High Cost Sharing and Specialty Drug Initiation Under Medicare Part D: A Case Study in Patients With Newly Diagnosed Chronic Myeloid Leukemia

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ABSTRACT

Objectives: Specialty drugs often offer medical advances but are frequently subject to high cost sharing. This is particularly true with Medicare Part D, where after meeting a deductible, patients without low-income subsidies (non-LIS) typically face 25% to 33% coinsurance (initial coverage phase with "specialty tier" cost sharing), followed by ~50% coinsurance (coverage gap phase), and then 5% coinsurance (catastrophic phase). Yet, no studies have examined the impact of such high cost sharing on specialty drug initiation under Part D. Oral tyrosine kinase inhibitors (TKIs) have revolutionized the treatment of chronic myeloid leukemia (CML), making it an apt case study.

Study Design: A retrospective claims-based analysis utilizing 2011 to 2013 100% Medicare claims.

Methods: TKI initiation rates and time to initiation were compared between fee-for-service non-LIS Part D patients newly diagnosed with CML and their LIS counterparts who faced nominal cost sharing of ≤$5.

Results: The first 30-day TKI fill "straddled" benefit phases, for a mean out-of-pocket cost of $2600 or more for non-LIS patients. Non-LIS patients were less likely than LIS patients to have a TKI claim within 6 months of diagnosis (45.3% vs 66.9%; *P* <.001) and those initiating a TKI took twice as long to fill it (mean = 50.9 vs 23.7 days; *P* <.001). Cox regressions controlling for sociodemographic, clinical, and plan characteristics confirmed descriptive findings (hazard ratio, 0.59; 95% CI, 0.45-0.76). Extensive sensitivity analyses confirmed the robustness of our findings.

Conclusions: High cost sharing was associated with reduced and/or delayed initiation of TKIs. We discuss policy strategies to reduce current financial barriers that adversely impact access to critical therapies under Medicare Part D.

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Specialty drugs commonly offer significant medical advances for chronic and/or life-threatening diseases, but they frequently carry high out-of-pocket costs that may impede patients' access to treatment.[1] The relationship between high out-of-pocket costs and specialty drug treatment access is particularly relevant for Medicare beneficiaries, who face complex cost-sharing arrangements under Medicare Part D's prescription drug benefit. Per CMS regulations, Part D plans may place any drug that exceeds a designated cost threshold ($600 per month from 2011-2015) on a "specialty tier," which typically requires patients to pay 25% to 33% coinsurance during each calendar year's initial coverage phase.[2,3] Once patients' total drug spending exceeds an initial coverage limit ($2840-$2960 from 2011-2015),[4] they enter a coverage gap phase, which requires even higher cost sharing (45%-50% coinsurance from 2011-2015)[5] until their total out-of-pocket Part D spending reaches a certain threshold ($4550-$4700 from 2011-2015). After patients reach that catastrophic coverage limit, they pay 5% coinsurance for the remainder of that calendar year.[4] Today, virtually all Part D plans using tiered benefit structures have a specialty tier.[2]

Initial access to specialty drug treatment is particularly important for those who are newly diagnosed with cancer, where prompt treatment is often essential. This is an increasingly common scenario given that oncology drugs represent one of the largest areas of specialty drug growth in terms of both innovation and spending.[6] Although the majority of Medicare patients experience high cost sharing for specialty drugs under Part D, patients who qualify for full low-income subsidies (LIS) face nominal cost sharing (≤$5) throughout the year. Thus, cancer treatment under Part D provides an ideal case study to explore the relationship between high cost sharing for specialty drugs and treatment initiation, with LIS patients serving as a natural control group.

We focused on newly diagnosed patients with chronic myeloid leukemia (CML) for several reasons. First, nearly half of new CML diagnoses occur in individuals 65 years or older.[7] Second,

the treatment of CML has been revolutionized by tyrosine kinase inhibitors (TKIs), a class of "targeted" specialty drugs that act on a unique oncogenic protein in CML cells known as the BCR-ABL fusion protein. These highly active oral medications limit the growth and progression of CML, transforming it into a chronic condition. With continuous and typically lifelong treatment, TKIs allow most patients with CML to enjoy a near-normal life expectancy compared with a median survival of less than 3 years in the pre-TKI era.[8,9] Third, all TKIs are covered under Medicare Part D. Unlike conditions for which some treatment options with lower out-of-pocket costs may be available (eg, infused drugs covered under Medicare's Part B benefit), elderly patients with CML do not have an equivalent lower-cost option. In this study, we examined the association between high cost sharing and TKI treatment initiation in a sample of patients with Medicare Part D who had been newly diagnosed with CML.

