The Association of Industry Payments to Physicians with Prescription of Brand-Name Intranasal Corticosteroids

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Abstract

Objectives. To examine the association of industry payments for brand-name intranasal corticosteroids with prescribing patterns.

Study Design. Cross-sectional retrospective analysis.

Setting. Nationwide.

Subjects and Methods. We identified physicians prescribing intranasal corticosteroids to Medicare beneficiaries 2014-2015 and physicians receiving payment for the brand-name intranasal corticosteroids Dymista and Nasonex. Prescription and payment data were linked by physician, and we compared the proportion of prescriptions written for brand-name intranasal corticosteroids in industry-compensated vs non-industry-compensated physicians. We associated the number and dollar amount of industry payments with the relative frequency of brand-name prescriptions.

Results. In total, 164,587 physicians prescribing intranasal corticosteroids were identified, including 7937 (5%) otolaryngologists; 10,800 and 3886 physicians received industry compensation for Dymista and Nasonex, respectively. Physicians receiving industry payment for Dymista prescribed more Dymista as a proportion of total intranasal corticosteroid prescriptions than noncompensated physicians (3.1% [SD = 9.6%] vs 0.2% [SD = 2.5%], respectively, P < .001). Similar trends were seen for Nasonex (12.0% [SD = 16.8%] vs 4.8% [SD = 13.6%], P < .001). The number and dollar amount of payment were significantly correlated to the relative frequency of Dymista (ρ = 0.26, P < .001 and ρ = 0.20, P < .001, respectively) and Nasonex prescriptions (ρ = 0.09, P < .001 and ρ = 0.15, P < .001, respectively). For Dymista, this association was stronger in otolaryngologists than general practitioners (P < .001). There was a stronger correlation between the percentage of prescriptions and the number and dollar amount of payments for Dymista than for Nasonex (P = .014 and P < .001).

Conclusions. Industry compensation for brand-name intranasal corticosteroids is significantly associated with prescribing patterns. The magnitude of association may depend on physician specialty and the drug’s time on the market.

Keywords

industry, Open Payments Database, Sunshine Act, allergic rhinitis, nasal steroids, conflict of interest

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As the fifth most common chronic illness in the United States, allergic rhinitis (AR) accounts for $2 to $5 billion of health care expenditures annually.¹ Intranasal corticosteroids (INCS) are effective in controlling symptoms in most patients and are universally recommended as primary treatment.²,³ Less common indications include chronic rhinosinusitis and nasal polyposis.⁴ No specific INCS have been shown to be superior, but there are significant cost differences between different subclasses.⁵ These differences are particularly obvious as some INCS are available generically while many are branded, with or without patent protection.

In addition, a combination INCS-intranasal antihistamine (fluticasone propionate-azelastine hydrochloride, Dymista) was recently approved to treat AR that is inadequately controlled by INCS.⁶ Treatment guidelines typically suggest the addition of an intranasal antihistamine to INCS as an option when INCS alone fail; however, there is limited evidence that the combination formulation is superior to the more cost-effective coadministration of separate INCS and intranasal antihistamines.²,⁷,⁸ With this lack of guidance, this decision relies on individual physician judgment.

There has been considerable work examining the effect of industry support on physician behavior. The Physician Open Payments Act, passed in 2010, reports all industry

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payments to physicians.\textsuperscript{9} Multiple studies using these data have associated industry payments with increased physician usage.\textsuperscript{10–15} However, in some drug classes, no effect of industry support has been observed. To our knowledge, this question has not been examined for INCS. INCS are relatively inexpensive and commonly prescribed medications and have over-the-counter (OTC) equivalents; therefore, they represent a unique drug class that may be affected differently by industry financial support.

In this study, we use the Open Payments Database and Medicare Part D payment database to examine the association between industry payments and prescription patterns in INCS. Specifically, we examined the association of compensation with prescribing patterns for 2 commonly prescribed and industry-supported INCS, Nasonex (mometasone furoate) and Dymista (azelastine hydrochloride and fluticasone propionate).

