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ORIGINAL REPORT

Rising Prices of Targeted Oral Anticancer Medications and Associated Financial Burden on Medicare Beneficiaries

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This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibility of the authors.

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ABSTRACT

Purpose

The high cost of oncology drugs threatens the affordability of cancer care. Previous research identified drivers of price growth of targeted oral anticancer medications (TOAMs) in private insurance plans and projected the impact of closing the coverage gap in Medicare Part D in 2020. This study examined trends in TOAM prices and patient out-of-pocket (OOP) payments in Medicare Part D and estimated the actual effects on patient OOP payments of partial filling of the coverage gap by 2012.

Methods

Using SEER linked to Medicare Part D, 2007 to 2012, we identified patients who take TOAMs via National Drug Codes in Part D claims. We calculated total drug costs (prices) and OOP payments per patient per month and compared their rates of inflation with general health care prices.

Results

The study cohort included 42,111 patients who received TOAMs between 2007 and 2012. Although the general prescription drug consumer price index grew at 3% per year over 2007 to 2012, mean TOAM prices increased by nearly 12% per year, reaching $7,719 per patient per month in 2012. Prices increased over time for newly and previously launched TOAMs. Mean patient OOP payments dropped by 4% per year over the study period, with a 40% drop among patients with a high financial burden in 2011, when the coverage gap began to close.

Conclusion

Rising TOAM prices threaten the financial relief patients have begun to experience under closure of the coverage gap in Medicare Part D. Policymakers should explore methods of harnessing the surge of novel TOAMs to increase price competition for Medicare beneficiaries.

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INTRODUCTION

Targeted oral anticancer medications (TOAMs) have been the focus of drug development for the past two decades.[1-3] These novel drugs not only substantially improve the survival of patients with several cancers, such as chronic myelogenous leukemia and renal cell cancer, but have also revolutionized cancer care delivery, moving it from an office-based setting to a home-based environment.[4] Despite their clinical benefit and ease of administration, the high prices of TOAMs have raised major concerns over their affordability.[5,6] A recent study of nonelderly patients with cancer with private insurance showed that of the two classes of targeted anticancer medications, TOAMs and targeted intravenous medications, the trends of rising prices at launch and sustained price increases postlaunch were more pronounced among TOAMs.[7] Other studies of commercially insured patients with cancer have shown similar trends.[8,9]

Patient financial burden has been increasingly recognized as a major toxicity of cancer treatment,[10,11] manifesting in several dimensions.[12] Material conditions include lost productivity, out-of-pocket (OOP) costs, bankruptcy, and medical debt.[13,14] Psychological responses include financial distress;[15,16] coping behaviors include poor adherence.[17,18] Some evidence has even linked financial burden to adverse health outcomes.[19] Analyses of commercial claims data have noted substantially lower OOP payments for privately insured patients with cancer receiving TOAMs under the pharmacy benefit, compared with those receiving targeted intravenous medications under the medical benefit, because of differences in insurance benefit design.[7]

ASSOCIATED CONTENT

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Appendix

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The low OOP costs of TOAMs observed among privately insured patients with cancer are largely attributable to patient cost sharing taking the form of coinsurance with an OOP max or copayments in the majority of pharmacy benefits for these patients.[20]

The situation is much different for the 70% of Medicare beneficiaries who are enrolled in Medicare Part D,[21] the Medicare prescription drug benefit program, and whose use of TOAMs is covered under this program. Understanding the financial burden for Part D enrollees is important because they are more likely than other Medicare beneficiaries to be members of vulnerable groups: older, in fair or poor health, racial and ethnic minorities, or with low income and educational status.[22] The standard Part D plan encompasses four phases, and beneficiaries spend their way sequentially through these phases: (1) deductible ($320 in 2015), with 100% cost-sharing; (2) initial coverage (up to $2,960 in total prescription drug costs), with 25% to 33% coinsurance for specialty drugs[23]; (3) the coverage gap, or donut hole (up to $6,680 in total costs), with 100% coinsurance; and(4) catastrophic coverage, with 5% cost-sharing and no OOP maximum. Under this less-generous coverage structure, the high prices of TOAMs can impose considerable financial burdens on Medicare Part D enrollees, especially given their sociodemographics. Sustained price increases postlaunch exacerbate this concern. Under the Affordable Care Act, the coverage gap is scheduled to gradually be closed, reducing the coinsurance in this benefit phase from 100% to 50% in 2011 and further down to 25% in 2020.