Take-Away Points

We used 100% Medicare claims data to examine initiation of tyrosine kinase inhibitors (TKIs) in patients newly diagnosed with chronic myeloid leukemia.

- Patients not eligible for low-income subsidies, who faced mean out-of-pocket costs of $2600 or more for the first 30-day fill, were less likely to have an initial TKI claim within 6 months of diagnosis and took twice as long to initiate TKI treatment compared with patients receiving low-income subsidies who faced nominal cost sharing (≤$5).
- High cost sharing was associated with reduced and/or delayed initiation of TKIs under Medicare Part D.
- Changes in Part D policies have the potential to increase access to lifesaving cancer treatments.

METHODS

Study Design

This retrospective claims-based study examined TKI initiation among patients covered by Medicare Part D, newly diagnosed with CML. We compared initiation of TKIs among non-LIS Medicare beneficiaries subject to high levels of cost sharing under Part D at the time of initial CML diagnosis (non-LIS group), against a contemporaneous comparison group of newly diagnosed full-LIS patients who faced only nominal cost sharing (LIS group).

Although both the initial coverage phase and the coverage gap phase involve high out-of-pocket costs, our primary analysis focused on patients with a new CML diagnosis during the initial coverage phase only, for 2 key reasons. First, since exiting the initial coverage phase is triggered by reaching an out-of-pocket spending threshold, individuals who had already reached the coverage gap phase at the time of CML diagnosis would have done so because of substantial out-of-pocket spending on other prescriptions, potentially biasing our selection process toward patients with significant comorbidity (ie, requiring multiple and/or expensive medications). Second, those patients would likely be balancing other substantial medical/prescription expenses and health conditions that might influence their decisions to initiate a TKI, thereby limiting our ability to interpret the degree to which initiation decisions may have been related specifically to the out-of-pocket expense for the TKI.

Data Source

We used a data extract of the 2011 to 2013 100% Medicare Chronic Condition Data Warehouse files, which contain data on all fee-for-service Medicare beneficiaries in the United States. We specifically extracted the Medicare inpatient (Part A), outpatient (Part B), and prescription drug (Part D) data files linked with beneficiary summary files and Part D prescription drug plan characteristics files for patients with at least 1 diagnosis of CML (*International Classification of Diseases, Ninth Revision, Clinical Modification* [*ICD-9-CM*] code 205.1).

Sample Selection

We applied several selection criteria to capture our main sample of Medicare patients with newly diagnosed CML. Patients were included if they had: a) at least 1 inpatient or outpatient claim with a diagnosis of CML (*ICD-9-CM* code 205.1) between July 1, 2011, and June 30, 2013 (the first of which represented the "index date"); b) continuous enrollment in both fee-for-service Medicare and a stand-alone Part D prescription plan in the 180 days (6 months) before and after the index date (pre-index period and postindex period, respectively); c) ≥2 CML claims occurring at least 30 days apart (ie, the index claim and at least 1 other claim during the postindex period); d) a claim for a molecular oncogene diagnostic test during the 30 days before or the 30 days after the index date; and e) an index date that fell within the beneficiary's Part D initial coverage phase.

Patients were excluded if they had: a) any CML claims during the pre-index period; b) any claim for a TKI during the pre-index period; c) any diagnosis of acute lymphocytic leukemia (ALL), defined as ≥2 ALL claims 30 days apart during the pre- or postindex period; or d) any change in LIS status during the pre- or postindex period.

Outcome Variables

Our main outcome variable was time to TKI initiation, defined as the number of days elapsed between the index date (first CML diagnosis claim during the study period)

and the date that the first TKI prescription was filled during the 6-month postindex period. Patients who did not have a TKI claim during the 6-month postindex period were considered censored. We also measured the percentage of patients filling a TKI prescription within 6 months of diagnosis and time to TKI initiation among TKI users. All TKIs approved for CML and available during our 2011 to 2013 study period (imatinib [Gleevec], dasatinib [Sprycel], nilotinib [Tasigna], bosutinib [Bosulif], and ponatinib [Iclusig]) were included in the outcome definition.