**Methods**

**Data Sources: Medicare Part D**

The Centers for Medicare & Medicaid Services (CMS) Provider Utilization and Payment Data (Part D Prescriber) Public Use File (Part D PUF) is publicly available and contains information on prescriptions prescribed to Medicare beneficiaries enrolled in Medicare’s prescription drug program.\textsuperscript{16} For each prescriber and drug, it identifies the total number of prescriptions and drug cost dispensed at a provider’s direction for each calendar year. It contains information on the physician’s National Provider Identifier (NPI), full name, specialty, and place of service. OTC drugs included in approved step-therapy protocols, as OTC nasal steroids often are, are also included in the PUF.\textsuperscript{17} To protect patient privacy, records derived from 10 or fewer claims are excluded. We identified all prescriptions made for the most commonly prescribed nasal steroids from 2014 to 2015. Specifically, we included Dymista (azelastine hydrochloride and fluticasone propionate; Meda, Solna, Sweden), Nasonex (mometasone furoate; Merck, Kenilworth, New Jersey), QVar (beclomethasone dipropionate; Teva, Petah Tikva, Israel), Beconase AQ (beclomethasone dipropionate; GlaxoSmithKline, Brentford, United Kingdom), QNasal (beclomethasone dipropionate; Teva), Omnaris (ciclesonide; Takeda), Zetonna (ciclesonide; Takeda, Deerfield, Illinois), Veramyst (fluticasone furoate; GlaxoSmithKline), and OTC fluticasone propionate. Dymista and Nasonex were chosen for analysis as these represented the INCS for which physicians most commonly received industry compensation.

**Data Sources: Open Payments Database**

The Physician Payment Sunshine Act was passed as part of the Affordable Care Act and collects information about payments made to physicians by drug and device companies. It contains all payments over $10 for things like travel, research, meals, gifts, and speaking fees. Each case contains the dollar value and nature of the payment, identifying information about the payment recipient and industry sponsor, as well as the medications or devices associated with each payment.\textsuperscript{9} All nonresearch, nonownership payments made for Dymista or Nasonex were identified from the 2014 and 2015 open payments data sets, including payments made from January 1, 2014, to December 31, 2015.

**Statistical Analysis**

Claims data from the Part D PUF were linked to payments data by physician first name, last name, and state of practice. The number of days of nasal steroid prescriptions written by a given provider was summed, and the percentage of prescription days written for Dymista was calculated. The total number and dollar value of payments to each physician for Dymista were summed. Physicians receiving open payments for Dymista (“compensated”) who did (“prescribers”) and did not (“nonprescribers”) prescribe Dymista were compared in terms of number and dollar value of payments. Of physicians who prescribed Dymista, those receiving open payments were compared to those who did not (“noncompensated”) in terms of the mean rate of Dymista prescribed. The mean rate was defined as the mean of individual physicians’ percentage prescriptions. The Wilcoxon rank-sum test was used for comparison of continuous variables; Fisher’s exact test was used for comparison of categorical variables. Of compensated prescribers, the number of payments and dollar value of payments were associated with percentage of Dymista prescriptions via Spearman rank correlation test.

Physicians were then classified by specialty as otolaryngologists, allergists, and other. The above analysis was repeated, stratified by physician specialty, and the correlations between payments and prescribing patterns were compared between specialties.

This analysis was repeated for Nasonex. The correlations between prescribing patterns and payment number and value were compared between Nasonex and Dymista. These databases are both publicly available and, therefore, were exempt from approval by the Yale University Institutional Review Board. All statistical analysis was performed in STATA 15.0 (StataCorp, College Station, Texas). Statistical significance was considered at $P < .05$.

**Results**

A total of 164,587 physicians prescribing nasal steroids were identified, including 7937 (5\%) otolaryngologists, 3349 (2\%) allergists, and 153,301 (93\%) general physicians or other specialists. Each physician wrote a mean (SD) of 4069 (5013) days of nasal steroid prescriptions. Mean (SD) days of prescriptions were 7692 (9320), 9107 (9943), and 3844 (4530) for otolaryngologists, allergists, and general practitioners, respectively.

