



Spending on World Health Organization essential medicines in Medicare Part D, 2011-15: retrospective cost analysis

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ABSTRACT OBJECTIVES

To characterize the trends, drivers, and potential modifiers of increased spending by US Medicare beneficiaries on medicines deemed essential by the World Health Organization.

DESIGN

Retrospective cost analysis of Medicare Part D Prescriber Public Use File, detailing annual generic and brand name drug prescribing and spending from 2011 through 2015 by Medicare Part D participants who filled prescriptions for WHO essential medicines.

SETTING

US Medicare System.

MAIN OUTCOME MEASURES

Total and per beneficiary Medicare spending, total and per beneficiary out-of-pocket patient spending, cumulative beneficiary count, claim count, and per unit drug cost. All spending measures were adjusted for inflation and reported in 2015 US dollars.

RESULTS

Medicare Part D expenditures on 265 WHO essential medicines between 2011 and 2015 was \$87.2bn (£68.4bn; €76.5bn), with annual spending increasing from \$11.9bn in 2011 to \$25.8bn in 2015 (116%). Patients' out-of-pocket spending for essential medicines over the same period was \$12.1bn. Total annual out-of-pocket spending increased from \$2.0bn to \$2.9bn (47%), and annual per beneficiary out-of-pocket spending on these drugs increased from \$20.42 to \$21.17 (4%). Total prescription count increased from 376.1m to 498.9m (33%), and cumulative beneficiary count grew from 95.9m to

135.8m (42%). Of the essential medicines included in the study, the per unit cost of 133 (50%) agents increased faster than the average inflation rate during this period. Overall, approximately 58% of the increase in total spending during this period can be attributed to the introduction of novel agents.

CONCLUSIONS

Spending associated with essential medicines grew substantially from 2011 to 2015, driven largely by the increased use of two expensive novel drugs used in treating hepatitis C. Approximately 22% of increased total spending during this period can be attributed to increases in per unit cost of existing drugs. These trends may limit patients' access to essential drugs while also increasing healthcare system costs.

Introduction

Pharmaceutical spending in the United States is a source of growing financial burden for payers and patients. Unlike many developed nations that negotiate drug prices directly with manufacturers, the US allows drug manufacturers to set their own prices.¹⁻³ As a result, brand name drugs are priced higher at launch in the US than in most other countries around the world.^{4,5} Between 2008 and 2015, the prices of commonly used brand name medicines in the US increased 164% more than the consumer price index.⁶⁻⁸

Although the generic drug market in the US is competitive, resulting in low prices close to the cost of production, insufficient competition related to nearly 400 generic drugs led to 100-fold price increases for these products between 2008 and 2015.⁹ Non-adherence to drug treatment resulting from high prices for brand name prescriptions may adversely affect patients' outcomes and increase long term healthcare spending.¹⁰⁻¹²

In the US, the effect of high drug prices on patients may be buffered by public and private health insurers, although this may not hold true in other settings. Across developing countries, spending on drugs accounts for 20-60% of cumulative healthcare expenditure, with upwards of 90% of the population purchasing medicines directly out of pocket.^{13 14} In locations where medicines are the greatest family expenditure item after food, high drug prices may disproportionately affect vulnerable people who have limited access to basic healthcare.¹⁵ Barriers that prevent patients from accessing essential drugs would most directly affect health outcomes.¹⁶

The World Health Organization's Model List of Essential Medicines (MLEM) defines a critical set of drugs that constitute the "minimum medicine needs for a basic healthcare system."¹⁷ The MLEM consists of the most efficacious and safest medicines for

WHAT IS ALREADY KNOWN ON THIS TOPIC

The World Health Organization's Model List of Essential Medicines defines a critical set of drugs that constitute the minimum medicine needs for a basic healthcare system

Although the generic drug market in the US is competitive, nearly 400 generics drugs had a greater than 100-fold increase in price between 2008 and 2015

Non-adherence to treatment resulting from high drug prices may adversely affect patients' outcomes and increase long term healthcare spending

WHAT THIS STUDY ADDS

Spending associated with essential medicines in the Medicare Part D database grew substantially between 2011 and 2015, driven largely by the increased use of two expensive new drugs used to treat hepatitis C

