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Trends in Prices, Market Share, and Spending on Self-administered Disease-Modifying Therapies for Multiple Sclerosis in Medicare Part D

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IMPORTANCE Before 2009, only 4 self-administered disease-modifying therapies (DMTs) were approved for the treatment of multiple sclerosis (MS). Since then, 7 new agents have entered the market.

OBJECTIVE To assess trends in prices, market share, and spending on self-administered DMTs for MS in Medicare Part D from 2006 through 2016.

DESIGN, SETTING, AND PARTICIPANTS This cohort study used claims data from 2006 through 2016 from a 5% random sample of Medicare beneficiaries (a mean of 2.8 million Medicare beneficiaries per year). All prescription claims for self-administered DMTs for MS (glatiramer acetate, interferon beta-1a, interferon beta-1b, fingolimod hydrochloride, teriflunomide, dimethyl fumarate, and peginterferon beta-1a) were extracted throughout the study period.

MAIN OUTCOMES AND MEASURES The main outcomes were the annual cost of treatment with each medication, based on Medicare Part D prescription claims gross costs and US Food and Drug Administration–approved recommended dosing; market share of each medication, defined as the proportion of pharmaceutical spending accounted by every drug; and pharmaceutical spending per 1000 Medicare beneficiaries for all drugs. The relative contributions of Medicare Part D Plans' payments, Medicare catastrophic coverage payments, low-income cost-sharing subsidies, patients' out-of-pocket costs, manufacturers' coverage gap discounts, and other payments toward pharmaceutical spending were further quantified.

RESULTS Annual costs of treatment with self-administered DMTs for MS more than quadrupled from 2006 to 2016, from a mean (SD) of $18 660 ($1177) to $75 847 ($16 956) and at a mean rate of 12.8% every year. Brand-name glatiramers accounted for the largest market share across the study period, ranging between $25 552 of $79 411 per 1000 Medicare beneficiaries (32.2%) and $10 342 of $21 365 per 1000 Medicare beneficiaries (48.4%). Platform therapies experienced a substantial drop from 2006 to 2016 in favor of newer therapies, with decreases in the market shares of brand-name glatiramers (per 1000 Medicare beneficiaries: $2861 of $7794 [36.7%] to $25 552 of $79 411 [32.2%]), interferon beta-1a (30 µg; per 1000 Medicare beneficiaries: $2521 of $7794 [32.3%] to $11 298 of $79 411 [14.2%]), interferon beta-1b (Betaseron; per 1000 Medicare beneficiaries: $1460 of $7794 [18.7%] to $3588 of $79 411 [4.5%]), and interferon beta-1a (8.8/22/44 µg; per 1000 Medicare beneficiaries: $951 of $7794 [12.2%] to $6588 of $79 411 [8.3%]) and increases in fingolimod (to $6311 of $79 411 per 1000 Medicare beneficiaries [7.9%]), teriflunomide (to $7177 of $79 411 per 1000 Medicare beneficiaries [9.0%]), and dimethyl fumarate (to $15 262 of $79 411 per 1000 Medicare beneficiaries [19.2%]). Throughout the study period, pharmaceutical spending per 1000 beneficiaries increased 10.2-fold (from $7794 to $79 411), and out-of-pocket patient spending per 1000 beneficiaries increased 7.2-fold (from $372 to $2673). The relative contribution of federal payments toward pharmaceutical spending increased from $5335 of $7794 (68.5%) to $58 620 to $79 411 (73.8%).

CONCLUSIONS AND RELEVANCE Per this analysis, prices of self-administered DMTs for MS increased dramatically between 2006 and 2016. This resulted in a 7.2-fold increase in patient out-of-pocket costs.