Using data from Medicare prescription drug plans on benefit designs and the average prices plans pay for oral anticancer drugs, Dusetzina and Keating[24] simulated the potential effects of closing the coverage gap for patients with cancer. Using assumptions on plausible patterns of drug use, and allowing for a conservative range of possible trajectories of drug price increases, the authors found that filling the coverage gap would result in OOP savings by 2020. To better understand the impact of increasing drug prices on the Medicare Part D and to explore whether the coverage gap closure could ease patients' financial burden, we examined recent cost trends of TOAMs and TOAM-related OOP payments for older patients with cancer with Medicare prescription drug coverage. We built on prior research by using patient-level data on drug costs, OOP expenses, and utilization patterns for the distribution of Part D enrollees taking TOAMs, and we estimated how these changed after the coverage gap began to be filled. Findings from our study offer important policy insights for policymakers contemplating reforms to Medicare prescription drug coverage.

METHODS

Data Source and Study Population

We analyzed SEER-Medicare data to examine trends in the financial burden of TOAMs on the Medicare Part D program and on beneficiaries enrolled in Part D. We determined the list of TOAMs from the National Cancer Institute's Targeted Cancer Therapy Fact Sheet[25] (Appendix Table A1, online only) and identified patients who take TOAMs via brand names, generic names, and National Drug Codes from the Part D claims files. We limited the study period to 2007 to 2012, because Part D data in SEER-Medicare were only available after 2007. We then linked patients who take TOAMs to the Patient Entitlement and Diagnosis Summary File via unique patient identifiers to extract information on patient demographics and tumor types. Last, we excluded patients younger than age 65 or who were not enrolled in Medicare Part D on the dates of use of TOAMs.

Cost Measures

Medicare Part D files included two cost variables: gross drug costs and patient pay amount. Gross drug costs represent total drug costs, including the portions of drug costs that are the responsibility of the Medicare program, prescription drug plans, beneficiaries, and other parties. Patient pay amount is the amount paid by beneficiaries that is not reimbursed by a third party; therefore, it captures the OOP payments for Medicare beneficiaries who are enrolled in the Part D program. Given that many TOAMs were prescribed monthly, we quantified the costs of TOAMs as per patient per month (PPPM) costs for each calendar year, which were calculated by aggregating all TOAM claims for gross drug costs and OOP payments, then dividing the aggregate costs by the total number of months a patient was treated with any TOAM in the calendar year. When reporting OOP payments, we limited our analysis to beneficiaries without low-income subsidies, for whom payments are substantially lower.

Growth in Drug Prices

We stratified gross drug costs PPPM for TOAMs by year of prescription, without inflation adjustment, and calculated the annual increase in drug prices from 2007 to 2012 as the ratio of costs PPPM between year $(t + 1)$ and year t. We then compared the annual growth rate of TOAM prices with two commonly cited health care price indices obtained from the Bureau of Labor Statistics: the medical care component of the consumer price index (MC-CPI) and the prescription drug category of the medical CPI (RX-CPI).[26] We used Medicare drug spending data accessible from the Centers for Medicare & Medicaid Services website to project annual growth rates from 2012 to 2015.[27] The data include aggregate drug spending from 2011 to 2015 for each drug covered under Part D. We extracted TOAMs from the data, estimated cost per patient per year (PPPY) by weighting total annual spending per patient of each TOAM by its respective patient share, and calculated annual PPPY growth rates. We then projected annual growth rates of TOAM prices, quantified as cost PPPM, by applying the relative ratio of the 2011 to 2012 growth rate calculated from PPPM versus that from PPPY to the 2012 to 2015 growth trend observed in PPPY. To determine the rate of inflation (denoted as R) from 2007 to 2012, we solved the equation: $\text{Cost}_{2007} \times (1 + R)^5 = \text{Cost}_{2012}$. We calculated the inflation rate for gross drug costs and OOP payments, both overall and for each TOAM agent included in our analysis. For TOAMs approved before 2007, we used years 2007 to 2012 to calculate the rate of inflation. For those approved after 2007, we calculated the inflation rate using data from all applicable years up to 2012.