Increases in per unit cost of existing drugs accounted for 22% of increased spending, with more than 20 essential medicines increasing by more than 50 times the rate of inflation

As high prices can lead to non-adherence, policy makers should pay attention to changes that can help to ensure that essential medicines remain accessible for people who need them in the US and around the world

priority conditions selected on the basis of current and projected relevance to public health and functions as a means to equalize access to and affordability of basic medicines globally.¹⁷⁻²⁰ Despite these efforts, availability and prices of essential medicines remain variable across different nations, with particular agents attracting public attention owing to price mark-ups.^{1 21-24}

In the US, most people aged 65 or older are enrolled in Medicare, a federal government program that provides health insurance to approximately 60 million people.²⁵ The Centers for Medicare and Medicaid Services provides publicly available data on the spending and use of prescription drugs covered by Medicare Part D, the insurance program that covers outpatient drugs. To evaluate spending on WHO MLEM drugs in the US, we reviewed trends in overall pharmaceutical spending and out-of-pocket spending that are directly borne by patients within Medicare Part D.

Methods

Datasets

We extracted a list of essential drugs from the core and complementary lists within the WHO Model List of Essential Medicines (WHO MLEM, 20th list, March 2017), which contains names of medicines, appropriate dosage forms, routes of administration, and 30 major drug categories.¹⁷ We evaluated spending on medicines by using population based claims data from the Medicare Part D Prescriber Public Use File, a database released by the Centers for Medicare and Medicaid Services in December 2016 that details annual spending for filled prescriptions of listed drugs between 2011 and 2015. The database contains information on prescriptions for approximately 70% of Medicare beneficiaries with a Medicare Part D prescription drug plan between 2011 and 2015.²⁶ The Medicare Part D Public Use File provides prescription drug name, claim count (including refills), unit count (total dosage units of drug dispensed across the calendar year in tablets, grams, milliliters, or other units), average cost per unit, beneficiary count, average beneficiary cost share, total annual spending per user, and total spending by Medicare. The Public Use File reports non-unique beneficiary counts for each drug, with overlapping beneficiaries across different drugs. As a result, we used cumulative beneficiary counts to calculate all values relating to beneficiary counts and per beneficiary outcomes to allow for cross comparisons.

Inclusion and exclusion criteria for essential medicines

We identified essential medicines from the WHO MLEM core and complementary lists and located them on the Medicare Part D Prescriber Public Use File, including all overlapping agents. We excluded vaccines, insulin agents, contraceptives and reproductive agents, and dialysis solutions, as these medicines sustained substantial variability in pricing resulting from diffuse market segmentation. Because Medicare Part D is used

for prescription drugs, we excluded medicines used primarily in the inpatient setting. We also excluded medicines with five year unit fills of fewer than 15 000. Application of inclusion and exclusion criteria resulted in 246 active ingredients corresponding to 265 dosage formulations as specified in the WHO MLEM (supplementary table A).

Generic and brand name drugs

We cross referenced all medicines included in the study with the List of Off-Patent, Off-Exclusivity Drugs without an Approved Generic to prevent misclassification of generic drugs as potential brand name agents.²⁷ When both brand name and generic options were available for a single drug, we preferentially included the generic drug for analysis. In cases for which the brand name drug had more units than the generic, we included both generic and brand formulations if the generic drug had cumulative five year units of greater than 10% of the brand formulation. For medicines for which the generic drug had fewer than 10% of the cumulative five year units of the brand name formulation, we included only the brand name formulation.

Cost calculations

We calculated Medicare spending on the basis of total annual drug spending data, which represent the aggregate spending by Medicare Part D (includes Medicare, plan, and beneficiary payments).²⁸ We calculated total out-of-pocket spending by patients by analyzing cumulative beneficiary counts and average beneficiary cost shares, which reflect the monetary amount paid by patients that was not reimbursed. We calculated changes in per unit cost by using average weighted values in cost per unit. All values were adjusted for inflation rates and reported in 2015 dollars (<https://data.bls.gov/cgi-bin/cpicalc.pl>). We made calculations for total Medicare spending and Medicare spending per beneficiary, claim and unit count, and out-of-pocket spending by patients in bulk within categories to reflect annualized changes.