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Editorial

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Before 2009, only 4 self-administered disease-modifying therapies (DMTs) were approved for the treatment of multiple sclerosis (MS), including glatiramer acetate, 20 mg (Copaxone), interferon beta-1a, 30 µg (Avonex), interferon beta-1a, 8.8/22/44 µg (Rebif), and interferon beta-1b (Betaseron). Since then, 7 new branded agents have entered the market: interferon beta-1b (Extavia) in 2009, fingolimod (Gilenya) in 2010, teriflunomide (Aubagio) in 2012, dimethyl fumarate (Tecfidera) in 2013, glatiramer acetate, 40 mg (Copaxone) and peginterferon beta-1a (Plegridy) in 2014, and generic glatiramer acetate, 20 mg (Glatopa) in 2015.[1] Prior studies have shown that prices of DMTs for MS have increased at rates substantially higher than specialty medications used to treat other disease states,[1-5] and these increases led to higher out-of-pocket costs for patients.[6] However, it remains unknown how these price increases have affected pharmaceutical spending in the last decade and how increased spending has been borne by different stakeholders.

In this study, we used Medicare claims data from 2006 through 2016 to examine the how rising prices of self-administered DMTs for MS affected Medicare Part D spending and the share of spending borne by each type of stakeholder. We also explored changes in the market share of each agent.

Key Points

Question How did prices, market share, and spending on self-administered disease-modifying therapies for multiple sclerosis change in Medicare Part D from 2006 through 2016?

Findings This cohort study found that between 2006 and 2016, the annual cost of treatment with self-administered disease-modifying therapies for multiple sclerosis more than quadrupled, from a mean of $18 660 to $75 847, increasing at a mean annual rate of 12.8%. Pharmaceutical spending per 1000 beneficiaries increased by 10.2-fold, from $7794 to $79 411, while out-of-pocket spending per 1000 beneficiaries increased by a factor of 7.2, from $372 to $2673.

Meaning In this study, prices of self-administered disease-modifying therapies for multiple sclerosis increased dramatically between 2006 and 2016, which resulted in a 7.2-fold increase in patients' out-of-pocket costs.

Methods

Using claims data from a 5% random sample of Medicare Part D beneficiaries, we extracted all prescription claims filled for self-administered DMTs for MS from January 1, 2006, to December 31, 2016. The study included 3 outcomes measured every year: (1) the annual cost of treatment with each medication, based on Medicare Part D prescription claims gross cost (before rebates) and US Food and Drug Administration–approved recommended dosing; (2) market share of each medication, defined as the proportion of pharmaceutical spending accounted by every drug; and (3) pharmaceutical spending per 1000 Medicare beneficiaries for all drugs. For drugs marketed in multiple formulations, we calculated annual costs of treatment as the mean annual cost of treatment of their formulations weighted by their relative market share. We further quantified the contributions of Medicare Part D Plans' payments, Medicare catastrophic coverage payments, low-income cost-sharing subsidies, patients' out-of-pocket costs, manufacturers' coverage gap discounts, and other payments toward pharmaceutical spending.

This study was approved by the institutional review board at the University of Pittsburgh as exempt from informed consent procedures because the use of unidentifiable data. All analyses were conducted with SAS version 9.4 (SAS Institute Inc) from October 2018 to January 2019. This was a descriptive study, and thus no *P* value was used to define a significance threshold.