Statistical Analyses

Descriptive statistics were generated for the main sample. Multivariable Cox regressions were used to examine the difference in time to TKI initiation between non-LIS and LIS patients. Model covariates included sociodemographic characteristics capturing patient age, sex, race, Census region of residence (Northeast, Midwest, South, West), and county-level per capita income. Clinical characteristics included CML disease complexity (mild, moderate, or severe; classified according to the algorithm used by Darkow et al [2007][10]), number of drug classes filled during the pre-index period, Charlson comorbidity score as adapted by the National Cancer Institute,[11] diagnosis of end-stage renal disease (yes/no), and whether the index CML claim was an inpatient claim. Plan characteristics included the Part D drug benefit type (defined standard benefit, actuarially equivalent standard, enhanced alternative, other), TKI formulary coverage (the proportion of TKI drugs available on the market that were covered by the plan during the index claim year), and TKI utilization management tools (the proportion of covered TKIs requiring prior authorization, quantity limits, or step therapy). Finally, covariates for the year of the index CML diagnosis were included to control for any temporal trends.

We conducted extensive sensitivity analyses to test the robustness of our results. First, we examined an alternative way of measuring time to TKI initiation. Since physicians may assign a working diagnosis of CML but delay TKI initiation until the diagnosis is confirmed via molecular oncogene testing, we examined time to initiation based on the days elapsed between the date of the second (rather than the first) CML claim and the date of the first TKI claim. Second, we examined an alternative model specification by using plan formulary-level fixed effects variables, including indicators of the plan formulary identifier for the plans in which patients were enrolled. This approach enabled us to compare non-LIS and LIS patients facing the same formulary, while controlling for a series of patient confounders, in order to isolate the effects of cost-sharing differences and to rule out the influence of other formulary restrictions (eg, formulary coverage, prior authorization, quantity limits, and step therapy requirements for TKIs and other medications).Third, we removed the sample selection requirement that a patient's index date fall within the initial coverage phase and allowed inclusion of all patients meeting our other primary sample selection criteria, regardless of the Part D coverage phase during which they were first diagnosed with CML.

Finally, we also conducted extensive sensitivity analyses to test the degree to which our sampling criteria were effective in achieving our goal of capturing patients newly diagnosed with CML. That is, we sought to maximize sensitivity (identifying all patients newly diagnosed with CML) while also maximizing specificity (excluding patients who may have had a CML claim prior to receiving a revised final diagnosis of a different form of cancer, as well as patients who may have received a TKI for another condition).

To examine how changes in our selection criteria would influence the resulting sample, we began with the most relaxed criterion (identifying new CML patients by requiring 2 or more CML claims, including the index claim) and then applied additional criteria in sequence to examine the impact: a) requiring ≥2 CML claims 30 days apart; b) requiring ≥2 CML claims 30 days apart and requiring a claim for a molecular oncogene diagnostic test (during the 30 days before or the 30 days after the index date); c) requiring ≥2 CML claims and excluding ALL patients (defined as ≥2 ALL claims during the pre- or postindex period); d) requiring ≥2 CML claims 30 days apart and excluding ALL patients (defined as ≥2 ALL claims 30 days apart during the pre- or postindex period); e) requiring ≥2 CML claims 30 days apart, excluding ALL patients (defined as ≥2 ALL claims 30 days apart during the pre- or postindex period), and requiring a molecular oncogene diagnostic test (as defined above); and f) excluding patients whose index CML claim occurred during an inpatient stay, since a lengthy stay may have included an initial course of a TKI during the hospitalization. (Oral drugs administered in inpatient settings are not captured in inpatient claims data.)

All statistical analyses were performed using SAS version 9.2 (SAS Institute, Cary, North Carolina) and STATA/MP version 13 (StataCorp LP, College Station, Texas). The University of Pennsylvania Institutional Review Board deemed the study exempt from informed consent procedures, as no data were collected directly from human subjects.

RESULTS

Our main sample selection criteria identified 1053 patients with newly diagnosed CML between 2011 and 2013.

Baseline characteristics for this sample are reported in Table 1. The non-LIS group was older and had a higher percentage of males and white patients, compared with the LIS group. The non-LIS group also had a lower mean Charlson comorbidity score but a larger proportion of patients with moderate to severe CML severity at diagnosis, as well as a greater percentage of patients who faced prior authorization requirements for TKIs, compared with the LIS group.

All non-LIS patients were subject to 25% to 33% coinsurance for TKIs during the initial coverage phase, regardless of whether their plan had a distinct specialty tier. Further, given mean total costs of ~$6800 per 30-day TKI prescription, the first drug fill "straddled" Part D benefit phases (pushing beneficiaries out of the initial coverage phase and into the coverage gap phase) and generated an out-of-pocket cost for the initial TKI fill of approximately $2600 or more for non-LIS patients (data not shown). On the other hand, the full LIS patients faced out-of-pocket costs of $5 or less for the initial TKI fill (data not shown).

