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ORIGINAL ARTICLE

Comparing Adoption of Breakthrough and "Me-too" Drugs Among Medicare Beneficiaries: a Case Study of Dipeptidyl Peptidase-4 Inhibitors

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Abstract
Purpose "Me-too" drugs are new pharmaceuticals with the mechanism of action of an existing drug and are considered less innovative than breakthrough drugs. The objective of this study was to evaluate whether the adoption patterns of the breakthrough drug sitagliptin and the "me-too" drug saxagliptin differed and to assess whether the patterns differed between Medicare stand-alone (PDP) and Medicare Advantage Part D (MA-PD) plans.
Methods Pharmacy claims from a 5% random sample of Medicare Part D beneficiaries were used to identify all prescriptions filled for sitagliptin (breakthrough drug) and saxagliptin ("me-too" drug) between October 1, 2006 and December 31, 2011. The number of new sitagliptin and saxagliptin users by month and type of plan were plotted and Bass diffusion models were constructed to estimate the rate of diffusion.
Results Sitagliptin had a longer adoption life than saxagliptin, and its adoption was quicker among MA-PD than PDP beneficiaries; it peaked at 51 and 66.7 months after its approval, respectively. However, the adoption of saxagliptin did not differ by type of plan; it peaked at 20.5 months in PDP and 22.9 months in MA-PD. At the end of our study, the market share of the innovative drug sitagliptin measured as the cumulative number of users since market entry was almost nine times higher than the "me-too" drug, saxagliptin.
Conclusions The breakthrough drug sitagliptin had a much longer adoption life compared to the "me-too" drug saxagliptin, and the breakthrough drug sitagliptin was adopted quicker among managed care plans compared to PDP plans.

Keywords Diffusion of innovation · Prescription drugs · Medicare Part D · Medicare Advantage

Introduction

Breakthrough drugs are the first pharmaceuticals within a drug class to reach the market and therefore are generally innovative drugs with large incremental value compared to the existing therapies [1]. In contrast, "me-too" drugs are new pharmaceuticals with the same mechanism of action of an existing drug and are characterized by a low degree of innovation [1, 2]. Previous researchers have analyzed the diffusion of new drugs, which is the rate at which a new innovation, in this case, a prescription drug, is adopted in a population over time [3] and have found the time to adoption ranging from 5 months to 8.2 years [4, 5], and that innovative therapies are adopted quicker in areas with higher managed care penetration [6, 7]. However, no studies have compared the diffusion and adoption patterns of breakthrough and "me-too" drugs. It also remains unclear whether the diffusion and adoption of breakthrough and "me-too" drugs differ between traditional fee-for-service and managed care organizations. Comparing the diffusion and adoption of breakthrough and "me-too" drugs will show whether the incremental value of a new therapy translates into a benefit in terms of market penetration and revenue

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generated, which may ultimately incentivize research on drugs with new mechanisms of action, rather than on "me-too" drugs. Evaluating the differences in the diffusion and adoption of breakthrough and "me-too" drugs between the fee-for-service and the managed care setting will provide evidence on the effect of managed care financial incentives on the use of new pharmaceuticals.

To answer these questions, dipeptidyl peptidase-4 (DPP-4) inhibitors were selected as a case study. DPP-4 inhibitors are oral hypoglycemic agents used in the treatment of type 2 diabetes. Sitagliptin was the first DPP-4 inhibitor, approved by the Food and Drug Administration in October 2006 as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Saxagliptin was approved in July 2009 for the same indication and it has a pharmacological profile very similar to sitagliptin; therefore, it constitutes a good example of a "me-too" drug. The diffusion of saxagliptin and sitagliptin was compared between Medicare Part D stand-alone (PDP) plans—fee-for-service plans that only cover prescription drugs, and Medicare Advantage Part D (MA-PD) plans—managed care plans that also cover medical services. Beneficiaries enrolled in PDP are on average older, more likely to be white and female, have a higher number of chronic conditions and use more prescription drugs than MAPD beneficiaries [8, 9]. Because MA-PD plans are incentivized to use high-value drugs to offset downstream medical costs as opposed to PDP plans, which do not benefit from offsets from nondrug medical expenditures, the rate of adoption of the breakthrough drug sitagliptin was hypothesized to be faster among MA-PD plans than among PDP plans.