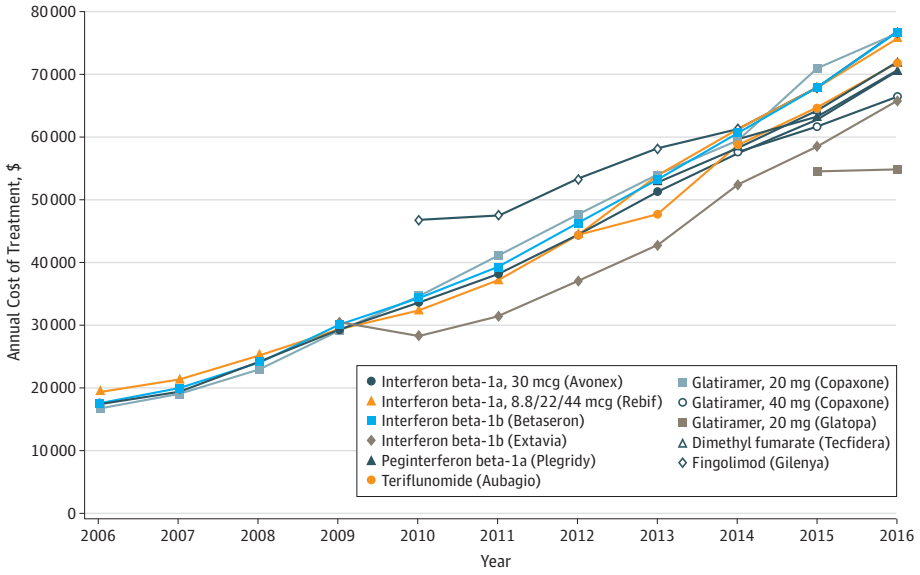
Results

The sample included a mean of 2.8 million Medicare beneficiaries every year. Annual costs of treatment with self-administered DMTs for MS more than quadrupled from 2006 to 2016, from a mean (SD) of $18 660 ($1177) to $75 847 ($6956) (**Figure 1**). Trends in annual costs of treatment with each agent increased in parallel at a mean rate of 12.8% every year. Only 4 agents deviated from the general trend at some point. Fingolimod and brand-name glatiramer, 20 mg, occupied the higher end of the range of annual costs of treatment throughout the study period, while interferon beta-1b (Extavia) and generic glatiramer, 20 mg, occupied the lower end.

Brand-name glatiramers accounted for the largest market share across the study period, ranging between $25 552 of $79 411 per 1000 Medicare beneficiaries (32.2%) and $10 342 of $21 365 per 1000 Medicare beneficiaries (48.4%) (**Figure 2**). Yet platform therapies experienced a substantial drop over time, with decreases in the market shares of brand-name glatiramers ($2861 of $7794 per 1000 Medicare beneficiaries [36.7%] to $25 552 of $79 411 per 1000 Medicare beneficiaries [32.2%]), interferon beta-1a (30 µg; $2521 of $7794 per 1000 Medicare beneficiaries [32.3%] to $11 298 of $79 411 per 1000 Medicare beneficiaries [14.2%]), interferon beta-1b (Betaseron; from $1460 of $7794 per 1000 Medicare beneficiaries [18.7%] to $3588 of $79 411 per 1000 Medicare beneficiaries [4.5%]), and interferon beta-1a (8.8/22/44 µg; from $951 of $7794 per 1000 Medicare beneficiaries [12.2%] to $6588 of $79 411 per 1000 Medicare beneficiaries [8.3%]) from 2006 to 2016. By 2016, the new therapies fingolimod, teriflunomide, and dimethyl fumarate reached market shares of $6311 of $79 411 per 1000 Medicare beneficiaries (7.9%), $7177 of $79 411 per 1000 Medicare beneficiaries (9.0%), and $15 262 of $79 411 per 1000 Medicare beneficiaries (19.2%), respectively. Throughout the study period, the mean (SD) market shares of interferon beta-1b (Extavia), peginterferon beta-1a, and generic glatiramer, 20 mg, were 1.1% (0.5%).

