and the timing of first orally administered anticancer drug use. Drugs of interest were covered by Medicare Part D and indicated for treating NSCLC by the end of 2014. Part D treatments included gefitinib, erlotinib, crizotinib, ceritinib, and afatinib (Supplementary Table 1, available online). We considered any use of these treatments as our primary outcome, regardless of the line of therapy and molecular subtype (which are not currently available in the SEER-Medicare data). Patients were followed starting from the date of diagnosis through the first occurrence of death, disenrollment, first Part D NCSLC treatment initiation, or 365 days post diagnosis.

Covariates

Covariates included patient demographics (age at diagnosis, sex, race/ethnicity, and marital status), year of diagnosis, cancer stage and histology, receipt of radiation and/or surgery as initial treatment, geographic region, urbanicity, socioeconomic status (census-level high school graduation rates, poverty rates, and household income), comorbidity status (22), and predicted disability status (23) (each measured during the 6 months before diagnosis).

Statistical Analysis

We used descriptive statistics (analysis of variance for continuous variables and χ^2 tests for categorical variables) to evaluate differences in baseline covariates by subsidy group. All tests were two-sided, and a *P* value of less than .05 was considered statistically significant. Next, we estimated unadjusted product-limit failure curves to compare the likelihood of initiating and time to initiate Part D medications among full LIS, partial LIS, and non-LIS populations. We also estimated unadjusted Cox proportional hazards models to compare the probability of initiating a Part D treatment and the time until Part D treatment uptake among each group.

Next, to account for potential differences among those who received LIS and those who did not, we estimated two models. First, we estimated a multivariable adjusted Cox proportional hazards model that included all patient demographic, geographic, clinical, and institutional characteristics from Table 2 in the regression model. Second, we estimated and applied inverse probability of treatment weights (IPTW) (25) to adjust for differences in patient characteristics among LIS groups using these same variables. Although both models provide similar results, the IPTW approach avoids potential violations of the proportional hazards assumption that are common in multivariable models. For each approach we generate hazard ratios and corresponding 95% confidence intervals (CIs) to indicate the relative likelihood of initiating Part D medication in three LIS groups (ie, non-LIS, partial LIS, and full LIS, as reference). We used Kaplan-Meier curves to compare the subsidy groups to confirm that the proportional hazards assumption was not violated for the primary exposure variable. We used SAS software, Version 9.4 (SAS Institute Inc., Cary, NC) for all analyses.

Sensitivity Analysis

In our primary analysis, we wanted to isolate the effect of high out-of-pocket spending on treatment uptake using LIS status as a marker for treatment affordability. However, patients who qualify for LIS are financially disadvantaged relative to their non-LIS peers and may face additional challenges starting and managing their medication use. To better understand the relationship between out-of-pocket costs and treatment uptake, we selected a negative control (26) scenario to explore the relationship between LIS and treatment initiation when out-of-pocket spending is expected to be low for both LIS and non-LIS groups. We used Part B medication uptake (see Supplementary Table 2, available online) as our negative control scenario because supplemental health insurance options are available to cover patient cost-sharing requirements for Part B services for patients who do not otherwise qualify for subsidies. This supplemental coverage results in lower, more consistent, and predictable expenses for patients using Part B services throughout the year. Conversely, supplemental plans are not available to cover patient cost-sharing requirements for treatments covered under a Medicare Part D plan, thus resulting in high out-of-pocket costs in non-LIS patients for Part D treatments but not for Part B treatments. More than 80% of fee-for-service Medicare beneficiaries have some source of supplemental coverage (27). Our hypothesis was that patients with no LIS but who presumably have supplemental coverage to lower their out-of-pocket spending would have shorter time to treatment initiation for Part B drugs relative to patients with partial or full LIS.

Finally, we estimated a multivariable Poisson regression model of the association between each covariate and the probability of using Part D medications to provide insight into factors outside of LIS that influence treatment uptake (Supplementary Table 3, available online).