**Dymista**

In total, 3512 (2\%) of nasal steroid prescribers prescribed Dymista, including 1202 (15\%) of otolaryngologists, 864 (26\%) of allergists, and 1446 (1\%) of other/general practitioners.
A total of 10,800 providers receiving payments for Dymista were identified, and 3328 (31%) of these compensated providers did not have any nasal steroid prescriptions recorded. The overlap between compensation, nasal steroid prescription, and Dymista prescriptions is shown in Figure 1. Compensated physicians who did not prescribe nasal steroids were excluded from subsequent analysis. Overall, 1557 of 7472 (21%) compensated nasal steroid prescribers prescribed Dymista, compared to 1955 of 157,115 (1%) noncompensated nasal steroid prescribers ($P < .001$). This remained true following stratification by specialty, with general physicians having the largest increase at 14-fold likelihood (Table 1). Compensated Dymista prescribers received a median payment value of $42 (S19-$113) and 2 (1-4) payments vs $21 (S14-$52) and 1 (1-2) for compensated nonprescribers ($P < .001$ and $P < .001$, respectively). The mean (SD) rate of Dymista prescriptions was $0.2\%$ ($0.26$, $P < .001$) and dollar value ($0.20$, $P < .001$) of payments (Figures 2 and 3). When stratified by specialty, there was a significant correlation between the percentage of Dymista prescriptions and number of payments for otolaryngologists ($\rho = 0.25$, $P < .001$), allergists ($\rho = 0.20$, $P < .001$), and general physicians ($\rho = 0.12$, $P < .001$). There was no significant difference between the degree of correlation for otolaryngologists and allergists ($P = 0.066$); however, there was a stronger correlation for both otolaryngologists and allergists than general practitioners ($P < .001$ and $P = .008$, respectively). There was also a significant correlation between the percentage of Dymista prescriptions and total dollar value of payments for otolaryngologists ($\rho = 0.18$, $P < .001$), allergists ($\rho = 0.13$, $P < .001$), and general physicians ($\rho = 0.09$, $P < .001$). There was no significant difference in the degree of correlation between otolaryngologists and allergists ($P = .144$) or allergists and general practitioners ($P = .190$); however, the degree of correlation for otolaryngologists was higher than for general practitioners ($P < .001$).

Nasonex

A total of 36,144 (22%) of physicians prescribed Nasonex, including 3274 (41%) otolaryngologists, 1702 (51%) allergists, and 31,150 (20%) general physicians.

In total, 3886 providers received payment for Nasonex, and 601 (15%) compensated providers did not have any INCS prescriptions and were excluded from subsequent analysis (Figure 4). Overall, 1832 of 3285 (56%) compensated nasal steroid prescribers prescribed Nasonex, compared to 34,312 of 161,302 (21%) noncompensated nasal steroid prescribers ($P < .001$). This remained true following stratification by specialty, with generalists having the greatest fold increase at 2.3 (Table 1). Compensated Nasonex prescribers received a median payment value of $14 (S11-$25) and 1 (1-2) payments vs $12 (S10-$20) and 1 (1-2) in noncompensated Nasonex prescribers ($P < .001$ and $P < .001$, respectively). The mean rate of Nasonex prescriptions was 4.8% (13.6%) in noncompensated physicians vs 12.0% (16.8%) in compensated physicians ($P < .001$).

For compensated INCS prescribers, there was a significant correlation between the percentage of Nasonex prescriptions and the number ($\rho = 0.09$, $P < .001$) and dollar amount ($\rho = 0.15$, $P < .001$) of payments (Figures 5 and 6). Stratified by physician specialty, there was a significant correlation between the percentage of prescriptions and the dollar amount of payments for otolaryngologists ($\rho = 0.10$, $P = .003$) and general practitioners ($\rho = 0.17$, $P < .001$) but not allergists ($\rho = 0.01$, $P = .709$). There was no significant

| Table 1. Percentage of Compensated and Noncompensated Physicians Prescribing Dymista and Nasonex. |
|---|---|---|---|---|---|
| & No. (%) of Physicians | & Prescribing Dymista | & No. (%) of Physicians | & Prescribing Nasonex | & Fold Increase | & Fold Increase |
| & Not Paid | & Paid | & Fold Increase | & Not Paid | & Paid | & Fold Increase |
| Ear, nose, and throat | 578/5970 (10) | 624/1967 (32) | 3.3 | 2700/7083 (38) | 574/854 (67) | 1.8 |
| Allergy | 331/1949 (17) | 533/1400 (38) | 2.2 | 1196/2520 (47) | 524/829 (63) | 1.3 |
| General | 1046/149,196 (1) | 400/4105 (10) | 13.9 | 30,416/151,699 (20) | 734/1602 (46) | 2.3 |
There was a significant correlation between the percentage of Nasonex prescriptions and the number of payments for otolaryngologists ($r = 0.09$, $P = 0.006$) and general practitioners ($r = 0.10$, $P = .001$) but not allergists ($r = 0.01$, $P = .7225$). There was no significant difference between the strength of the correlation between otolaryngologists and general practitioners ($P = .810$).