RESULTS

The study cohort included 42,111 patients with cancer who received TOAM between 2007 and 2012; these patients formed the 73,209 person-years used in our analysis. Table 1 shows that between 2007 and 2012, the top five cancers among patients taking TOAMs were lung (31.2%), myeloma (23.1%), kidney (8.3%), liver (7.8%), and leukemia (7.7%). The distribution by calendar year shows a higher proportion of observations in more recent years; this reflects the compound effect of the entry of new TOAMs into the market in addition to the accumulation of patients from previous years, because TOAMs have transformed several cancers into chronic illnesses. The comparison of patient characteristics by year shows that although the demographic characteristics and geographic distribution of patients taking TOAMs stayed stable,

Table 1. Descriptive Statistics of Medicare Part D Beneficiaries Using TOAMs in Person-Years, 2007 to 2012

Patient Characteristic	Year						
	2007-2012	2007	2008	2009	2010	2011	2012
No. of patients (%)	73,209 (100)	9,987 (14)	10,636 (15)	11,656 (16)	12,586 (17)	13,849 (19)	14,495 (20)
Age, years (SD)	72.17 (9.93)	72.46 (9.83)	72.32 (9.89)	72.40 (9.86)	72.20 (9.86)	72.06 (9.95)	71.75 (10.08)
Sex							
Male	21,191 (49.2)	4,712 (47.2)	5,062 (47.6)	5,572 (47.8)	6,013 (47.8)	6,791 (49.0)	7,213 (49.8)
Female	21,920 (50.9)	5,275 (52.8)	5,574 (52.4)	6,084 (52.2)	6,573 (52.2)	7,058 (51.0)	7,282 (50.2)
Race/ethnicity							
Non-Hispanic white	28,274 (65.6)	6,620 (66.3)	6,885 (64.7)	7,503 (64.4)	7,953 (63.2)	8,865 (64.0)	9,556 (65.9)
Non-Hispanic black	5,158 (12.0)	1,227 (12.3)	1,326 (12.5)	1,474 (12.7)	1,629 (12.9)	1,695 (12.2)	1,760 (12.1)
Hispanic or others	9,679 (22.5)	2,140 (21.4)	2,425 (22.8)	2,679 (23.0)	3,004 (23.9)	3,289 (23.8)	3,179 (21.9)
US region							
Northeast	6,726 (15.6)	1,543 (15.5)	1,677 (15.8)	1,786 (15.3)	1,836 (14.6)	1,997 (14.4)	2,445 (16.9)
South	9,044 (21.0)	1,959 (19.6)	2,112 (19.9)	2,420 (20.8)	2,701 (21.5)	3,067 (22.2)	3,071 (21.2)
Midwest	3,693 (8.6)	892 (8.9)	936 (8.8)	1,073 (9.2)	1,004 (8.0)	1,103 (8.0)	1,259 (8.7)
West	23,648 (54.9)	5,593 (56.0)	5,911 (55.6)	6,377 (54.7)	7,045 (56.0)	7,682 (55.5)	7,720 (53.3)
Top five cancers among patients taking TOAMs							
1	Lung	Lung	Lung	Lung	Myeloma	Myeloma	Myeloma
No. of patients (%)	13,041 (31.2)	3,185 (32.7)	2,986 (28.8)	3,186 (28.1)	3,460 (28.3)	3,866 (28.7)	3,653 (26.0)
2	Myeloma	Myeloma	Myeloma	Myeloma	Lung	Lung	Lung
No. of patients (%)	9,646 (23.0)	2,536 (26.1)	2,797 (27.0)	3,045 (26.8)	3,189 (26.1)	3,282 (24.4)	2,788 (19.9)
3	Kidney	Leukemia	Leukemia	Leukemia	Leukemia	Leukemia	Leukemia
No. of patients (%)	3,464 (8.3)	1,180 (12.1)	1,309 (12.6)	1,435 (12.6)	1,667 (13.6)	1,862 (13.8)	1,920 (13.7)
4	Liver	Kidney	Kidney	Kidney	Kidney	Kidney	Breast
No. of patients (%)	3,276 (7.8)	840 (8.6)	786 (7.6)	840 (7.4)	922 (7.5)	1,068 (7.9)	1,159 (8.3)
5	Leukemia	Pancreas	Liver	Liver	Liver	Liver	Kidney
No. of patients (%)	3,220 (7.7)	492 (5.1)	695 (6.7)	797 (7.0)	881 (7.2)	988 (7.3)	1,125 (8.0)

NOTE: Data presented as No. of patients (%) unless otherwise noted.
Abbreviations: SD, standard deviation; TOAMs, targeted oral anticancer medications.

there were some variations in the top-five list, with breast cancer entering the list and liver cancer dropping off the list in 2012.