Results

We identified 19 746 patients diagnosed with advanced NSCLC from July 2007 to December 2013: 6989 (35.4%) with full LIS; 11 778 (59.6%) with no LIS; and 989 (5.0%) with partial LIS (Figure 1, Table 2). Across groups, around 70% were diagnosed with stage IV cancers, and around half had adenocarcinoma subtype. Compared with those with full LIS, patients without full LIS were generally older and were more likely to report race/ethnicity as non-Hispanic white, and this group consisted of more women than men. Most of the population lived in the West or South regions (79.5% full LIS vs 67.0% partial LIS vs 61.1% non-LIS) and big metro/metro areas (80.4% full LIS vs 73.2% partial LIS vs 81.1% non-LIS). Patients with full or partial LIS were more likely to live in an area with lower median incomes and education levels compared with those without any subsidy. Patients with full LIS had poorer health status (comorbidity score of 2+: 35.6% full LIS vs 30.7% partial LIS vs 24.9% non-LIS) and predicted disability status (Poor 3–4: 17.1% full LIS vs 5.7% partial LIS vs 4.5% non-LIS). After the application of IPTW, characteristics between groups were well balanced (Table 2; Supplementary Table 4, available online). In our study, 22.5% of full LIS, 26.8% of partial LIS, and 29.5% of non-LIS were followed for 12 months after diagnosis. Approximately 62.7% of the patients died or disenrolled from Medicare during the follow-up.

Uptake of Part D Medications

During the 12-month period following NSCLC diagnosis, approximately 10% of patients initiated Part D treatments (11.4% full LIS, 7.4% partial LIS, and 9.9% non-LIS) (Figure 2). Compared with patients with full LIS, those without full LIS (ie, non-LIS and partial LIS) were 21% and 39% less likely to initiate Part D treatments, respectively, in unadjusted models (Figure 3, Model 1). The effects remained even after controlling for other factors (Figure 3, Model 2) or applying IPTW (Figure 3, Model 3) to reduce the imbalance among groups (non-LIS vs full LIS $HR_{IPTW} = 0.87$ [95% CI = 0.79 to 0.95, $P = .02$]; partial LIS vs full LIS $HR_{IPTW} = 0.77$ [95% CI = 0.62 to 0.97, $P = .03$]).

The time to initiate Part D treatments was shorter among patients with full LIS compared with those with partial LIS or with no LIS. The mean [SD] time to initiation of orally administered targeted therapies was 10.8 [0.04] months full LIS, 11.3 months (SD = 0.08) partial LIS, and 11.1 months (SD = 0.03) non-LIS, respectively ($P < .001$) (Figure 2).

Uptake of Part B Medications

Uptake of Part B drugs differed in important ways from what was observed for Part D drugs. As expected, Part B drugs were used more often by patients diagnosed with advanced NCSLC over our study period: 35.0% of full LIS beneficiaries initiated Part B treatment; 40.6% partial LIS; and 51.6% non-LIS during the 12 months post diagnosis (Figure 4). However, patients without LIS were more likely to initiate Part B treatments compared with those with full LIS (non-LIS vs full LIS $HR_{IPTW} = 1.42$ [95% CI = 1.35 to 1.48; $P < .001$]) (Figure 5). The time to initiate Part B treatments was shorter among the non-LIS group compared

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Table 2. Baseline patient characteristics before and after IPTW