In a subgroup analysis of factors contributing to increased total spending, we created a volume and cost index (change in drug volume based on fixed set of costs and vice versa) to analyze the proportion of increased total spending attributable to variations in unit count and per unit cost. Using this model, we varied drug volume (units) and cost (per unit cost) from 2011 to 2015 to determine the relative contributions of both entities to increased spending. We excluded essential medicine formulations lacking Medicare Part D total spending data from 2011 or 2015 and formulations with decreased total spending during this five year period.

Secondary analysis: number of manufacturers and drug costs

To investigate a potential association between number of drug manufacturers and increases in drug costs among essential medicines, we collected the number of distinct manufacturers for each formulation listed

in the Food and Drug Administration's Orange Book corresponding to 2011 and 2015 (32nd and 36th editions). Because the Medicare Part D Prescriber Public Use File does not distinguish spending across different formulations of a single agent, we included only essential medicines with a single formulation (for example, oral, intravenous, or topical) for this secondary analysis. Next, we extracted the absolute and percentage change in per unit costs for the included drugs within the Medicare Part D Prescriber Public Use File from 2011 to 2015. We analyzed the association between number of manufacturers and change in drug cost descriptively by using means and percentages. Finally, we compared the average annual percentage change in per unit costs for all 265 formulations with the average rate of inflation over this time period.

Patient and public involvement

No individual patients were involved in our study. We analyzed de-identified, population data from the Medicare population. The findings of this manuscript will be shared through the institutional newsletter at Harvard Medical School and its affiliated hospitals, in addition to various online news and media platforms.

Results

Cross referencing the WHO MLEM with all 4498 drugs in the Medicare Part D Prescriber Public Use File resulted in 319 essential medicines. We excluded 73 products (fig 1) and added 19 generic formulations of already included medicines for cases in which the brand name was prescribed more frequently than the generic, resulting in 265 essential medicines of which 197 (74%) were generic (complete list in supplementary table A).

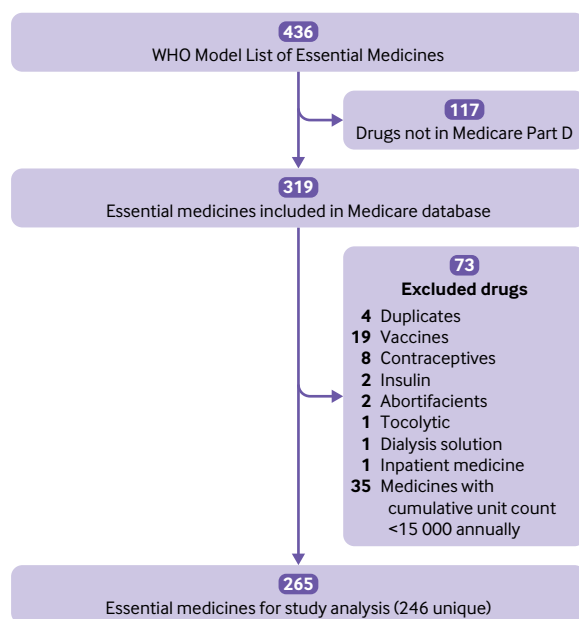


Fig 1 | Inclusion and exclusion of World Health Organization essential medicines. 436 essential medications were initially screened with Medicare Part D Prescriber Public Use File, of which 246 drugs corresponding to 265 essential medicine formulations were included for analysis

Spending trends

Total spending for the 265 essential medicines was \$87.2bn (£68.4bn; €76.5bn) (from 2.2bn prescriptions) between 2011 and 2015, an increase of 116% from \$11.9bn in 2011 to \$25.8bn in 2015 (net increase of \$13.8bn) (table 1). Cumulative beneficiary count increased from 95.9m in 2011 to 135.8m in 2015 (42%). The total number of prescriptions (original and refills) increased from 376.1m to 498.9 m (33%), and total spending per beneficiary increased from \$124.3 to \$189.7 (53%) over the study period (fig 2).