Trends in Gross Drug Costs

Figure 1A shows that the mean gross drug costs PPPM increased from $4,427 in 2007 to $7,719 in 2012. Similar trends were observed at the median (Fig 1B), 75th (Fig 1C), and 95th percentile (Fig 1D), with median gross drug costs more than doubling, increasing from $3,484 in 2007 to $7,673 in 2012.

For each TOAM agent, Figure 2 compares its median gross drug cost PPPM in 2007 or the year of launch (whichever is later) with that in 2012. Because Part D data were not available before 2007, the launch price for drugs approved before 2007 was based on cost PPPM calculated using 2007 data. The top panel portrays an increasing trend in the launch cost PPPM, moving from the $3,000 to $6,000 range for most drugs approved before 2010 to $8,000 to $10,000 for those approved after 2010. However, the bottom panel of Figure 2, plotting the final cost PPPM for 2012, shows that many drugs approved before 2012 had sustained price increases and moved toward the price range ($8,000 to $10,000) of those approved in 2012. Of the 16 TOAMs approved before 2012, five exhibited double-digit annual rates of inflation during 2007 to 2012: imatinib (15.5%), dasatinib (13.7%), erlotinib (10%), sorafenib (12%), and everolimus (11%).

Figure 3 compares the annual changes, from 2007 to 2015, in TOAM costs PPPM with two medical-related price indices. Both MC-CPI and RX-CPI remained relatively stable between 2007 and 2015, with an annual price change generally around 3% to 4%. Gross drug costs PPPM for TOAMs exhibited sustained increases at a rate $>$ 10% annually up to 2012. This trend was projected to continue and even accelerate in more recent years. Figure 4 shows that the inflation rate for TOAMs was close to 12% over 2007 to 2012, which was more than three times higher than the MC-CPI and RX-CPI.

Trends in OOP

Mean OOP payments for those without low-income subsidies increased steadily from $980 in 2007 to $1,200 in 2010 but dropped below $850 in 2011 when the coverage gap began to close (Fig 1A). Although similar trends were found at the median, 75th, and 95th percentiles, the magnitude of financial relief from closure of the coverage gap was most pronounced for Part D enrollees whose TOAM-related OOP payments were in the top five percentile. Those patients' OOP PPPM dropped by $>$ 40% from 2010 ($4,176) to 2011 ($2,491; Fig 1D). We also calculated the inflation rate for OOP PPPM. Figure 4 shows that the rate over 2007 to 2012 was negative (−3.7%) because the coverage gap began to close in 2011 but was positive (7%) between 2007 and 2010.

DISCUSSION

This study analyzed Part D claims in the 2007 to 2012 SEER-Medicare data to examine the cost trend of TOAMs for the Medicare Part D program and its enrollees. We found that gross drug costs PPPM increased from the $3,000 to $6,000 price range