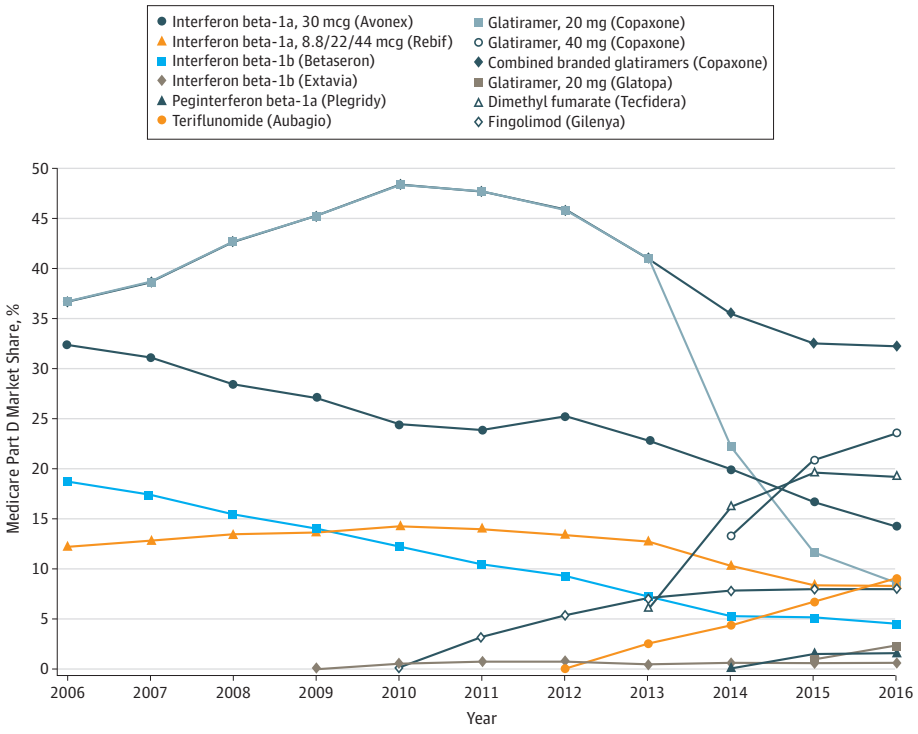
From 2006 to 2016, pharmaceutical spending per 1000 Medicare beneficiaries on self-administered DMTs for MS increased 10.2-fold, from $7794 to $79 411 (**Figure 3**). The share of pharmaceutical spending borne by Medicare's catastrophic coverage payments increased 14.1-fold, from $3798 to $53 705, while Medicare Part D plans' payments increased

Figure 1. Trends in Annual Cost of Treatment With Self-administered Disease-Modifying Therapies for Multiple Sclerosis in Medicare Part D, 2006-2016



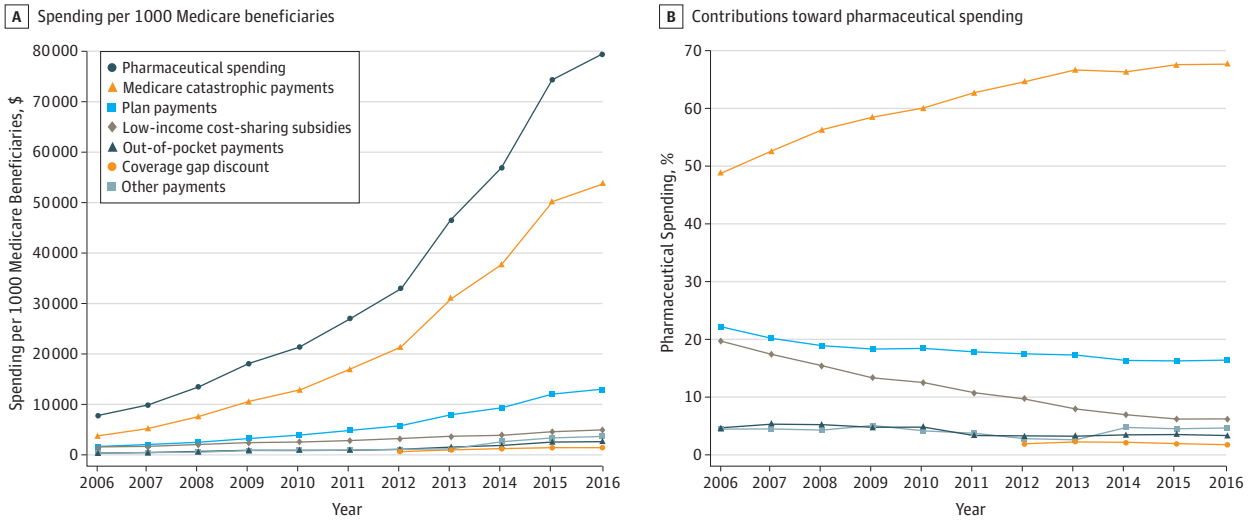
The annual cost of treatment with each medication was calculated based on Medicare Part D prescription claims gross cost (before rebates) and US Food and Drug Administration–approved recommended dosages. For drugs marketed in multiple formulations, annual costs of treatment were calculated as the mean annual cost of treatment of their formulations, weighted by their relative market share every year. There are 2 different formulations of glatiramer: 20 mg (once daily) and 40 mg (3 times a week). Brand-name glatiramer in a 20-mg dose was approved in 1996, and the 40-mg branded formulation was approved in 2014. The first generic glatiramer in a 20-mg dose (Glatopa) was approved in 2015. Subsequently, a second generic of glatiramer at 20 mg and a new generic glatiramer at 40 mg were approved in 2017. Finally, a second generic of glatiramer at 40 mg was approved in 2018. Since this study period goes up to December 2016, this study only includes the first generic version of glatiramer in a 20-mg dose (Glatopa).