Methods

Pharmacy data was obtained for a 5% random sample of Medicare Part D beneficiaries from the Centers for Medicare and Medicaid Services (CMS). All prescriptions filled for sitagliptin and saxagliptin between October 1, 2006 and December 31, 2011 were extracted. Our case study focused on DPP4-inhibitors because it is the only example of well-defined therapeutic class with a first-to-market and a "me-too" drug approved during 2006–2011.

Outcomes included number of new users by month, cumulative number of users by month, time to peak adoption, and time to full adoption, all of them defined for each drug and by type of Medicare Part D plan. The first two outcomes were obtained from the analysis of Medicare part D claims, and the last two outcomes were produced by Bass models.

New users were defined based on the first prescription filled for sitagliptin or saxagliptin. The type of plan (MA-PD or PDP) that the beneficiary was enrolled in the month of the first prescription for sitagliptin or saxagliptin was identified. Existing Medicare beneficiaries with only Parts A and B coverage may initiate Part D coverage in January, which resulted in a peak of new users in January every year. These beneficiaries do not represent new users, but rather existing users whose pharmacy claims were not captured in our data before. Therefore, beneficiaries who previously had Parts A and/or B coverage but joined Part D in January of any study year were excluded from the analysis. However, beneficiaries joining Part D in January because they became eligible for Medicare coverage due to their birthday in January were included in the study, because the distribution of birthdays is random in a year. The number of sitagliptin and saxagliptin new users was plotted by month and type of plan, and the cumulative number of sitagliptin and saxagliptin users by month was also calculated to compare market penetrations by drugs [8].

Bass diffusion models were constructed to estimate the rates of diffusion for each drug, by type of plan. The Bass formula describes the number of new users at a given time on the basis of four parameters: the time of market introduction (t_0), the total number of users after full penetration (m), the likelihood that somebody not using the product will start using it because of external factors (p), and the likelihood that somebody not using the product will start using it because of internal influences (q) [10]. To construct Bass models, the number of new sitagliptin and saxagliptin users by month and type of plan was specified as input data, and start points for the parameters p, q, and m were provided. Specifically, the start points for p and q were 0.03 and 0.4, respectively, because these have been found to be the average values of each parameter [11]. The start point for m was the cumulative number of new users observed at the end of our study period. In sensitivity analysis, the start point for p was varied between 0.01 and 0.1, and the start point for q was varied between 0.1 and 1. Further details on the mathematical representation and assumptions of Bass models can be found in the Supplemental Material. Bass models were constructed using nlmrt package in the statistical software R 3.0.3.

Results

The final estimates for p and q calculated by the Bass model algorithm can be found in the Supplemental Material.

Adoption Cycle

Our study yielded two main results with regard to the adoption cycle of sitagliptin and saxagliptin. First, Bass diffusion models predicted that the breakthrough drug sitagliptin had a longer adoption life than "me-too" drug saxagliptin, whose diffusion model showed a large peak soon after the market introduction (Fig. 1). The time to full adoption was predicted

