How Direct-To-Consumer Television Advertising For Osteoarthritis Drugs Affects Physicians’ Prescribing Behavior

DTC advertising of COX-2 inhibitors appears to have increased the number of prescriptions written for these products.

by W. David Bradford, Andrew N. Kleit, Paul J. Nietert, Terrence Steyer, Thomas McIlwain, and Steven Ornstein

ABSTRACT: Concern about the potential pernicious effect of direct-to-consumer (DTC) drug advertising on physicians’ prescribing patterns was heightened with the 2004 withdrawal of Vioxx, a heavily advertised treatment for osteoarthritis. We examine how DTC advertising has affected physicians’ prescribing behavior for osteoarthritis patients. We analyzed monthly clinical information on fifty-seven primary care practices during 2000–2002, matched to monthly brand-specific advertising data for local and network television. DTC advertising of Vioxx and Celebrex increased the number of osteoarthritis patients seen by physicians each month. DTC advertising of Vioxx increased the likelihood that patients received both Vioxx and Celebrex, but Celebrex ads only affected Vioxx use. [Health Affairs 25, no. 5 (2006): 1371–1377; 10.1377/hlthaff.25.5.1371]

The U.S. Food and Drug Administration (FDA) issued new regulations in August 1997 governing television advertising of prescription drugs. Shortly thereafter, spending on direct-to-consumer (DTC) advertising for prescription drugs soared—from $596 million in 1995 to approximately $1.2 billion in 1997 and an estimated $3.8 billion by 2004. The effects of this spending have been the subject of much debate, although little is known about its actual impacts. We studied this issue by examining the use of a popular (and controversial) class of prescription drugs: the anti-inflammatory and pain-relieving cyclooxygenase-2 (COX-2) inhibitors. The most popular of these were Vioxx (Merck) and Celebrex (Pfizer). We studied how prescriptions for these two drugs for patients with osteoarthritis responded to changes in television advertising during 2000–2002.

The Vioxx effect. One of the most

David Bradford (bradfowd@musc.edu) is a professor at the Center for Health Economic and Policy Studies, Department of Health Administration and Policy, at the Medical University of South Carolina (MUSC) in Charleston. Andrew Kleit is a professor in the Department of Meteorology, Center for Health Care and Policy Research, at the Pennsylvania State University in University Park. At MUSC, Paul Nietert is an assistant professor in the Department of Biostatistics, Bioinformatics, and Epidemiology; Terrence Steyer is an assistant professor in the Department of Family Medicine; Thomas McIlwain is an assistant professor in the Department of Health Administration and Policy; and Steven Ornstein is an associate professor in the Department of Family Medicine.
heavily advertised products in recent years was Vioxx (rofecoxib). In calendar year 2000, Merck spent more than $160 million on advertising this product to consumers.\(^2\) Merck withdrew Vioxx from the market in September 2004 because of evidence of increased risk of myocardial infarction and stroke associated with its use.\(^3\) Its side effects have sparked much criticism of Merck's advertising strategy.\(^4\)

### Previous studies
Published studies on the impact of television advertising for prescription drugs have yielded conflicting results. Advancing an argument made by Alison Masson and Paul Rubin, Alison Keith found that patients' suggestions regarding drugs (aspirin for cardiovascular disease) were important determinants in prescription decisions and that advertising tended to lead to more appropriate care.\(^5\)

Other studies found that drug companies' TV promotional activities preserved market share for existing products and also caused patients to be less responsive to price.\(^6\) The post-1997 era presented an opportunity for examination of the new policy regime for DTC advertising. As Woodie Zachry and Diane Ginsburg pointed out, however, few studies examine the actual effects of DTC advertising.\(^7\) In one of these studies, John Calfee and colleagues examined whether the 1997 FDA policy change increased the demand for statins but were unable to find any significant direct effect.\(^8\) There are also studies that examined DTC advertising, using survey data. These studies tended to find that patients were positively disposed toward DTC advertising and that advertising had some effect on patient-physician interactions.\(^9\)

### Study Data And Methods
To assess the impact of DTC advertising, we examined separate models for (1) the average patient flow into each physician practice, (2) prescribing for Vioxx, and (3) prescribing for Celebrex, using the practice as the unit of analysis. We examined data on visits to fifty-seven primary care practices each month over three years (2000–2002). After exclusions (discussed below), this resulted in 1,589 observations in the form of visits per practice per month.