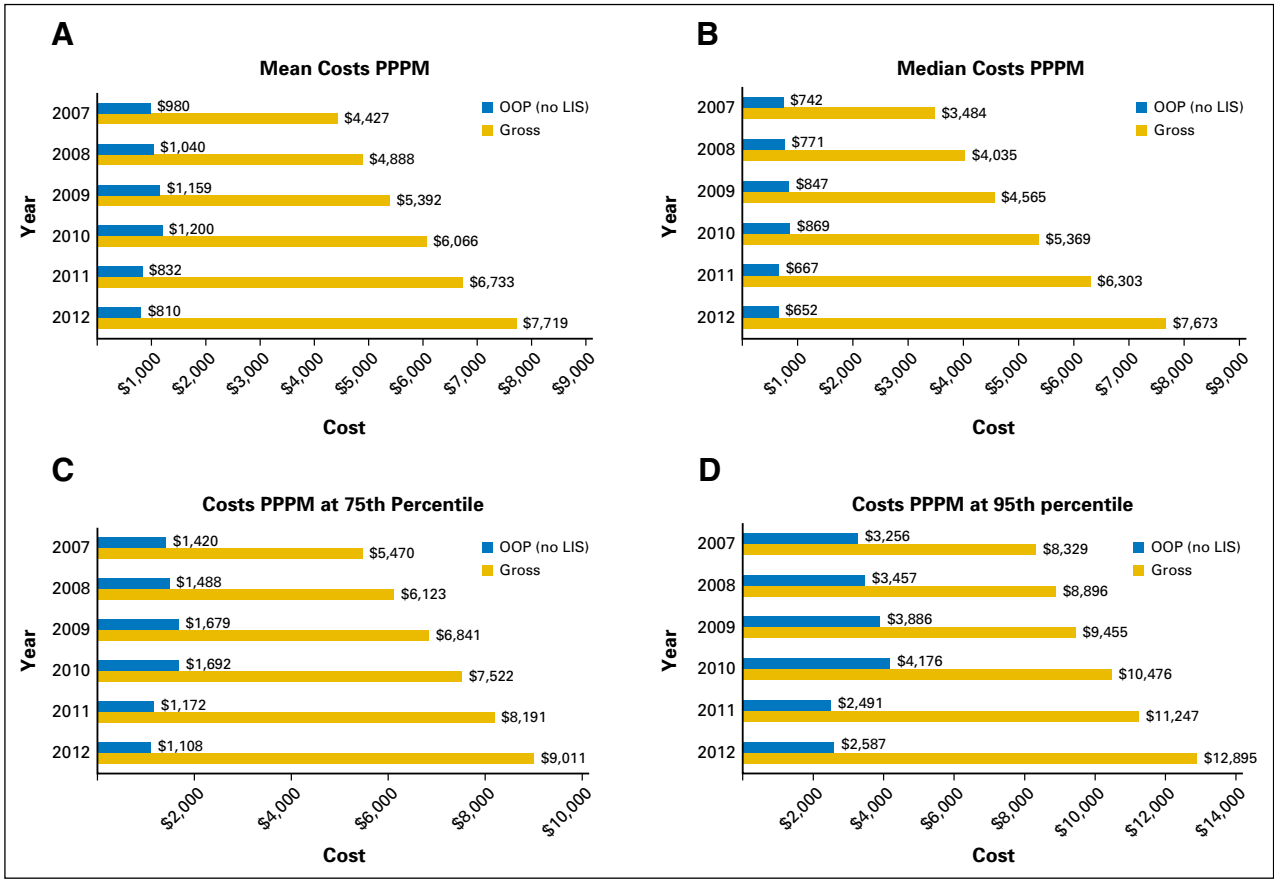

Fig 1. Annual targeted oral anticancer medication costs of Medicare Part D beneficiaries, 2007 to 2012. (A) Mean costs per patient per month (PPPM); (B) median costs PPPM; (C) costs PPPM at 75th percentile; (D) costs PPPM at 95th percentile. LIS, low-income subsidy; OOP, out-of-pocket.

for TOAMs launched before 2010 to the $8,000 to $10,000 range for those launched after 2010. In addition, with sustained price increases, costs PPPM for several TOAMs launched earlier had approached or passed $8,000 by 2012. The combination of increasing prices at drug launch and sustained price increases postlaunch was associated with an inflation rate of nearly 12% over 2007 to 2012, outpacing the growth of the prescription drug CPI by more than three-fold. This rate of inflation was projected to continue and even accelerate in more recent years.

The trends in OOP PPPM reported in our analysis documented the early experience of a legislative provision to phase in closure of the coverage gap by 2020. We found a sizable (approximately 20%) reduction in OOP PPPM when measured at the median, after the coinsurance rate in the coverage gap phase was reduced from 100% to 50% in 2011. A similar magnitude of reduction was reported in a study of coverage gap closure and specialty drug use among beneficiaries in Medicare Advantage plans.[28] Had OOP payments continued to increase along the trajectory observed before 2011, they would have grown by 50% by 2012, implying a substantial impact of closing the coverage gap. The largest financial relief was for beneficiaries with high OOP PPPM. Some of these high spenders could be patients who were taking TOAMs but who discontinued their medication because of cost concerns while in the coverage gap phase with 100% coinsurance, and were unable to reach the catastrophic phase with 5% coinsurance. The closure of the coverage gap is especially beneficial for such individuals by allowing them to continue their life-saving medications.