Patients paid a total of \$12.1bn out of pocket for these drugs between 2011 and 2015 (fig 2). Total annual out-of-pocket spending increased from \$2.0bn to \$2.9bn (47%), and annual per beneficiary out-of-pocket spending increased from \$20.4 to \$21.2 (4%).

Drug costs

The per unit cost of 133 (50%) drugs increased faster than the rate of inflation between 2011 and 2015 (fig 3; detailed list in supplementary table B). During this period, 9 (3%) of 265 essential medicines sustained escalations in per unit cost of more than 100 times the inflation rate from 2011 to 2015, and 11 (4%) had per unit cost increases of between 50 and 100 times the inflation rate. Medicines with per unit cost increases of more than 100 times the average inflation rate included the brand name drugs albendazole (Albenza), pyrimethamine (Daraprim), and penicillamine (Cuprimine) and the generic drugs tetracycline, clomipramine, mannitol, griseofulvin, chlorpromazine, and doxycycline hyclate (fig 3).

Among the drugs that increased in total spending from 2011 to 2015, we created a cost-volume index encompassing 152 (57%) essential medicine formulations to analyze the proportion of increased total spending attributable to changes in unit count and per unit cost (expanded list in supplementary table C). This cohort excluded 25 formulations lacking Medicare Part D total spending data and 88 formulations that sustained decreased total spending from 2011 to 2015.

The introduction of novel agents and variations in unit count, per unit cost, or both among existing agents led to a \$15.7bn increase in total spending from 2011 to 2015 (not including drugs sustaining a decrease in total spending). Of this, 20% (\$3.2bn) and 22% (\$3.5bn) can be attributed to increases in unit count and per unit cost, respectively, among existing essential medicines. Of the remaining \$9.1bn related to the introduction of novel agents, sofosbuvir (Sovaldi) and ledipasvir-sofosbuvir (Harvoni)—two drugs introduced during the study period as transformative treatments for hepatitis C virus infection—account for \$8.35bn (92%) of the increase.

Market competition and drug costs

To investigate the association between number of manufacturers and cost changes, we evaluated a subgroup of 170 (64%) drug formulations that existed in a single dosage form, representing 59% of total Part

Table 1 | Medicare Part D total and per beneficiary spending on essential medicines, 2011 to 2015

Spending	2011	2012	2013	2014	2015
Cumulative inflation rate*	5.4%	3.2%	1.7%	0.1%	2015 dollars
Total Medicare spending (\$)†	11 920	13 204	15 400	20 875	25 761
Per beneficiary spending (\$)	124	124	126	162	190
Total out-of-pocket spending (\$)†	1958	2094	2461	2687	2874
Per beneficiary out-of-pocket spending (\$)	20	20	20	21	21
Total prescription count†	376	410	469	485	499
Total beneficiary count†	96	107	123	129	136

*Calculated using <https://www.usinflationcalculator.com/>.

†Values reported in millions.

D spending on essential medicines across the five year period. We compared the top and bottom quarters of essential medicine formulations organized by percentage increase in unit drug cost. Drug formulations in the top quarter (n=43) had unit cost increases of at least 41% and had an average of 3.2 manufacturers (table 2). Twenty one (49%) formulations were produced by two or fewer manufacturers. By contrast, drug formulations in the bottom quarter (n=43) had unit cost decreases of at least 36%. These drugs had an average of 10.7 manufacturers, and only one was produced by two or fewer manufacturers.

Discussion

Expenditure on 265 WHO essential medicines in Medicare Part D between 2011 and 2015 was \$87.2 billion, increasing from \$11.9bn to \$25.8bn (116%) during this period and outpacing the growth in out-of-pocket spending (47%) and total prescriptions (33%). The increase in spending on essential medicines is primarily attributable to increasing costs of existing drugs as well as the introduction of two expensive essential medicines for hepatitis C.