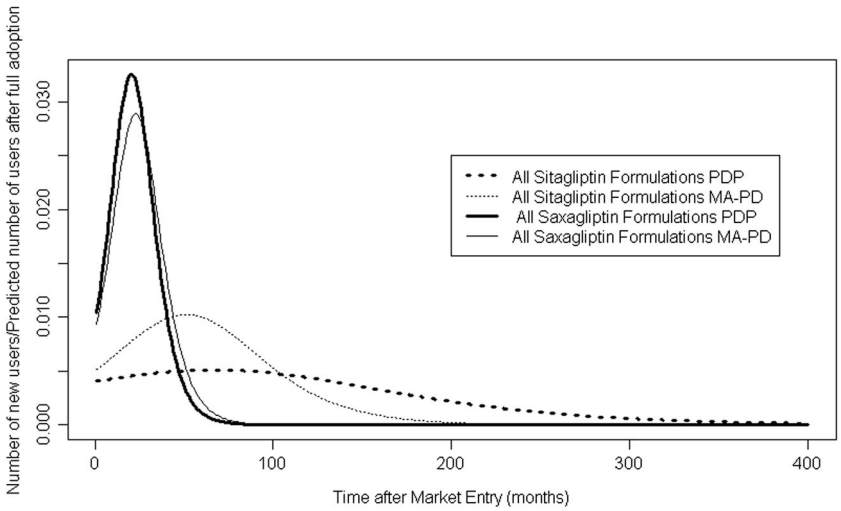

Fig. 1 Adoption cycle of breakthrough drug sitagliptin and "me-too" drug saxagliptin. Predicted bass diffusion models, by drug and type of Medicare enrollment. *PDP* stand-alone prescription drug plan, *MA-PD* Medicare Advantage prescription drug plan. The *y*-axis shows the proportion of predicted number of new users among the predicted total number of users after full adoption. The *x*-axis shows time after market entry, measured in months

at 400 months for sitagliptin in the PDP market, and 200 months among MA-PD plans. In contrast, saxagliptin was estimated to achieve full adoption at 100 months after market entry in both PDP and MA-PD markets.

Second, the adoption of the innovative drug sitagliptin was faster in the MA-PD than in the PDP setting. In particular, the rate of sitagliptin adoption peaked at 66.7 months after its approval among PDP and at 51 months among MA-PD. However, the diffusion of the "me-too" drug saxagliptin was similar in both types of plans, and it started to decline at 20.5 and 22.9 months after market entry among PDP and MA-PD, respectively.

Market Penetration

Our study yielded three main results with regard to the market penetration of sitagliptin and saxagliptin. First, the market share of the innovative drug, sitagliptin, measured as the cumulative number of users, was almost nine times the market share of the "me-too" drug, saxagliptin, in December 2011 (Fig. 2). Specifically, at the end of our study, the total number of sitagliptin users was 58,433, in comparison to 6662 saxagliptin users.

Second, the number of beneficiaries who started using sitagliptin every month did not decrease after the market introduction of saxagliptin. For instance, the number of new sitagliptin users in March and July of 2009, before saxagliptin approval, was 1052 and 867, compared to 1050 and 960 in March and July of 2010, after saxagliptin became available.

Third, the uptake of the breakthrough drug sitagliptin during the first months after approval was considerably greater than that of the "me-too" drug (Fig. 2). The number of beneficiaries who initiated drug 6 months after approval was 15 times higher for sitagliptin than saxagliptin: 667 vs 42. In