Characteristic	Pre-IPTW				Post-IPTW			
	Full LIS, % (n = 6979)	Partial LIS, % (n = 989)	Non-LIS, % (n = 11778)	P	Full LIS, % n = 6911	Partial LIS, % (n = 948)	Non-LIS, % (n = 12046)	P*
Age, y				<.001				0.27
65–69	26.6	29.8	21.9		23.1	25.3	24.0	
70–74	28.1	26.9	26.7		27.2	28.0	27.9	
75–79	22.2	22.1	22.6		22.4	22.0	22.2	
80+	23.1	21.1	28.7		27.3	24.7	25.9	
Sex				0.03				0.90
Male	50.6	49.6	48.6		49.4	48.9	49.6	
Female	49.4	50.4	51.4		50.6	51.1	50.4	
Race/Ethnicity				<.001				0.004
Non-Hispanic white	52.7	73.2	89.4		75.0	74.4	73.5	
Non-Hispanic black	19.2	17.0	4.4		10.5	9.6	10.3	
Hispanic	11.4	4.4	2.6		5.9	6.5	5.7	
Other	16.7	5.4	3.6		8.6	9.5	10.5	
Marital status				<.001				0.53
Married	30.5	34.1	54.7		43.7	40.7	43.1	
Single	65.6	61.6	41.6		52.5	55.2	53.1	
Unknown	3.9	4.3	3.7		3.9	4.1	3.8	
Region				<.001				<0.001
North East	11.8	18.3	23.5		21.6	17.8	19.4	
South	32.0	46.7	25.9		28.2	31.9	28.0	
North Central	8.7	14.7	15.4		12.4	12.8	13.3	
West	47.5	20.3	35.2		37.9	37.6	39.3	
Urban/Rural residence				<.001				0.77
Big metro	53.3	45.8	51.1		49.8	48.8	50.8	
Metro	27.1	27.4	30.0		30.1	30.0	29.4	
Urban	5.5	6.4	6.6		6.8	7.5	6.5	
Less urban	11.4	16.5	9.9		10.8	10.7	10.7	
Rural	2.8	3.9	2.4		2.5	3.0	2.6	
% of Non–high school degree				<.001				0.41
00–05%	6.5	8.2	21.9		14.9	12.9	15.4	
05–10%	14.0	17.3	29.5		23.9	23.8	23.2	
10–20%	29.4	35.8	30.1		30.4	32.0	30.4	
20–100%	50.1	38.7	18.5		30.8	31.3	31.0	
% Below poverty				<.001				0.30
00–05%	8.1	9.7	22.5		17.2	15.3	16.3	
05–10%	14.8	19.9	29.2		22.9	21.9	23.5	
10–20%	31.1	36.0	30.4		31.1	31.0	31.5	
20–100%	46.0	34.4	17.9		28.8	31.8	28.7	
Household median income				<.001				0.24
1st quartile (≤$38 187)	40.0	33.8	15.4		25.0	26.8	24.9	
2nd quartile ($38 187–52 684)	25.7	29.6	24.2		25.5	26.8	25.7	
3rd quartile ($52 685–73 391)	20.0	22.3	28.2		24.1	25.0	24.7	
4th quartile (>$73, 391)	14.4	14.3	32.2		25.4	21.4	24.7	
Comorbidity Index†				<.001				0.51
0	35.4	40.8	45.2		40.7	41.9	40.6	
1	29.0	28.4	29.9		29.3	30.8	29.4	
2+	35.6	30.7	24.9		30.1	27.3	30.0	
Predicted DS‡				<.001				0.62
Good 0–2	82.9	94.3	95.5		90.9	91.7	90.7	
Poor 3–4	17.1	5.7	4.5		9.1	8.3	9.3	
Year of diagnosis				<.001				0.98
2007	7.7	9.2	7.1		7.0	7.3	7.3	
2008	15.0	18.1	14.5		14.4	15.3	14.7	
2009	15.3	16.4	14.8		14.9	14.5	15.3	
2010	15.6	15.8	14.1		14.7	15.3	14.6	
2011	15.2	15.6	13.8		14.3	14.9	14.2	
2012	15.6	13.7	16.8		16.5	16.4	16.3	
2013	15.6	11.3	19.0		18.1	16.5	17.6	

(continued)

Table 2. (continued)

Characteristic	Pre-IPTW				Post-IPTW			
	Full LIS, % (n = 6979)	Partial LIS, % (n = 989)	Non-LIS, % (n = 11778)	P	Full LIS, % n = 6911	Partial LIS, % (n = 948)	Non-LIS, % (n = 12046)	P*
Cancer stage				0.006				0.25
IIIB	29.1	28.7	27.0		28.4	28.1	27.3	
IV	70.9	71.3	73.0		71.6	71.9	72.7	
Cancer histology								
Adenocarcinoma	48.2	46.1	54.3	<.001	50.8	51.4	51.2	0.85
Squamous	30.1	30.4	24.1	<.001	26.7	27.1	26.6	0.95
Large cell	2.4	2.5	2.6	0.83	2.5	2.5	2.5	0.98
Other	19.3	20.9	19.1	0.35	20.0	19.0	19.7	0.74
Radiation as first course of therapy	36.3%	41.9	43.9	<.001	41.9	39.6	41.1	0.45
Surgery as first course of therapy	4.9%	5.5	7.4	<.001	6.4	6.8	6.3	0.63
Receipt of care from hospital affiliation with§								
NCI designation	13.0	11.3	18.4	<.001	17.4	16.1	16.9	0.46
Major affiliation with medical school	32.8	39.7	40.9	<.0001	38.8	36.9	38.6	0.54
Teaching hospital	63.6	64.8	68.4	<.001	66.8	65.0	67.0	0.42