Among essential medicine formulations with increased cumulative spending, rising claim and beneficiary counts accounted for 20% of the increased spending over the study period. This increase in

healthcare use may reflect demographic changes in the US, as well as the growing prevalence of chronic diseases resulting from the widespread use of life prolonging drugs.^{29 30} Increases in per unit cost of existing drugs accounted for 22% of increased spending, and between 2011 and 2015 more than 20 essential medicines increased by more than 50 times the rate of inflation. The brunt of these cost increases was borne by Medicare, with only modest increases in direct per patient out-of-pocket spending. These increases in cost are transmitted to patients in the form of higher premiums, deductibles, and copayments/coinsurance. Ultimately, these increases in cost are absorbed by US taxpayers and divert spending from other governmental priorities.

Comparison with other studies and policy implications

Our findings support and expand on existing literature on the increasing burden of pharmaceutical spending on healthcare systems. We showed increases in drug cost to be correlated with a decrease in the number of drug manufacturers, with essential medicines in the bottom quarter (by percentage increase in unit cost) having, on average, 7.5 more manufacturers than those in the top quarter. This finding is consistent with previous literature suggesting that market entry of a generic drug manufacturer is most beneficial for reducing costs among a subset of drugs with limited market competition.³¹⁻³³ New policy from the Food and Drug Administration that provides for expedited review of drugs with limited market competition may therefore help to reduce some of the excessive increases in spending on essential medicines in the future.³⁴

High prices for off-patent drugs can also be attenuated by legislative measures to facilitate import of prescription drugs into the US along with precautionary measures to assure manufacturing quality,^{35 36} although some potential savings may be offset by increased costs from regulatory efforts to ensure high quality drug imports.³⁷ Legislation permitting Medicare to negotiate prices for drugs within Medicare Part D plans could also help to lower prices of prescription drugs, particularly for those that face little or no market competition. Such a change would entail legislative changes to Medicare Part D.³⁸

Strengths and limitations of study

Strengths of our study include the five year follow-up period, systematic methods, and robust pricing database. Additionally, literature examining the trends in spending among WHO essential medicines is scarce. However, our results are limited by the fact that the Medicare Part D Public Use File contained only 319 (73%) of the 436 essential medicines listed in the WHO MLEM, and after applying the exclusion criteria we included in our study 265 formulations corresponding to 246 (56%) essential medicines. Some drugs in the MLEM were covered by other parts of Medicare (for example, Part B for infused chemotherapy) and were excluded from our analysis.

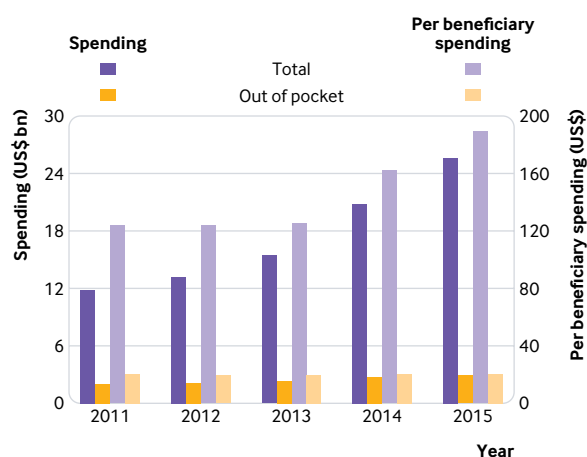


Fig 2 | Medicare Part D total and out-of-pocket spending on essential medicines, 2011 to 2015. Total and out-of-pocket spending depicted on left axis. Per beneficiary total spending and out-of-pocket spending shown on right axis (accompanying values listed in table 1). Introduction of sofosbuvir and ledipasvir-sofosbuvir accounts for sharp increase in per beneficiary total spending after 2013