#### Patient data
Data were obtained from the Practice Partner Research Network (PPRNet), located at the Medical University of South Carolina (MUSC). PPRNet is a practice-based learning and research organization among primary care practices across the United States that use a common electronic medical record (EMR) (Practice Partner by Physician Micro Systems Inc. in Seattle). PPRNet pools longitudinal data on diagnoses, laboratory studies, medications, vital signs, and other nonidentifiable information quarterly for research and quality improvement activities. PPRNet has access to all EMR extracts of ninety-one community-based primary care practices in thirty-two states. To create our practice-level data set, we extracted data on all patients who had a diagnosis for osteoarthritis from practices active during 2000–2002. Because many unobservable factors might drive prescribing, we restricted the original data to osteoarthritis patients.

These patient data were then aggregated to the practice level by month. Also, we eliminated practices located more than 100 miles from the geographic center of the nearest media market. We also eliminated practices that were in the database for fewer than twenty months or that wrote fewer than ten COX-2 inhibitor prescriptions cumulatively over the three-year study period. Fifty-seven practices from forty-four markets remained after these restrictions were implemented.

#### Advertising data
We obtained national and local advertising information from Competitive Media Reporting Inc. (CMR), which collects data on media advertising for all products, including pharmaceuticals, at the market (for example, city) level. The data are specific to the product's brand name and show which products were advertised and how many times they were advertised on both national and local television each month. We used counts of ads broadcast by month as our measure of DTC advertising. Patients and practices were assigned to the nearest local media market. (In the advertising data we received, media markets were identified by metropolitan area,
such as Philadelphia or Denver.)

Dependent variables. We examined the impact of DTC ads on three dependent variables: (1) the number of visits (for any reason) to the practice each month by osteoarthritis patients; (2) the fraction of these visits associated with a prescription (new or renewed) for Celebrex; and (3) the fraction of these visits associated with a prescription (new or renewed) for Vioxx (Exhibit 1). We could not distinguish reliably between the number of new and renewed prescriptions, although this is not a limitation with respect to our study’s goal.

Explanatory variables. Advertising exposure. We measured advertising exposure as the number of ads broadcast for each brand advertised. We included separate measures for national and local advertising, because national and local ads tend to be shown during different times of the day and during different programs.

Retained information from ads. Since information presented in ads will not be immediately forgotten, we needed to account for retained information. To do this, we constructed two versions of each of our three models. First, we estimated models for the three dependent variables that included the number of ads placed in the current month. Second, we estimated models for the three dependent variables that included the number of ads placed in both the current month and the previous month.10

Clinical and income variables. We also included variables we expected to affect either the demand for treatment by patients or the supply of office visits (and therefore treatment) by practices. Factors expected to affect patients’ demand for treatment were patients’ clinical comorbidities, average age, and sex. These clinical variables were calculated using the PPRNet data on osteoarthritis patients in the practice. The income variable was taken from the Area Resource File (ARF) and was measured at the county rather than the patient or practice level (and is thus a crude measure of average patient income for the practice).