Although our findings provide support for patient financial improvements under this policy change, it is important to note that the financial burden for patients enrolled in Medicare Part D who take TOAMs remains substantially higher than for those with private insurance. The comparison of the 2011 mean OOP PPPM ($832) reported in our study and that reported in a study of privately insured patients who take TOAMs ($198)[7] indicates that without the added protection of the OOP maximum, Part D enrollees are especially vulnerable to high drug prices. Previous research has shown that for Medicare beneficiaries taking TOAMs, many individuals quickly pass through the coverage gap and enter catastrophic coverage.[24] With monthly costs of $>$ $10,000 for TOAMs, even a 5% coinsurance can amount to a substantial financial burden, because most patients who take TOAMs continue taking these medications for months or years. Indeed, Dusetzina and Keating[24] projected that median OOP costs would remain high ($>$ $5,500 annually) for individuals taking any of several TOAMs, even after the coverage gap is closed in 2020.

The patterns we documented in Medicare drug price inflation are mirrored in studies using commercial insurance

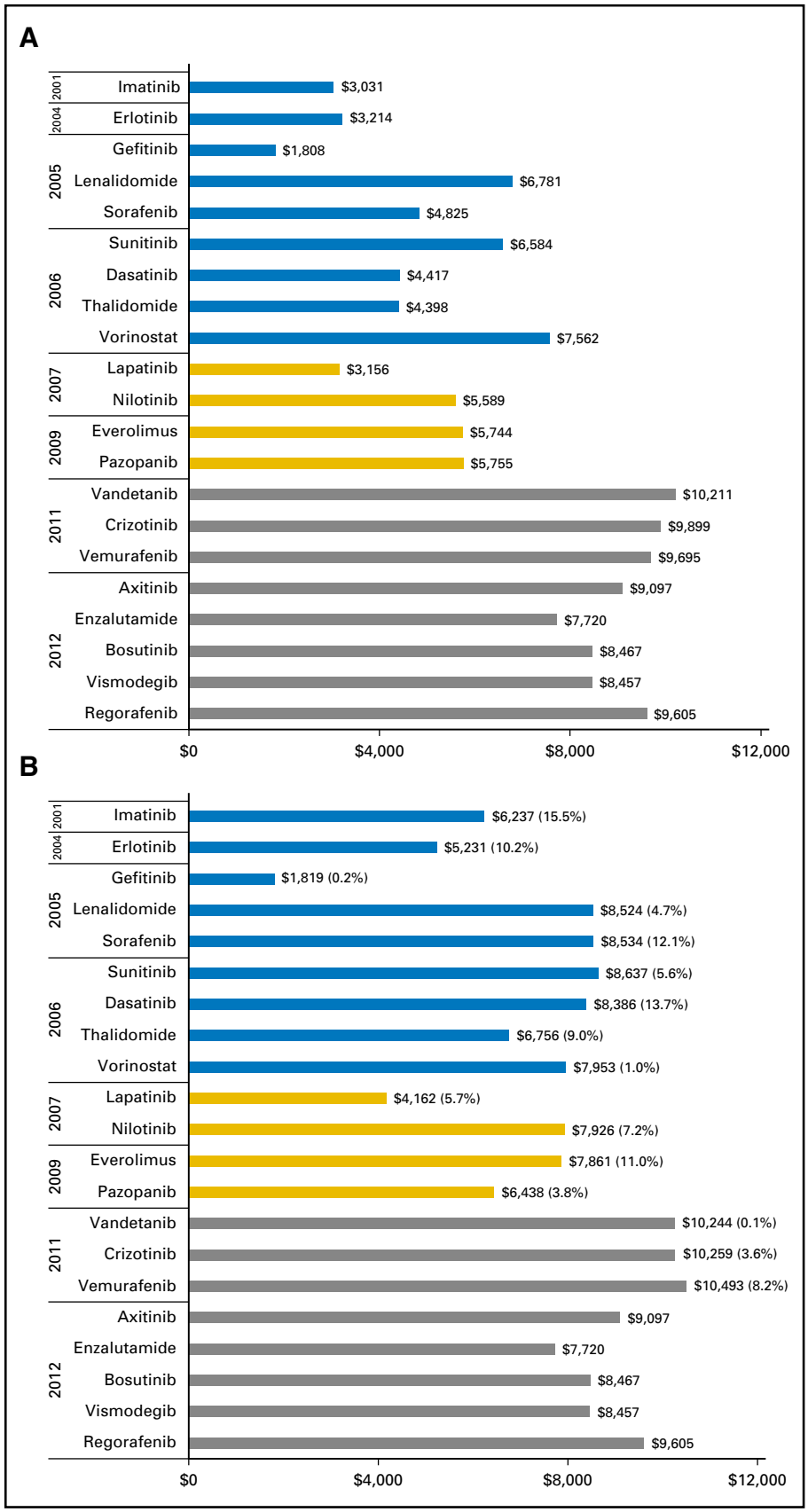

Fig 2. Launch prices and 2012 prices of targeted oral anticancer medication in Medicare Part D by year of launch, 2007 to 2012. (A) Launch year or 2007 (whichever was later); (B) 2012 prices.

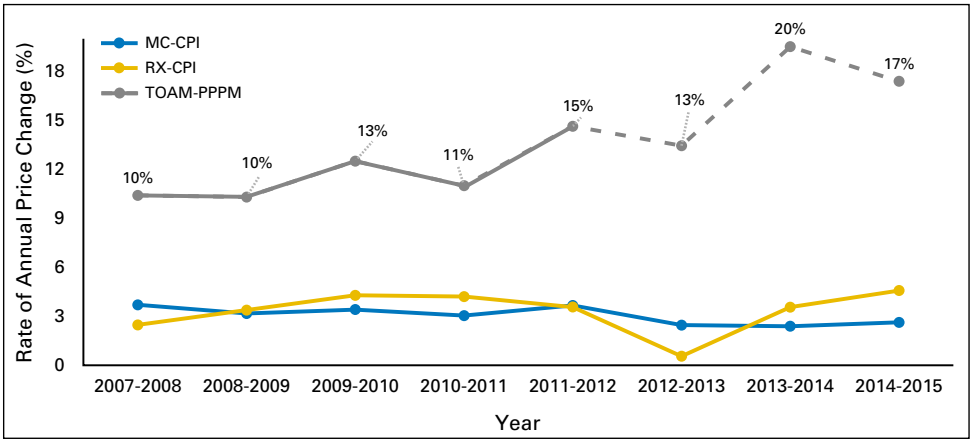

Fig 3. Rate of annual price change, 2007 to 2015. Dashed gray line represents projection on the basis of data published by Centers for Medicare & Medicaid Services. CPI, Consumer Price Index; MC, medical care; OOP, out-of-pocket; PPPM, per patient per month; RX, prescription drug; TOAM, targeted oral anticancer medication.