*Analysis of variance was used for comparison for continuous variables and χ^2 tests for categorical variables. All tests were two-sided, and a P value of less than .05 was considered statistically significant. The standardized mean differences (24) post IPTW (25) were all below 0.10 between groups (non-LIS vs full LIS; partial LIS vs full LIS), suggesting negligible imbalance in patient baseline characteristics between groups for the analysis (Supplementary Table 3, available online). DS = disability status; IPTW inverse probability of treatment weights; LIS = low-income subsidy; NCI = National Cancer Institute.

†Klabunde's adaptation of the Charlson comorbidity index (22) was used to assess cancer-specific comorbidity index with Charlson comorbidity index included comorbidities other than cancer.

‡Predicted DS (23) was calculated based on a validated claims-based algorithm as a proxy measure of PS among older cancer population.

§Statistical models also adjusted for urbanicity, quarter of the year when diagnosed, and receiving care from the Eastern Cooperative Oncology Group–affiliated hospital.

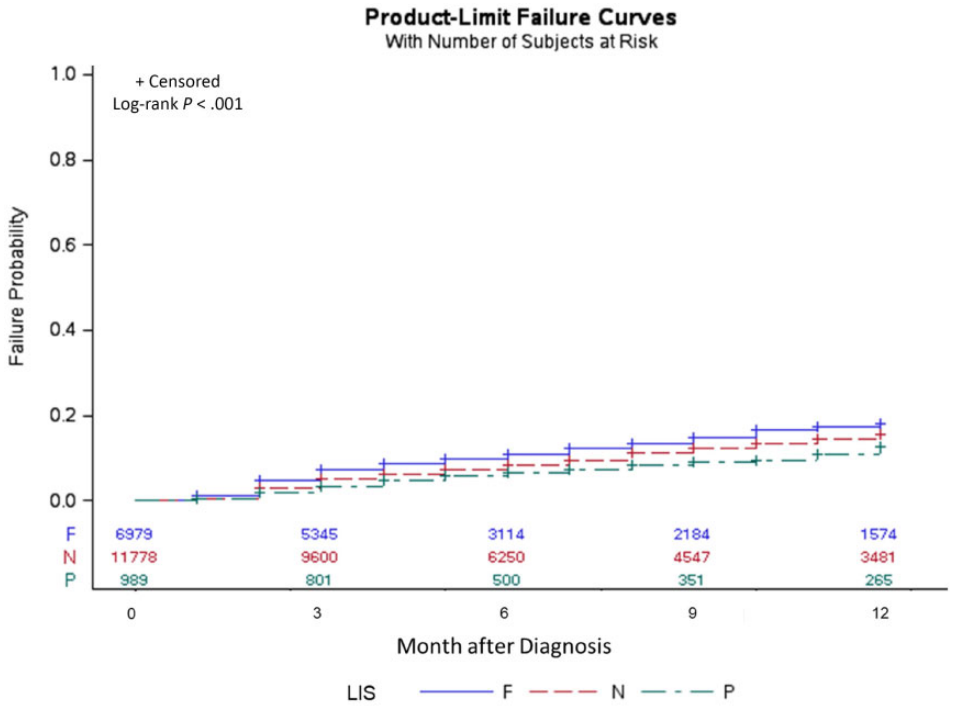

Figure 2. Time initiate Part D treatments by LIS status. LIS = low-income subsidy; F as full LIS, N as non-LIS, and P as partial LIS. "Failure" indicates the outcome of interest, which is the initiation of Part D treatments. *P* values are based on the log-rank test and are two-sided.

with those with any LIS; the mean [SD] time to initiation was 8.4 [0.06] months for full LIS, 7.9 [0.15] months for partial LIS, and 7.0 [0.04] months for non-LIS, respectively ($P < .001$) (Figure 4).