Figure 2. Market Share of Self-administered Disease-Modifying Therapies for Multiple Sclerosis in Medicare Part D, 2006-2016



Market share was calculated as the proportion of pharmaceutical spending accounted by every drug each year.

Figure 3. Trends in Spending and Relative Contribution of Stakeholders Toward Pharmaceutical Spending on Self-administered Disease-Modifying Therapies for Multiple Sclerosis in Medicare Part D, 2006-2016



A, Spending per 1000 Medicare beneficiaries for all self-administered, disease-modifying therapies approved for the treatment of multiple sclerosis. Spending per 1000 Medicare beneficiaries was defined as the absolute annual spending on self-administered disease-modifying therapies for multiple sclerosis in this sample, divided by the total number of beneficiaries in the sample each year, and multiplied it by 1000. B, The relative contribution (expressed as a percentage) toward pharmaceutical spending made by Medicare catastrophic coverage payments, Medicare Part D Plans payments, low-income cost-sharing subsidies, patients' out-of-pocket payments, manufacturers' coverage gap discounts, and other payments. The low-income cost-sharing subsidy provides assistance to certain low-income individuals to supplement patients' cost-sharing (deductible and copayments) associated with the Part D benefit. Other payments include payments made by the Part D plan for benefits beyond the standard Part D benefit, payments made by third-party payers (eg, group health plans, worker's compensation, and governmental programs, such as the Veterans Administration and Tricare), and payments made by qualified state pharmacy assistance programs or charities. As an example, the Medicare Part D standard benefit design in 2016 was structured as (1) a deductible up to $360 (with beneficiaries bearing 100% of the spending); (2) an initial coverage period up to $3310 of spending (with beneficiaries bearing 25% and Medicare Part D plans 75% of the spending); (3) a coverage gap up to an out-of-pocket threshold of $4850 (with beneficiaries bearing 45%, Medicare Part D plans 5%, and manufacturers' discounts 50% of the spending for brand-name drugs and beneficiaries bearing 58% and generic manufacturers' discounts 42% of the spending for generic drugs); and (4) catastrophic coverage (with beneficiaries bearing 5%, Medicare Part D plans 15%, and Medicare 80% of the spending).

7.5-fold, from $1740 to $13 031. Low-income cost-sharing payments increased 3.2-fold, from $1536 to $4914, and patients' out-of-pocket costs increased 7.2-fold, from $372 to $2673. In relative terms, the contribution of Medicare's catastrophic coverage payments toward pharmaceutical spending increased from $3798 of $7794 (48.7%) to $53 705 of $79 411 (67.6%), while the relative contribution of plans' spending (from $1740 of $7794 [22.3%] to $13 031 of $79 411 [16.4%]), low-income cost-sharing subsidies (from $1536 of $7794 [19.7%] to $4914 of $79 411 [6.2%]), and out-of-pocket costs (from $372 of $7794 [4.8%] to $2673 of $79 411 [3.4%]) decreased. Combined, federal contributions toward pharmaceutical spending increased from $5335 of $7794 (68.5%) to $58 620 of $79 411 (73.8%). Manufacturers' discounts in the coverage gap accounted for a mean (SD) of 2% (0.2%) of the spending. We estimate that, from 2006 to 2016, Medicare Part D spending on self-administered DMTs for MS increased from $396.6 million to $4.4 billion, while patients' out-of-pocket spending increased from $18.9 million to $149.4 million.