The Figure shows Kaplan-Meier curves for TKI initiation, stratified by LIS status. The time to TKI initiation was significantly longer in the non-LIS group compared with the LIS group (log-rank P <.001). A significantly lower proportion of the non-LIS group initiated a TKI within 1 month (21% vs 53%; P <.001) and within 3 months (36% vs 65%; P <.001) of initial CML diagnosis compared with the LIS group. Six months after the first CML claim, the non-LIS group was still less likely than the LIS group to have initiated a TKI (45% vs 67%; P <.001) (Table 2).

On average, non-LIS patients who did fill a TKI took twice as long to do so (mean = 50.9 vs 23.7 days; P <.001). After controlling for sociodemographic, clinical, and plan characteristics in Cox regression analysis, LIS status remained highly associated with TKI initiation, with the non-LIS group having a lower hazard of TKI initiation compared with the LIS group (hazard ratio, 0.59; 95% CI, 0.45-0.76; P <.001) (eAppendix Table [available at **www.ajmc.com**]). Subgroup analyses in elderly versus disabled Medicare beneficiaries showed consistent findings, with non-LIS patients having a lower hazard of TKI initiation than LIS patients (data not shown). Extensive sensitivity analyses using varying outcome definitions, analytic techniques, and sample selection criteria showed findings consistent with the main results (Table 2).

Table 1. Sample Characteristics by Low-Income Subsidy Status

	Non-LIS Group (n = 769)	LIS Group (n = 284)	P[a]
Sociodemographic Characteristics			
Age, years: mean (SD)	75.8 (7.9)	66.7 (14.1)	<.001
Age group, years: n			<.001
<65	26 (3.4%)	109 (38.4%)	
65-69	127 (16.5%)	39 (13.7%)	
70-74	223 (29.0%)	45 (15.8%)	
75-79	144 (18.7%)	39 (13.7%)	
≥80	249 (32.4%)	52 (18.3%)	
Sex, n			.004
Male	420 (54.6%)	127 (44.7%)	
Female	349 (45.4%)	157 (55.3%)	
Race, n			<.001
White	738 (96.0%)	179 (63.0%)	
Black	19 (2.5%)	59 (20.8%)	
Hispanic	0 (0.0%)	19 (6.7%)	
Other	12 (1.6%)	27 (9.5%)	
Region, n			.013
Northeast	109 (14.2%)	44 (15.5%)	
Midwest	234 (30.4%)	61 (21.5%)	
South	301 (39.1%)	115 (40.5%)	
West	125 (16.3%)	64 (22.5%)	
County-level per capita income,[b] mean (SD)	4.29 (1.23)	4.17 (1.37)	.160
Clinical Characteristics			
CML severity, n			<.001
Mild	345 (44.9%)	159 (56.0%)	
Moderate	326 (42.4%)	84 (29.6%)	
Severe	98 (12.7%)	41 (14.4%)	
Number of drug classes (pre-index period[c]), mean (SD)	6.3 (3.3)	6.6 (3.7)	.170
Charlson comorbidity score, mean (SD)	0.86 (1.35)	1.08 (1.55)	.021
Diagnosis of end-stage renal disease, n	NR[d]	NR[d]	.015
Index CML claim was an inpatient claim, n	62 (8.1%)	35 (12.3%)	.034

(continued)

DISCUSSION

Our study offers new insights into the relationship between high cost sharing and cancer treatment initiation

Table 1. Sample Characteristics by Low-Income Subsidy Status *(continued)*

	Non-LIS Group (n = 769)	LIS Group (n = 284)	*P*[a]
Plan Characteristics			
Part D drug benefit type, n			<.001
Defined standard benefit	NR[d]	38 (13.4%)	
Actuarially equivalent standard	116 (15.1%)	180 (63.4%)	
Enhanced alternative	335 (43.6%)	11 (3.9%)	
Other	314 (40.8%)	55 (19.4%)	
Formulary coverage and utilization management tools for TKIs, mean (SD)			
Proportion of TKIs available on market covered by the plan	0.99 (0.03)	0.99 (0.05)	.002
Proportion of covered TKIs requiring prior authorization	0.89 (0.29)	0.75 (0.41)	<.001
Proportion of covered TKIs subject to quantity limits	0.41 (0.47)	0.40 (0.45)	.790
Proportion of covered TKIs subject to step therapy	0.00 (0.00)	0.00 (0.00)	
Index year (CML diagnosis), n			.610
2011	153 (19.9%)	64 (22.5%)	
2012	394 (51.2%)	138 (48.6%)	
2013	222 (28.9%)	82 (28.9%)	