Discussion

This study examined the effect of LIS for Medicare Part D medications on treatment initiation among patients with advanced

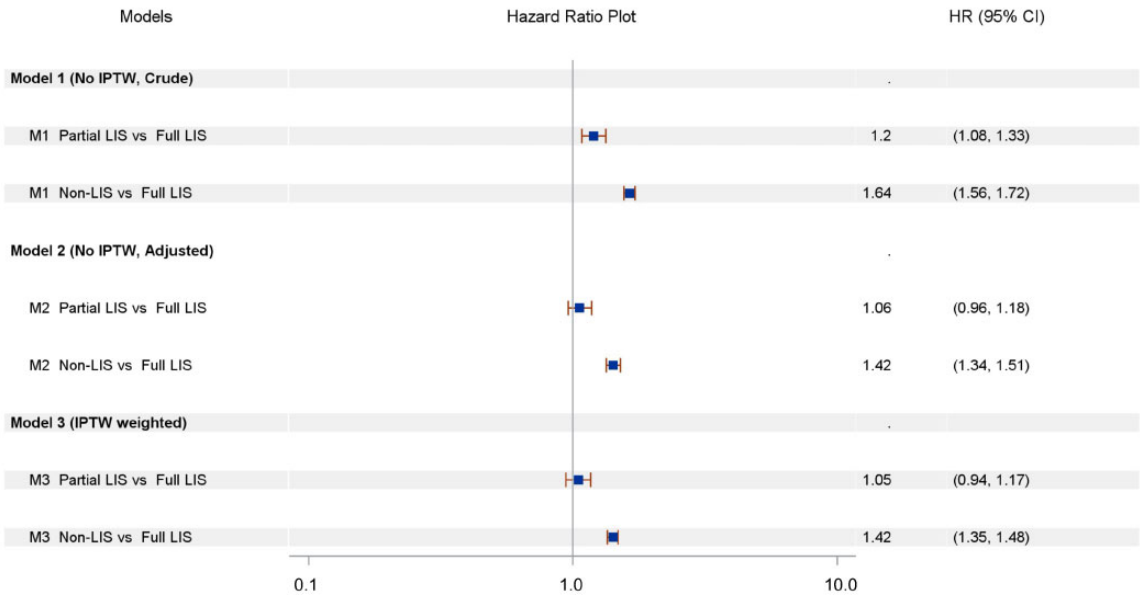

Figure 3. Association between LIS status and time from diagnosis to initiation of Part D treatments. Model 1 applied unadjusted Cox proportional hazards models to estimate crude HRs. To account for potential differences among different LIS groups, we estimated adjusted results using a multivariable Cox proportional hazards model that included all patient demographic, geographic, clinical, and institutional characteristics from Table 2 in the regression model (Model 2) and also applied IPTW (25) to adjust using these same variables (Model 3). The HR plot was plotted on log scales. CI= confidence interval; HR= hazard ratio; IPTW= inverse probability of treatment weight; LIS= low-income subsidy. Error bars represent the 95th percentile of the HR.

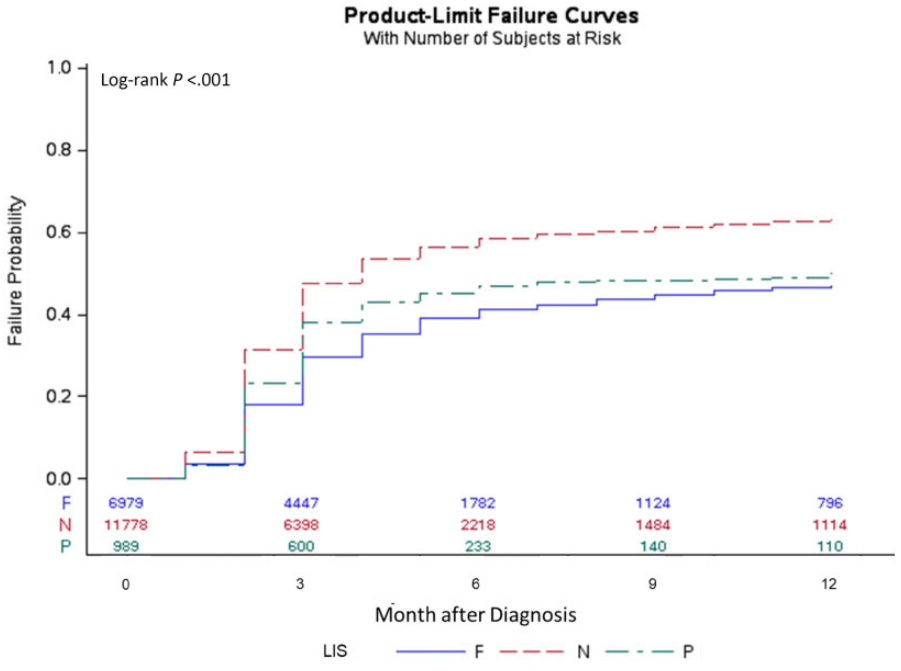

Figure 4. Time initiate Part B treatments by LIS status. LIS= low-income subsidy; F as full LIS, N as non-LIS, and P as partial LIS. "Failure" indicates the outcome of interest, which is the initiation of Part B treatments. *P* values are based on the log-rank test and are two-sided.