Discussion

Using Medicare Part D data, we observed that annual costs of treatment of self-administered DMTs for MS more than quadrupled from 2006 to 2016. Pharmaceutical spending on these medications increased more than 10-fold, with patients' out-of-pocket spending increasing more than 7-fold. Although brand-name glatiramers accounted for most of the market, platform therapies experienced a market share drop over time in favor of newer therapies.

While prices of most self-administered DMTs for MS increased in parallel, defying standard market expectations, certain deviations from the general cost trend were observed. First, interferon beta-1b (Extavia) and fingolimod, both manufactured by Novartis, occupied the lower and upper end of the price range in 2010 through 2014. This could have represented an attempt from the manufacturer to encourage the use of its lower-priced interferon beta-1b while launching its new therapy fingolimod at a much higher price than incumbent agents. Second, although Teva launched the branded glatiramer, 40 mg, at a similar price as the branded 20-mg version in 2014, the price of the 20-mg branded formulation increased substantially the following year. This could have represented an attempt to encourage the use of the 40-mg formulation in anticipation of the entry of a generic version for the 20-mg formulation.

Pharmaceutical spending, and patients' and Medicare's financial burdens particularly, were largely affected by the strong year-over-year increases observed in drug prices.

Moreover, soaring prices of self-administered DMTs for MS have progressively moved Medicare Part D spending from the initial phases of coverage to the catastrophic phase of coverage (in which Medicare bears 80% of the spending), leading to an increased relative contribution of Medicare payments toward pharmaceutical spending. Additionally, high and rising prices of self-administered DMTs for MS have led to a 7.2-fold increase in patients' out-of-pocket spending, which could have resulted in lower access for patients to these medications.

These rising prices are not only concerning because of the strong effect they had on spending, but because they demonstrate that the approval of new therapies did not ameliorate and could have even contributed to high inflation rates observed for incumbent drugs.[7,8] However, it is possible that the similarity of trends and the high price increases observed could represent competition for rebates, which unfortunately cannot be accounted for because of the unavailability of rebate data at the product level.

Limitations

This study is subject to 3 additional limitations. First, the analyses only include self-administered DMTs for MS and not those administered in physician offices, because they are reimbursed under Medicare Part B. Second, the results are only generalizable to the Medicare Part D population. Third, only glatiramer, 20 mg, faced direct within-molecule competition. Yet according to economic theory, prices of incumbent agents should decrease after the entry of competitors, even if those only present within-class competition.[9]

Conclusions

As health care costs become unsustainable, these findings suggest that market entry of new MS drugs may have contributed to higher drug prices among incumbent agents. These higher prices were associated with large increases in Medicare spending and patient out-of-pocket costs.

ARTICLE INFORMATION

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Concept and design: San-Juan-Rodriguez, Good, Heyman, Shrank, Hernandez.
Acquisition, analysis, or interpretation of data: San-Juan-Rodriguez, Heyman, Parekh, Hernandez.
Drafting of the manuscript: San-Juan-Rodriguez, Good, Shrank, Hernandez.
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Conflict of Interest Disclosures: Drs Good and Parekh are current employees of UPMC Health Plan Insurance Services Division. Dr Shrank is a current employee of Humana but formerly worked at UPMC Health Plan Insurance Services Division, during the initial drafting of this article; Dr Shrank also reports serving as an advisor to the GetWellNetwork Inc outside the submitted work. Dr San-Juan-Rodriguez reported grants from the Myers Family Foundation during the conduct of the study. Dr Hernandez reports personal fees from Pfizer outside the submitted work. No other disclosures were reported.

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