Factors affecting general demand for health care. Factors expected to affect the general demand for health care were county population; county per capita income; the average price of a physician office visit; and the percentage of county population that is over age sixty-five, employed, and either Caucasian or African American. We imputed the price of an intermediate-length office visit with an established patient from the Council for Community and Economic Research’s (ACCRA’s) quarterly Cost of Living Index (using the average price

EXHIBIT 1  
Means And Standard Deviations Of Dependent And Key Explanatory Variables, Study Of Direct-To-Consumer Television Ads And Prescribing For Osteoarthritis (OA), 2000–2002

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of monthly office visits by OA patients</td>
<td>341.952</td>
<td>420.814</td>
</tr>
<tr>
<td>Number of monthly Celebrex prescriptions per OA office visit</td>
<td>0.014</td>
<td>0.035</td>
</tr>
<tr>
<td>Number of monthly Vioxx prescriptions per OA office visit</td>
<td>0.012</td>
<td>0.028</td>
</tr>
<tr>
<td>Number of local Vioxx ads</td>
<td>0.259</td>
<td>0.761</td>
</tr>
<tr>
<td>Number of national Vioxx ads</td>
<td>105.848</td>
<td>37.742</td>
</tr>
<tr>
<td>Number of local Celebrex ads</td>
<td>12.296</td>
<td>22.980</td>
</tr>
<tr>
<td>Number of national Celebrex ads</td>
<td>102.262</td>
<td>54.018</td>
</tr>
<tr>
<td>Number of local Vioxx ads, previous month</td>
<td>0.243</td>
<td>0.727</td>
</tr>
<tr>
<td>Number of national Vioxx ads, previous month</td>
<td>104.274</td>
<td>38.237</td>
</tr>
<tr>
<td>Number of local Celebrex ads, previous month</td>
<td>11.755</td>
<td>23.057</td>
</tr>
<tr>
<td>Number of national Celebrex ads, previous month</td>
<td>97.820</td>
<td>55.620</td>
</tr>
</tbody>
</table>

SOURCE: Authors’ calculations, using data from PPRNet and the Centers for Medicare and Medicaid Services.  
NOTE: N = 1,589.
in the metropolitan area nearest the primary care practice site). Finally, we captured the market-level supply of services by including the number of full-time physicians (both primary and specialty care) actively engaged in patient care in the county per thousand population, taken from the ARF.

**Clinical publications.** Besides DTC advertising and demand/supply-side economic factors, articles in medical journals might affect physicians’ prescribing habits. We controlled for confounding effects of clinical publications in two ways. First, we conducted a Medline search using the keywords rofecoxib, celecoxib, Vioxx, Celebrex, and osteoarthritis (restricting the range to English-language journals and the years 2000–2002). We included measures of the number of articles each month that focused on Celebrex or Vioxx, or both. We did not attempt to characterize whether the articles were favorable or unfavorable. We also included a variable that equals 0 when the month of publication is before an important August 2001 publication by Debabrata Mukherjee and colleagues, and 1 otherwise. This article was the first in a major clinical journal to document concerns about Vioxx’s cardiovascular side effects.

**Statistical analysis.** Two of the three models had dependent variables that were numbers of prescriptions written to osteoarthritis patients divided by the number of visits by such patients. By measuring these dependent variables as percentages of the potentially “treated” population, we normalized the results for differences in practice size. We also included practice-level fixed effects in each of the three models (which controlled for any time-invariant practice characteristics). We estimated these models as linear regressions and adjusted the standard errors for clustering at the practice level (to control for the fact that we had repeated monthly observations on each practice) using the Stata “xtreg” procedure. We adjusted for clustering at the practice level rather than at the media-market level because we generally have only one practice per media market.

**Study Results**

Although Merck (Vioxx) invested in nearly twice as many ads as Pfizer (Celebrex) for the first nine months of 2000, advertising exposure for the two brands was roughly comparable over the remaining 2000–2002 time period (Exhibit 2). However, a different picture emerged at the local level throughout this period: Celebrex local ads aired slightly more than twelve times a month on average, while Vioxx local ads aired fewer than once a month on average (data not shown). There was also evidence in the raw data of a more concentrated

**EXHIBIT 2**

Monthly Counts Of Direct-To-Consumer Television Advertising Of Drugs For Osteoarthritis, Nationally And In Local Markets, By Brand Name, 2000–2002

<table>
<thead>
<tr>
<th>Number of monthly ads</th>
<th>Total Vioxx ads</th>
<th>Total Celebrex ads</th>
</tr>
</thead>
<tbody>
<tr>
<td>200</td>
<td></td>
<td></td>
</tr>
<tr>
<td>150</td>
<td></td>
<td></td>
</tr>
<tr>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td></td>
<td></td>
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<tr>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MONTHS SINCE JANUARY 2000