NSCLC. We found that cost-sharing support through full LIS or dual eligibility for Medicaid was associated with increased likelihood of initiating an orally administered anticancer drug on Medicare Part D. Specifically, patients with partial or no LIS were less likely to initiate Part D treatments compared with those with full LIS. Notably, uptake was lowest among the partial LIS group, those not poor enough to receive the full subsidy but still responsible for substantial out-of-pocket costs for initiating Part D treatments. This is a novel finding and one that has important consequences for policy as efforts are made to improve access to high-priced drugs under the Part D benefit, particularly for those who have low income but are not eligible for Medicaid.

Our results illustrate how the high up-front cost for initiating a Part D treatment may be limiting patient access to novel

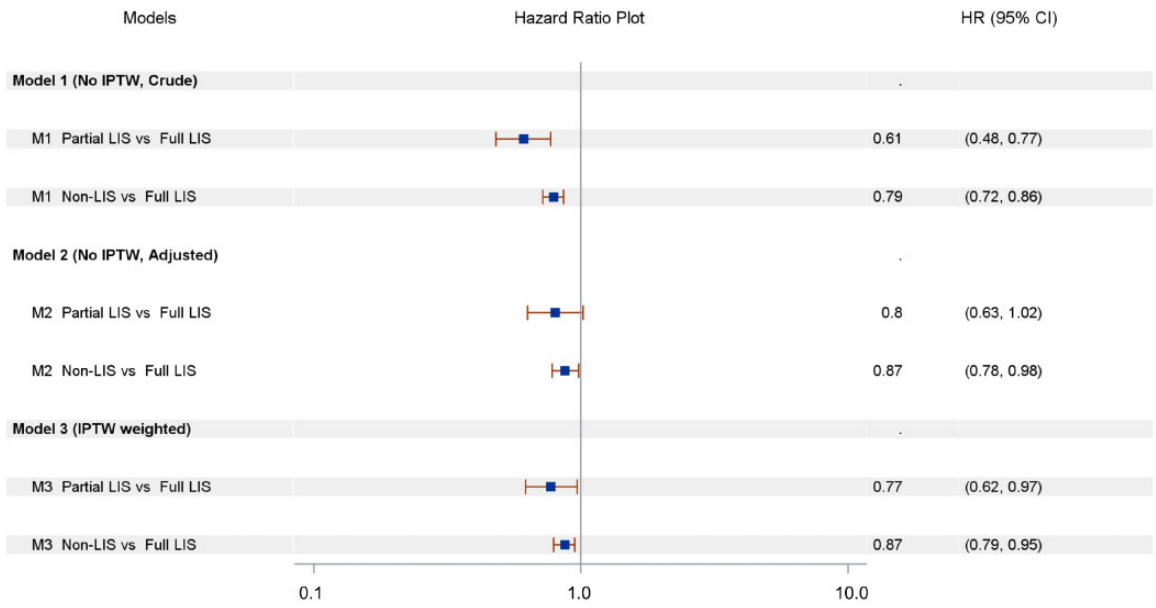

Figure 5. Association between LIS status and time from diagnosis to initiation of Part B treatments. Model 1 applied unadjusted Cox proportional hazards models to estimate crude HRs. To account for potential differences among different LIS groups, we estimated adjusted results using a multivariable Cox proportional hazards model that included all patient demographic, geographic, clinical, and institutional characteristics from Table 2 in the regression model (Model 2) and also applied IPTW (25) to adjust using these same variables (Model 3). HR plot was plotted on log scales. CI= confidence interval; HR= hazard ratio; IPTW= inverse probability of treatment weight; LIS= low-income subsidy. Error bars represent the 95th percentile of the HR.

therapies. As list prices for most anticancer treatments now exceed $14 000 per month on Medicare Part D, expected out-of-pocket costs for treatment initiation exceeds $2000 for patients with no LIS and over $1000 for patients with partial LIS (17,18). In contrast, patients with full cost-sharing support pay less than $10 for the same prescription. It is possible that patients with no or partial subsidies may delay their uptake of treatments while they seek funds to cover their out-of-pocket drug costs. They may also settle for alternative treatments that have lower out-of-pocket costs, particularly those offered under Medicare Part B.