Overall, the strength of the correlations between the percentage of prescriptions and both the dollar amount and number of payments was stronger for Dymista than Nasonex ($P < .001$ and $P = .014$, respectively).

**Discussion**

In this study, we found that industry payments were significantly associated with physician prescriptions of the
brand-name INCS Nasonex and Dymista. Physicians receiving industry payment were more likely to prescribe these drugs and prescribed a higher percentage of these drugs than physicians not receiving payment. In addition, both the number and dollar value of payments were related to prescription rates, and the strength of association of prescription rates with industry payments varied by physician specialty.

Nasal steroids are commonly prescribed by otolaryngologists, allergists, and primary care physicians. Many different preparations are available, and none have been shown to be superior to another, with the possible exception of Dymista. Even for Dymista, there are no clear guidelines indicating its use. INCS therefore represent an excellent opportunity to explore the effect of industry payments on prescription patterns. Most physicians in this study received nominal payment amounts (medians of $26 and $13 for Dymista and Nasonex, respectively); however, this amount was still significantly associated with prescribing behavior. Not only were compensated physicians more likely to prescribe brand-name INCS at all, but they also prescribed a higher proportion than noncompensated physicians. This association of payment with prescribing behavior agrees with multiple previous studies. Fleischman et al recently examined the association of physician payments for marketed oral anticoagulants and noninsulin diabetes drugs, and they found that increased payments were associated with increased prescriptions at a regional level; however, they did not examine this at the individual physician level. These results have been replicated at the individual physician level for other drug classes and specialties. Bandari et al examined this question in 4 different prostate cancer drugs and found that payment was significantly associated with prescribing patterns for 2 of 4 drugs. The reasons for the differences between drugs are unclear, but the authors speculated that the limited number of treatment options for advanced prostate cancer may have made prescribers relatively insensitive to payments. In contrast, there are a multitude of options available for allergic rhinitis treatment, and we speculate that this may have contributed to the association observed here.

Few studies have examined the effect of industry payments on brand-name prescriptions as a proportion of total prescriptions within a given drug class as was done in this study. DeJong et al recently used this methodology to examine prescription patterns in 4 classes of commonly prescribed drugs and found, in agreement with our findings, that even a single payment was associated with a higher proportion of brand-name prescriptions. In addition, in agreement with the findings here, they found that higher numbers and dollar amounts of payments were associated with further increases in relative prescription rate. Importantly, most of the physicians in this study received small payment amounts and prescribed low rates of Dymista and Nasonex, with a few physicians receiving high payment values and prescribing at high rates. This is particularly notable for Dymista, and these few physicians likely account for much of the correlation observed. Examining relative rather than absolute frequency of prescriptions allowed us to control for drug company targeting of physicians treating a higher volume of a relevant disease. These physicians likely prescribe more of the entire drug class, including the marketed drug, so the relative rather than absolute frequency of prescribing is more indicative of preferential behavior.

We also found that physician specialty affected the degree to which industry payments were related to relative prescription rates. For Nasonex, otolaryngologists and general practitioners were more sensitive to industry payments, whereas for Dymista, otolaryngologists and allergists were more sensitive to industry payments. Dymista is indicated as an option for patients refractory to other treatments who are also more likely to be referred to a specialist. This may account for the stronger association observed in otolaryngologists and allergists. Nonspecialists, in contrast, are less likely to care for patients in whom Dymista is considered appropriate treatment, which could explain the weaker correlation observed.

The finding of a stronger correlation in specialists vs nonspecialists has been replicated in previous studies. Nasonex, however, is indicated for all rhinosinusitis patients, who may be cared for by either specialists or generalists. This may explain the equivalent associations seen in otolaryngologists and generalists; however, the cause of the weaker association observed in allergists remains unknown.