claims.[7-9] It is possible that sustained price increases for TOAMs could outweigh the savings patients are expected to achieve through the coverage gap closure, eventually causing OOP payments to grow again. Dusetzina and Keating[24] estimated that if TOAM drug prices increased by 50% from 2010 to 2020, the projected OOP savings from coverage gap closure would drop from $2,550 to $621. With the 11.8% inflation rate estimated from our study, it will take < 4 years to reach a 50% increase in drug prices, and drug prices are projected to triple from 2010 to 2020. These observations underscore how drug price escalation is as crucial as insurance coverage gaps in determining the risk of financial toxicity for elderly patients who take TOAMs. Conversely, too-generous coverage desensitizes patients and prescribing oncologists to the high drug prices, preventing pressure within the cancer care community from building against price inflation. This point has been made with regard to drug manufacturers' copay assistance programs,[29] which serve a similar function. Absent countervailing measures, this provides free rein to drug manufacturers to further increase prices.[30,31]

Our study has several limitations. First, our measures of drug prices are calculated from claims data on the basis of invoices at the point of purchase. These include discounts provided at the point of sale but do not subtract out rebates negotiated between Part D plans and drug manufacturers, and thus, overestimate the net prices paid by plans.[32] Across all payers, the growth in net prices of branded oncology drugs has been estimated to be 1% to 2% points lower than invoice price growth.[33] Second, although our OOP measure should by construction exclude third-party payments by nonprofit charity or patient-assistance programs and coupons that contribute toward required OOP payments, some of these may be erroneously captured in our analyses. For example, a recent study found that despite Medicare's ban on the use of coupons, 6% to 7% of seniors reported using coupons in Medicare.[34] Last, we reported costs PPPM instead of annual costs. Although normalizing costs into monthly units offers a better proxy for price and forms a more reasonable analytical unit to calculate annual price changes and inflation rates, we note that one cannot simply multiply costs PPPM by 12 to obtain annual costs, because these are also determined by the starting month and the duration of treatment.