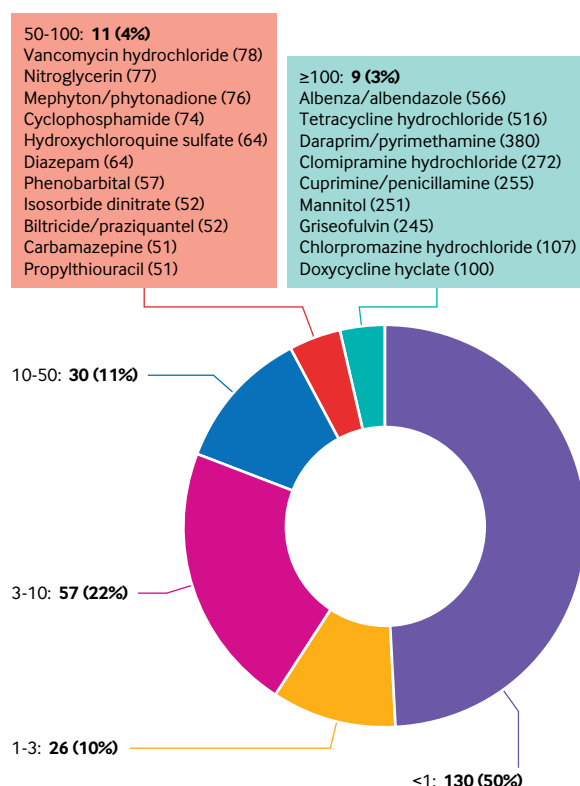


Fig 3 | Ratio of annual percentage change in per unit cost to annual inflation rate. Ranges represent ratio of annual percentage change in per unit cost to annual inflation rate. Numerical values represent number and percentage of formulations. Overall, 133/265 (50%) essential medicine formulations increased in per unit cost faster than average rate of inflation, with 9 (3%) and 11 (4%) formulations sustaining increases of greater than 100 times and between 50 and 100 times rate of inflation, respectively. Linezolid and daclatasvir are not included in this chart because these drugs had only 1 year of pricing data

Both cost and population data are specific to Medicare Part D and may not reflect prescribing patterns and expenses in private markets.

The study findings are also limited by reporting methods regarding beneficiary counts included in the Medicare Part D Prescriber Public Use File. Consequently, all beneficiary counts and reported per beneficiary spending outcomes represent cumulative rather than discrete values. Additionally, although we showed trends in patients' out-of-pocket spending, we could not account for the effect of manufacturers' rebates to individual Medicare Part D plan sponsors as these data were not contained in the Public Use File. The Medicare Part D Prescriber Public Use File represents drug events corresponding to Medicare beneficiaries, and these findings may not be representative of the larger US patient population. Furthermore, our

findings on increased spending on prescription drugs do not account for the changing health distributions of the Medicare population over the period analyzed. Finally, although we found an inverse association between the number of manufacturers and change in drug costs among essential medicines included in our sample, these findings cannot be used to conclude the existence of consolidative practices in the pharmaceutical industry.

We examined the trends in spending on essential medicines through the scope of the Medicare Part D Prescriber Public Use File within the US healthcare system, but similar analyses should be done in other countries. Future research may benefit from longer follow-up periods and exploration of other pricing databases not specific to the Medicare population.

Conclusions

Spending associated with essential medicines among US Medicare beneficiaries increased substantially between 2011 and 2015. Although the introduction of novel agents and increasing numbers of beneficiaries partially account for increases in spending, modifiable cost drivers such as increases in the price of generic drugs also contributed to increases in overall spending. As high prices can lead to non-adherence to drug treatment, policy makers should pay attention to changes that can help to ensure that essential medicines remain accessible for people who need them in the US and around the world.

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Contributors: DGL and AM were responsible for study concept and design, obtained funding, and did the statistical analysis. All authors were involved in acquisition, analysis, and interpretation of data; drafting of the manuscript; and critical revision of the manuscript for important intellectual content. ASK and AM supervised the study. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. DGL and AM are the guarantors.

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Ethical approval: This study was granted institutional review board exemption by the Partners Healthcare IRB.

Data sharing: No additional data available.

Transparency declaration: The manuscript's guarantors affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Table 2 | Cost and manufacturer trends among essential medications, analysis by quarters

Parameter	Top quarter by % change in cost	Bottom quarter by % change in cost
No of drugs	43	43
No of drugs (%) produced by ≤2 manufacturers	21 (49)	1 (2)
Mean (range) No of manufacturers	3.2 (1-15)	10.7 (1-31)
Mean change in cost (%)	497.8	-54.5

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Supplementary materials