CML indicates chronic myeloid leukemia; LIS, low-income subsidy; NR, not reported; TKI, tyrosine kinase inhibitor.
[a]Continuous variables were compared using ANOVA. Categorical variables were compared using Pearson's χ^2 test.
[b]In $10,000s.
[c]Pre-index period refers to the 180 days (6 months) prior to the index CML claim.
[d]Not reported separately due to cell size of 10 or less, per CMS data use agreement.

in Medicare Part D beneficiaries. We found significantly lower fill rates and significantly longer time to initiation of TKIs among beneficiaries newly diagnosed with CML who were responsible for high out-of-pocket costs compared with their counterparts who faced minimal out-of-pocket costs due to receipt of LIS. The robustness of these results was confirmed via a wide range of sensitivity analyses, suggesting that patient out-of-pocket burden is associated with delayed and/or reduced initiation of critical treatments under Medicare Part D.

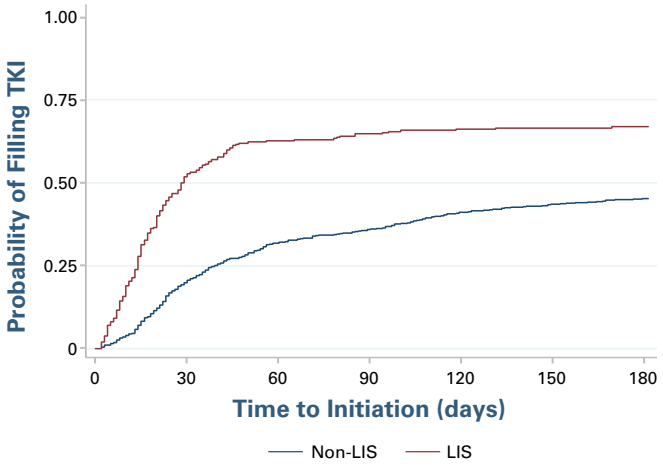
To our knowledge, this is the first study to utilize a 100% data extract of national Medicare Part A, B, and D claims linked with Part D plan and formulary characteristics information to explore the relationship between high cost sharing and access to specialty cancer drugs. Use of this data set allowed us to extend prior findings on this topic in a number of ways. First, most prior evidence in this area comes from data on privately insured populations from 2009 or earlier, wherein specialty drugs were subject to substantially lower levels of cost sharing.[12-16] In fact, the specialty drugs examined in all of these studies had median monthly out-of-pocket payments of $30 or less.[1] As a result, those findings have limited generalizability to the complicated cost-sharing structure and high out-of-pocket costs currently present under Medicare Part D. Two prior studies that included data on Medicare patients using specialty cancer drugs either did not conduct subgroup analyses in Medicare patients[17] or averaged cost-sharing amounts across the high and low cost-sharing coverage phases under Part D,[18] and thus, the specific impact of out-of-pocket costs on treatment during periods of high cost sharing was obscured. Furthermore, both studies lacked medical claims data and were unable to control for important clinical characteristics.[17,18]

Second, all prior studies lacked information on plan formulary characteristics and, hence were unable to account for the confounding effect of utilization management tools, such as prior authorization, quantity limits, and step therapy, which are increasingly applied to specialty drugs as a complement or substitute to cost-sharing strategies.[12-18] Our study is the first to use detailed information on Part D plan formularies to control for the extent of formulary coverage and utilization management for the studied cancer drug class. Finally, although the literature in general suggests a stronger association between cost sharing and treatment initiation than treatment adherence and/or discontinuation,[1] prior studies examining specialty cancer drug treatment initiation have lacked a large sample size (given their data source) and/or a more clinically nuanced approach to identify patients newly diagnosed with cancer, or to examine treatment history in a way that would reveal whether patients may have delayed treatment initiation.[12,13,15,17]

The magnitude of the discrepancies in the outcomes we measured—double-digit differences in the percentage of patients initiating TKI treatments within 6 months of initial diagnosis and, on average, those filling Part D TKI prescriptions within 6 months taking roughly twice as long to start treatment—are striking. This is especially notable given that, unlike some cancer treatments that extend survival by months, TKIs can extend survival by many years and allow most patients to live with CML as a chronic disease.[8] Further, oral TKIs do not carry additional burdens associated with many specialty drugs that require self-injection

or infusions (eg, needle anxiety, pain with administration, need for refrigeration or special handling, travel to an infusion center), so there may be fewer potential barriers beyond out-of-pocket burden for patients to consider when deciding to initiate treatment promptly or at all. In these ways, TKIs represent particularly high-value medications from a patient perspective. Although the relatively short duration of follow-up in our observational analyses did not allow us to assess the impact of TKI delay on long-term clinical outcomes, recent data suggest that prolonged delays in TKI initiation can have a deleterious effect on survival in patients with CML.[19]

Figure. Kaplan-Meier Curves for Time to TKI Initiation (in days), by Low-Income Subsidy Status[a]



LIS indicates low-income subsidy; TKI, tyrosine kinase inhibitor.
[a]Log-rank test comparing Kaplan-Meier curves between LIS and non-LIS groups indicated $P < .05$.