There are significant differences in drug costs among nasal steroids. Allergic rhinitis costs the US health care system $2 to $5 billion annually, almost 50% of which is attributable to prescription drugs. Total Medicare reimbursement for fluticasone propionate averaged $11 (SD = $5) for a 30-day supply, while costs for Nasonex and Dymista were $206 (SD = $19) and $164 (SD = $10), respectively. In the Medicare patients examined here, much of this additional cost is passed on to the patients and thus may affect treatment compliance and outcomes. If similar associations exist in patients covered under private insurance, the differences in prescribing patterns seen here may produce a significant cost burden on the health care system without improving patient outcomes.

An increasing number of studies are showing an association between industry payments and physician behavior. This is not necessarily a negative force, as industry involvement plays an important role in the health care system; however, in an age of increasing pressure for cost-effective care, avoiding industry influence that will needlessly increase spending is prudent. There are multiple ways this can be approached, such as through the development of clinical practice guidelines and in-class exchange programs. Clinical practice guidelines, while interpreted by some physicians as overly restrictive, may assist physicians in making evidence-based decisions and therefore reduce industry’s impact. In cases where there are significant cost differences within a given drug class, electronic medical record therapeutic exchange may reduce costs effortlessly.
and without affecting outcomes and has been effective in INCS prescriptions in the past.24

There are significant limitations to this study. As a retrospective study, we were only able to establish a correlation between payments and prescription patterns, and the associations found here may not represent a causative relationship. It is possible that physicians who are prescribing more of a brand-name INCS are more likely to subsequently receive industry support rather than the other way around. We attempted to control for this by examining brand-name INCS prescriptions as a percentage of total INCS prescriptions; however, this possibility remains. Furthermore, our use of Medicare prescription data limits our analysis to physicians treating Medicare-covered patients. This population differs in terms of age, socioeconomic factors, and illness severity from the general population, and therefore the trends identified here may not be generalizable. We speculate that physicians are likely to be more cost-conscious in a publicly insured population compared to privately insured, as has previously been shown; therefore, the trends seen here may be amplified in a broader population.25 However, we are unable to test this hypothesis with the current data set. In addition, the Medicare prescription record only reports physicians with 10 or more prescriptions to Medicare beneficiaries each calendar year, which may have excluded some of the compensated physicians identified. Last, many patients use OTC INCS, which are only included in the Medicare PUF when part of an approved step therapy protocols. We were, therefore, unable to control for some of these prescriptions, which may represent the most cost-effective method in many cases.

Future work should establish effective ways of reducing the prescriptions of equivalent, more costly drugs. The potential advantages of Dymista over pure INCS formulations and the patients in whom this therapy is indicated should continue to be delineated. The associations of industry support with physician behavior should be examined for other drugs and devices to delineate the extent of industry influence. Industry payments to physicians are heterogeneous, and further work should establish how different interactions, such as meals vs consultantship, influence prescribing patterns. Consultants typically receive higher-value payments but dedicate significant time and are privy to scientific data surrounding the product. These factors may affect the association of payments with physician behavior, either positively or negatively. Industry plays a vital role in the health care system, and industry events, meals, and other financial incentives often allow physicians to become familiar with new products that their patients may benefit from. Physician and pharmaceutical leaders should work together to find a way that these beneficial results of industry-physician interaction can be maintained while preventing excessive physician spending or negative changes in patient care.

Overall, we found here that industry support for 2 commonly prescribed INCS, Nasonex and Dymista, are associated with prescribing patterns for these drugs. We found that the number and dollar amount of payments were linked to the percentage of brand-name prescriptions for these drugs. Industry support may play a significant role in physician behavior.

**Author Contributions**

Elliot Morse, conception and design, analysis and interpretation, including all statistical analysis, original draft of the manuscript, critical revision of the manuscript for intellectual content, final approval of the version to be published, agreement to be accountable for all aspects of the work; Rance J. T. Fujiwara, conception and design, critical revision of the manuscript for intellectual content, final approval of the version to be published, agreement to be accountable for all aspects of the work; Saral Mehra, conception and design, analysis and interpretation, critical revision for intellectual content, supervision, final approval of the version to be published, agreement to be accountable for all aspects of the work.

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