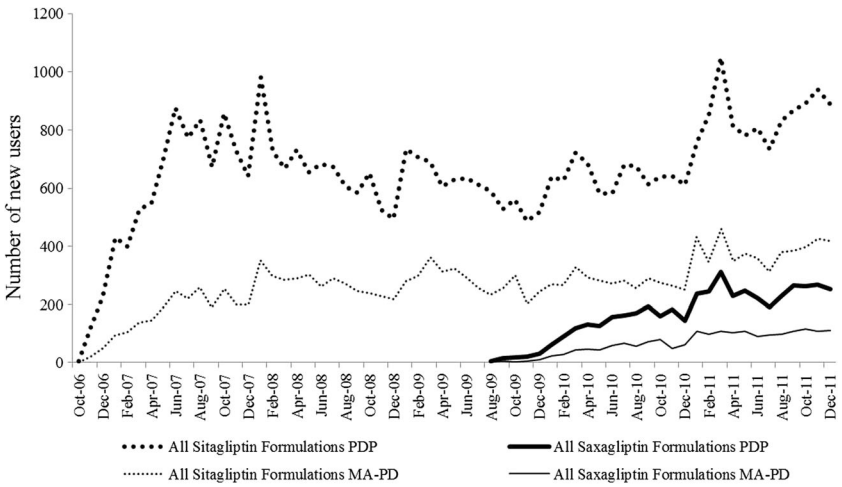

Fig. 2 Market penetration of breakthrough drug sitagliptin and "me-too" drug saxagliptin. Number of new users between October 1, 2006 and December 31, 2011, by month and type of Medicare enrollment. *PDP* stand-alone prescription drug plan, *MA-PD* Medicare Advantage prescription drug plan. New users were defined on the basis of the first prescription filled for sitagliptin or saxagliptin. New users were categorized into PDP and MA-PD by the type of plan they were enrolled in the month of the first prescription for sitagliptin or saxagliptin

addition, the cumulative number of sitagliptin users 6 months after approval was over 18 times the number of saxagliptin users, 2115 vs 115.

Discussion

Our study found that the adoption cycle of the breakthrough drug sitagliptin was longer than that of the "me-too" drug, saxagliptin, and that the market penetration of the breakthrough drug sitagliptin was considerably higher than that of the "me-too" drug saxagliptin. In addition, the diffusion of the breakthrough drug sitagliptin was quicker in the managed care setting than among PDP part D plans; whereas the adoption of "me-too" drug saxagliptin did not differ between two settings.

Our estimates for the time to full adoption (100–400 months) are larger than those previously reported in the literature, because we analyzed the diffusion of pharmaceuticals from the user level, rather than the prescriber or the prescription level [4, 5]. Nevertheless, our results are consistent with previous studies that found that managed care plans adopt breakthrough therapies faster than traditional plans [6, 7]. The observed seasonal trend in the uptake of both drugs characterized by annual peaks every January is consistent with the "January effect" described in the literature for medication use among Medicare Part D beneficiaries [12].

Our study has four main limitations. First, our study only evaluated the adoption of two pharmaceuticals, since they were the only examples of breakthrough and "me-too" drug approved within the time frame we have data for. Second, the conclusions of our study only apply to "me-too" drugs that did not present substantial advantages over breakthrough drugs, as it is the case of saxagliptin. The diffusion and adoption of "me-too" drugs that introduced relevant innovation to the available therapeutic arsenal may not fit the patterns observed in this study. Third, only 18 months of input data were available for saxagliptin; this can limit the ability of our model to predict the diffusion of this drug. However, previous studies have shown that the uptake of new drugs can be reliably predicted with only 15 months of data after market introduction [13]. Fourth, Bass diffusion models do not account for the influence of marketing strategies [10]. In future research, it would be adequate to examine the reasons to explain the differences observed in the diffusion of sitagliptin and saxagliptin, using data on prescriber characteristics, spending on marketing, and rebates to plans.

Nevertheless, our case study shows an example of an innovative pharmaceutical that is adopted quicker in the Medicare market than a "me-too" drug. Our results may incentivize research in drugs with new mechanisms of action, breakthrough drugs, rather than "me-too" drugs. In addition, our case study suggests that only breakthrough drugs, not "me-too" drugs, are adopted faster in the managed care setting compared to the PDP Part D market. This difference in the rate of adoption of the breakthrough may be explained by the differential incentives to maximize value of drugs in PDP and MA-PD plans, because only MA-PD plans benefit from medical costs offsets related to the use of high-value pharmaceuticals. Under the current healthcare reform, payments to providers are directly aligned with overall healthcare costs and quality of care. Providers thus have incentives to provide effective medications that can prevent downstream medical costs. Under this environment, prescribers may adopt innovative drugs faster than in our study period. As newer data become available, similar analyses could be repeated for new therapeutic classes to study whether the healthcare reform has promoted the adoption and diffusion of innovative drugs.

In summary, our case study found that the adoption life of the breakthrough drug sitagliptin was longer than that of the "me-too" drug saxagliptin and that the market penetration of the breakthrough drug sitagliptin was considerably higher. In addition, our case study found that the diffusion of the breakthrough drug sitagliptin was quicker among MA-PD than PDP Part D plans.

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Compliance with Ethical Standards

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