Our findings are consistent with previous research showing delays in initiation of orally administered anticancer drugs covered under Part D among individuals with high out-of-pocket cost and those without LISs (11–15). Importantly, our study distinguishes between those with full, partial, and no LIS. Other studies have combined these groups, masking challenges that may be unique to patients in the partial LIS program. Future work should explicitly examine differences in uptake and treatment use among patients by subsidy level as sample size permits.

Approximately 10% of our sample initiated Part D drugs over the study period, with approximately 11 months between diagnosis and the first Part D drug fill among initiators. These patients were likely treated with other medications before their Part D drug use, as most orally administered anticancer drugs were used as second-line therapy, particularly in earlier years of our study period when few orally administered treatments were available. Further, differences in the timing of initiation between groups were relatively short (~2 weeks of delay between full and partial LIS groups). It is unclear whether such delays are clinically significant. Even so, treatment delays and paying for or seeking out financial support for treatment can be a source of anxiety among patients, making these gaps important even if clinical outcomes are not impacted (14). With many more oral medications approved as frontline treatments for lung cancer since 2014 and the accompanying high prices, policies to reduce or limit patients' out-of-pocket burden are needed (28,29).

Importantly, counter to our findings related to the role of subsidies in Part D, for physician-administered treatments (Part B treatments), patients without LISs were more likely to initiate Part B treatments compared with those with full or partial LIS. We believe that uptake among patients prescribed Part B drugs may mimic a scenario in which patients have similar (and low) out-of-pocket costs because of the prevalence of supplemental health insurance among higher income beneficiaries (27). These findings supported our hypothesis that financial barriers unique to the Medicare Part D benefit may result in lower access to anticancer drugs for patients with insufficient financial support. This was particularly true for treatment initiation and among patients receiving partial LIS (eg, those with low incomes and assets but who still face substantial out-of-pocket costs for medications filled on Part D.).

Our study has limitations. First, tumor biomarkers could potentially influence the need for and response to oral targeted treatments for NSCLC, particularly as indications for orally administered therapy changed over our study period to target specific molecular subtypes (30–32). Information on tumor mutations and molecular testing results is not regularly collected in population-level registry-linked claim databases to date. However, tumor histology or molecular alteration is not likely to vary by subsidy status, which minimizes the concern in the study. Second, given the nature of claims data, only filled prescriptions were observed. Therefore, we cannot distinguish whether differences in treatment use were due to physician prescribing behavior (the patient did not receive a prescription for a drug) or patient filling behavior (the patient received a prescription but did not fill the medication). Third, to maximize sample size, we included only 6 months of prediagnosis data (vs 1 year, which is more commonly used) for measuring clinical status at baseline, including comorbidity and disability status, which could under-capture such measures. Because our

primary interest was in balancing characteristics among LIS and non-LIS groups rather than focusing on the role of comorbidity and disability for treatment uptake, we felt the trade-off in increased sample size was worth this loss of precision with the measures. Fourth, only two of the orally administered anticancer treatments studied were available over the full study period, which may reflect lower-than-expected uptake of novel oral anticancer treatments, although comparisons by LIS status remain valid. Finally, prices for advanced NSCLC drugs covered under Part D were increasing over our study period, and, at the same time, the Medicare Part D benefit generosity was increasing (6).This might have changed out-of-pocket spending requirements for some patients using Part D treatments, but it is unlikely to have a major impact on affordability, given the high up-front costs for initiating treatment among those without subsidies.

Our study highlights potential barriers to timely uptake of orally administered anticancer drugs. Given the growing number of cancer treatments available under Part D, modifications to the Part D benefit, including increasing the generosity of the partial LIS (Extra Help) program and redesigning the benefit to include an out-of-pocket spending limit, could improve access to and affordability of anticancer medications.

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Notes

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