Limitations

Several study limitations should be noted. First, this was a cross-sectional analysis that used LIS patients as a control group and, hence, the study documents associations and is not able to establish causal relationships between high cost sharing and treatment initiation. As with all observational studies, there is the potential for unobserved confounding (eg, related to additional clinical or treatment history variables not available in our claims data) to contribute to observed differences in initiation. Of note, many of the issues that are relevant for other oncology studies, such as differences in patient perceptions of the benefits and costs of an expensive treatment that may have more limited potential to improve quality of life or extend survival, would be expected to play less of a role in decisions about whether to initiate a TKI. In addition, whereas patient-level demographic and clinical differences could have contributed to the observed differences in TKI initiation, evidence suggests that age and comorbidities have little effect on the success of TKI treatment for CML.[20] Thus, all patients would be expected to be similarly eligible for TKI treatment. Further, we sought to offset the limitations of our observational design by employing multivariable regression to control for a variety of sociodemographic, clinical, and plan-level characteristics that could influence treatment decisions. We also conducted extensive sensitivity analyses, with consistent findings that suggest our results are robust.

Second, although 100% sample Medicare claims should include data for all beneficiaries who accessed TKIs through their Part D benefit (barring coding errors or omissions), we note 2 circumstances that may not be reflected in the claims data. On one hand, our data set did not capture patients who may have been receiving medication outside of their Part D benefit, such as through a manufacturer program that provides free or reduced-cost prescription drugs. Thus, it is possible that some patients who were classified as not initiating treatment, or as delaying initiation, may have been receiving medication via other means that would not have resulted in a Medicare Part D prescription claim.[21] Regardless, our results are an accurate reflection of access issues under the Medicare Part D program, which was specifically created to improve access to drug therapy. On the other hand, some non-LIS patients in our sample who accessed TKIs under Medicare Part D may have been able to do so only because of supplemental cost-sharing help from patient assistance programs sponsored by nonprofit foundations. (Federal law constrains manufacturer-sponsored patient assistance programs from offering cost-sharing assistance to Part D beneficiaries.[21]) In those cases, our results would underestimate the true adverse impact of high cost sharing. In both circumstances, the need to seek additional assistance has the potential to add stress at an overwhelming time, when individuals and families are coping with the impact of a new cancer diagnosis.

Third, in order to isolate a newly diagnosed population that would be subject to high cost sharing, we required that our sample be diagnosed during Medicare Part D's initial coverage period. As a result, our patient population may have been healthier overall than patients newly diagnosed with CML who did not meet this criterion. That is, patients who had already reached the initial coverage limit through spending on other pharmaceutical treatment (presumably due to the number and/or severity of other medical condi-

Table 2. TKI Initiation Among Patients Newly Diagnosed With CML, by Low-Income Subsidy Status

	Number of Patients			Probability of Using a TKI Within 6 Months of Index Claim[a]		
	All	Non-LIS	LIS	Non-LIS	LIS	Difference[b]
Primary analysis						
	1053	769	284	45.3%	66.9%	–21.7%
Sensitivity analysis: index date defined as 2nd CML claim						
	938	706	232	40.4%	59.9%	–19.5%
Sensitivity analysis: plan formulary fixed effects models						
	1053	769	284	45.3%	66.9%	–21.7%
Sensitivity analysis: inclusion of patients newly diagnosed with CML in any Part D coverage phase[c]						
	1292	877	415	46.9%	70.8%	–24.0%
Sensitivity analysis: alternate sample selection criteria to identify CML patients						
≥2 CML claims	2790	1931	859	23.6%	37.4%	–13.8%
≥2 CML claims 30 days apart	2269	1589	680	28.3%	45.7%	–17.5%
≥2 CML claims 30 days apart and with molecular oncogene diagnostic test[d]	1293	934	359	42.0%	60.5%	–18.5%
≥2 CML claims and excluding ALL patients	1831	1248	583	30.0%	46.1%	–16.2%
≥2 CML claims 30 days apart and excluding ALL patients	1688	1179	509	33.8%	53.4%	–19.6%
≥2 CML claims 30 days apart, with molecular oncogene diagnostic test,[d] and excluding both ALL patients and patients whose index CML claim occurred as an inpatient	956	707	249	45.0%	67.5%	–22.5%