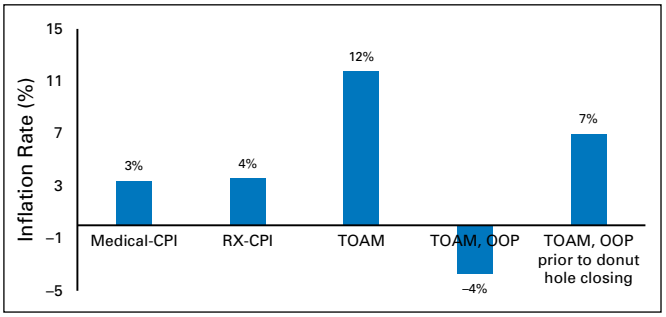

Fig 4. Inflation rates for various medical goods, 2007 to 2012. CPI, Consumer Price Index; OOP, out-of-pocket; RX, prescription drug; TOAM, targeted oral anticancer medication.

Several policies have been proposed to deal with the twin problems of increasing prices and high OOP payments for oral therapies.[35-39] Although the Medicare Payment Advisory Commission has proposed reforms to the Part D program, the program as currently structured is fundamentally limited in how much pressure is brought to bear on drug prices. However, the advancement of new cancer therapies means that in a growing number of indications, multiple therapies exist for cancer treatment and are included in recognized Clinical Practice Guidelines.[40-44] More effective ways should be tested to use price competition among these agents to limit price inflation. First, Part D plans could be allowed to have two specialty drug tiers, similar to plans enrolling a majority of enrollees in the commercial market,[20] rather than just one. Patient cost sharing would be capped for drugs on the preferred specialty drug tier, which would include best-in-class drugs for a given indication and drugs for which plans can negotiate lower prices, when similar therapeutic competitors exist. The current specialty tier with coinsurance, even in the catastrophic phase, would be reserved for competitor drugs with higher prices. This value-based insurance design would improve patient financial protection while incentivizing patients and physicians to become more aware of drug prices than they currently are[45] and retaining plan, patient, and physician pressure on competing drugs to reduce prices. Second, the Centers for Medicare & Medicaid Services is testing an episode-based payment model for chemotherapy—the Oncology Care Model—in 195 oncology practices serving patients enrolled with Medicare and 16 other payers. Practices share in savings by better coordinating care, including through value-based selection among competing intravenous drugs in Medicare Part B and oral drugs in Part D.[46] Although monitoring of the effects of

such reforms on cancer care quality and access will be essential, the incentives embodied in these policies could move Medicare toward more efficient and equitable purchasing of oral drugs for cancer patients.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at jco.org.

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Rising Prices of Targeted Oral Anticancer Medications and Associated Financial Burden on Medicare Beneficiaries

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Appendix

Table A1. Targeted Oral Anti-Cancer Medications Approved Before December 31, 2012

Drug Name	Year of FDA Approval	Approved Indication
Imatinib	2001	CML, dermatofibrosarcoma protuberans, GIST, myelodysplastic/myeloproliferative disorders
Erlotinib	2004	NSCLC, pancreatic
Gefitinib	2003	NSCLC
Lenalidomide	2005	Multiple myeloma, lymphoma
Sorafenib	2005	RCC, liver, thyroid
Sunitinib	2006	RCC, GIST, pancreatic
Dasatinib	2006	CML
Thalidomide	2006	Multiple melanoma
Vorinostat	2006	Lymphoma
Lapatinib	2007	Breast
Nilotinib	2007	CML
Everolimus	2009	RCC, breast, pancreatic
Pazopanib	2009	RCC, soft tissue sarcoma
Vandetanib	2011	Thyroid
Crizotinib	2011	NSCLC
Vemurafenib	2011	Melanoma
Axitinib	2012	RCC
Bosutinib	2012	CML
Vismodegib	2012	Basal cell
Regorafenib	2012	Colorectal cancer, GIST

Abbreviations: CLL, chronic lymphocytic leukemia; CML, chronic myelogenous leukemia; FDA, US Food and Drug Administration; GBM, glioblastoma multiforme; GIST, gastrointestinal stromal tumor; NHL, non-Hodgkin lymphoma; NSCLC, non–small-cell lung cancer; RCC, renal cell carcinoma.