ALL indicates acute lymphocytic leukemia; CML, chronic myeloid leukemia; LIS, low-income subsidy; TKI, tyrosine kinase inhibitor.
[a]Except where indicated otherwise, index claim refers to the first inpatient or outpatient claim with a diagnosis of CML (*International Classification of Diseases, Ninth Revision, Clinical Modification* code 205.1) between July 1, 2011, and June 30, 2013. Outcomes were captured during the 180 days (6 months) after the index claim.
[b]All differences were statistically significant at $P < .001$ level.
[c]Removed primary sample selection criterion requiring that new CML diagnosis occur within the Part D initial coverage phase.
[d]Refers to a claim for the molecular oncogene diagnostic test within the 30 days before or 30 days after the date of the index CML claim.

tions) were excluded from our sample. A sensitivity analysis examining patients who received a new diagnosis of CML at any point during the coverage year showed consistent results, however, suggesting that this sampling decision did not significantly limit the generalizability of our findings. Finally, since Medicare claims available from CMS only include data on Medicare fee-for-service patients, our results may not be generalizable to Medicare Advantage patients.

Policy Implications

Insurance coverage, as per economic theory, is intended to help protect patients against the risk of catastrophic loss, where the loss itself is a relatively rare and low-likelihood event, and beneficiaries of that coverage are not likely to alter their behavior in the presence of insurance.[12] The oncology context is an excellent example of how insurance coverage can be used to reduce the risk of high spending for patients: many specialty drugs are very expensive, and they are often used to treat conditions that have a low probability of occurring. With 1% to 5% of patients using specialty drugs,[22-24] insurance can serve its intended purpose to spread the risk of such occasional losses over a large insured population so that sick patients are not burdened with inordinately high costs for potentially life-saving or life-extending treatments. The potential for such burden is particularly of concern under Medicare Part D, where beneficiaries who do not qualify for low-income subsidies face specialty tier cost sharing of 25% to 33% in the initial coverage phase followed by 45% cost sharing in the coverage gap phase. Individuals currently need to spend up to $4700 out of pocket before their cost sharing drops to 5% during the catastrophic coverage period.[4] Although the 2010 Affordable Care Act is scheduled to gradually close the Part D coverage gap by 2020, patients will still be responsible for 25% to 33% coinsurance during the coverage gap phase, effectively extending the high cost sharing that is currently in place for specialty drugs during the initial coverage phase. Thus, patients will continue to face financial barriers that may inadvertently discourage use of high-value treatments.[5]

Our results point toward the critical need for regulators to consider approaches to provide Medicare Part

Time (in days) to Initiate a TKI (among those initiating within 6 months of index CML claim)[a]			Cox Regression Results		
Non-LIS	LIS	Difference[b]	Hazard Ratio	95% CI	*P*
50.9	23.7	27.2	0.59	(0.45-0.76)	<.001
45.6	19.4	26.2	0.61	(0.45-0.82)	.001
50.9	23.7	27.2	0.51	(0.39-0.68)	<.001
48.6	24.5	24.1	0.60	(0.47-0.78)	<.001
50.6	27.1	23.4	0.72	(0.58-0.88)	.002
50.3	27.0	23.3	0.68	(0.55-0.83)	<.001
49.9	24.8	25.1	0.66	(0.52-0.85)	.001
51.1	26.7	24.5	0.70	(0.56-0.88)	.002
51.5	25.9	25.5	0.65	(0.52-0.81)	<.001
51.2	23.8	27.3	0.56	(0.43-0.73)	<.001

D patients with additional protection against extremely high cost sharing for these medications. Several policy solutions may be considered. First, CMS should reconsider its policies permitting assignment of drugs to Part D specialty tiers based solely on the fact that their monthly acquisition cost exceeds a certain threshold, as well as the application of across-the-board high levels of coinsurance for all specialty drugs and for all patients requiring these drugs. Specialty drug cost sharing that accounts for medication value, as is the case with value-based insurance design approaches, may be more appropriate than these current one-size-fits-all Part D policies, wherein cost sharing is directly a function of the medication cost.[23] That is, it makes sense to reduce or limit cost sharing to modest amounts so as to remove it as a barrier to patient initiation of and adherence to high-value specialty medications. Policy changes to lower cost sharing for high-value specialty drugs may be financially feasible, given a recent actuarial analysis that indicated that the cost of eliminating Part D specialty tiers could be offset by implementing relatively minor increases in traditional 3-tiered co-payments.[24]

Second, creating greater consistency in out-of-pocket costs throughout the benefit year has the potential to reduce burden on patients who are currently subject to front-loaded out-of-pocket costs during the Part D initial coverage period and coverage gap. The complex and variable cost sharing required by the current Medicare Part D benefit structure likely poses challenges, particularly for elderly beneficiaries who are on a fixed income. Our study documented a mean out-of-pocket payment for the first TKI prescription fill of ~$2600 or more; this amount far exceeds the average monthly Social Security benefit (<$1350), which provides a substantial portion of income for many Medicare beneficiaries.[25]

To help preserve the stability of monthly budgets for Medicare beneficiaries, approaches allowing patients to distribute total out-of-pocket costs more evenly throughout the benefit year should be considered. This would be analogous to strategies used to help individuals and families manage energy bills by distributing high winter heating costs throughout the calendar year. Finally, given that entry into the catastrophic coverage period still leaves Medicare Part D beneficiaries responsible for 5% cost sharing for the remainder of the calendar year—resulting in sums that can be substantial for specialty medications (eg, ~$350 per monthly TKI fill)—CMS should consider annual out-of-pocket maximums akin to those in the health insurance exchange plans and many private insurance plans. A combination of these approaches, which would distribute out-of-pocket costs as well as limit annual out-of-pocket liabilities for beneficiaries, has the potential to not only reduce the risk of initiation delays, but also to reduce cost-related adherence and persistence problems.[26,27]

CONCLUSIONS

As more specialty drug treatments for cancer become available and part of standard care, there is increasing need to examine the impact of out-of-pocket costs on treatment initiation, adherence, and continuity of care, and to document how delays or interruptions in care impact clinical outcomes and overall healthcare costs. Our study suggests out-of-pocket costs may limit and/or delay initiation of life-sustaining oral medication for Medicare patients with newly diagnosed CML, providing evidence that policy changes are needed to ensure optimal access to specialty medications under Medicare Part D.

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eAppendix Table. Time to TKI Initiation in the 6 Months Following New CML Diagnosis (primary sample)

	Hazard Ratio	95% CI	*P*
Sociodemographic Characteristics			
Non-LIS status	0.59	0.45-0.76	.000
Age, years			
<65	1.30	0.95-1.76	.099
65-69		ref	
70-74	0.94	0.72-1.22	.624
75-79	0.73	0.54-0.98	.039
≥80	0.63	0.48-0.83	.001
Race			
White		ref	
Black	1.07	0.78-1.47	.678
Hispanic	1.31	0.74-2.30	.350
Other	1.61	1.08-2.40	.018
Female sex	1.22	1.02-1.45	.030
Region			
Northeast	1.04	0.76-1.43	.813
Midwest	0.97	0.74-1.28	.838
South	1.05	0.81-1.36	.694
West		ref	
County-level per capita income[a]	0.99	0.91-1.07	.800
Clinical Characteristics			
CML severity			
Mild		ref	
Moderate	0.45	0.37-0.56	.000
Severe	0.61	0.46-0.81	.001
Charlson comorbidity score	1.02	0.95-1.10	.564
Number of drug classes (pre-index period[b])	1.01	0.99-1.04	.337
Diagnosis of end-stage renal disease	1.48	0.79-2.79	.220
Index CML claim was an inpatient claim	0.99	0.74-1.33	.956
Plan Characteristics			
Part D drug benefit type			
Defined standard benefit	1.18	0.76-1.85	.462
Actuarially equivalent standard	0.90	0.69-1.17	.413
Enhanced alternative	1.01	0.80-1.29	.914
Other		ref	
Formulary coverage and utilization management tools for TKIs			
Proportion of TKIs available on market covered	0.30	0.02-3.56	.338

by the plan			
Proportion of covered TKIs requiring prior authorization	1.18	0.85-1.64	.327
Proportion of covered TKIs subject to quantity limits	0.99	0.80-1.21	.896
Proportion of covered TKIs subject to step therapy	1.00	1.00-1.00	.
Index year (CML diagnosis)			
2011		ref	
2012	0.93	0.74-1.16	.513
2013	1.19	0.91-1.56	.210

CML indicates chronic myeloid leukemia; LIS, low-income subsidy; ref, reference; TKI, tyrosine kinase inhibitor.
[a]In $10,000s.
[b]Pre-index period refers to the 180 days (6 months) prior to the index CML claim.