MONTHS

SOURCE: Authors’ analysis of data from Competitive Media Reporting Inc.
strategy for Vioxx—with ads appearing often in some local markets and never in others.12

- **Ads’ impact on physician visits.** Here we discuss results from the fixed-effects regressions on the number of monthly visits to a practice by osteoarthritis patients. Because we estimated linear models, the parameters have a straightforward interpretation, implying how much of a change in the dependent variable would be induced by one additional television ad per month (in either a local or national context). We found consistent evidence in favor of the hypothesis that DTC advertising attracted patients to practices. Current-month local Vioxx advertising had a positive and significant ($p = .01$ or better) effect in both specifications. National Vioxx advertising also had a positive and significant effect in the first specification. In terms of magnitudes, a 100 percent increase in local Vioxx ads would, on average, have increased the number of osteoarthritis visits per month by approximately 0.8 percent, while a 100 percent increase in national Vioxx ads would have led to a 7.4 percent increase in physician visits per month. In the second specification, a similar national Vioxx effect was measured for the lagged monthly advertising, although not for the current-month DTC advertising.

Celebrex TV advertising was effective only at inducing changes in patient flows at the national level (and only in our second specification), although the effect was somewhat complex. We found that current-month national DTC ads increased osteoarthritis patient flow, while lagged-month national DTC ads reduced patient flow. However, the net effect was positive, such that a 100 percent increase in DTC advertising for both time periods would have led to a 2 percent increase in monthly visits from osteoarthritis patients. Thus, on net, we did find support for the hypothesis that DTC advertising for COX-2 inhibitors increased patient flow into physician practices.13

- **Ads’ impact on prescribing.** In general, we found little effect from DTC ads on the rate of prescribing for Celebrex. Local DTC advertising for Vioxx had a marginally significant ($p = .06$) and a positive effect on the number of Celebrex prescriptions per patient visit. However, none of the other measures of the DTC levels was significantly associated with changes in Celebrex prescribing. Thus, although there could be a cross-brand effect for Celebrex, it appeared only weakly in our data.14

Our results were somewhat stronger for Vioxx prescribing. Current-month local Vioxx DTC ads had a positive and significant effect ($p = .04$ or better) in both specifications. The magnitude of the effect was more modest, however; our results suggest that a tenfold increase in local Vioxx DTC spots (0.25–2.5, on average) would have induced about a 0.5 percent increase in the rate of Vioxx prescribing each month. Interestingly, national Celebrex ads had a positive and significant ($p = .01$ or better) effect on the rate of Vioxx prescribing. The effect was larger than the impact of local Vioxx DTC advertising; a 50 percent increase in monthly national Celebrex advertising (102–153, on average) would have led to an increase of about 0.5 percent in Vioxx prescribing.

- **Impact of other factors.** There was no evidence that journal articles on Celebrex and Vioxx affected prescribing.15 In particular, while there has been much discussion of Mukherjee and colleagues’ paper, we could not find a consistent effect of the publication in our linear model of prescribing.16

**Discussion**

The issue of what impact, if any, DTC advertising has on the behavior of patients and physician practices is of major policy importance. Pharmaceutical spending represents a large percentage of total spending in state Medicaid programs. Even moderate changes in prescribing for a small number of products can lead to dramatic changes in Medicaid spending. The FDA has recently held public hearings to gather input for a reevaluation of its policy toward DTC advertising.

This paper sheds light on the impact of advertising of the two major COX-2 inhibitors available from 2000 to 2002: Vioxx and Celebrex. Following Merck’s withdrawal of Vioxx, the New England Journal of Medicine published an editorial that expressed skepticism about the
benefits to society from DTC advertising of COX-2 inhibitors.17

- **Patient flow.** The results presented here bear directly on these issues. In general, we found that DTC advertising for Vioxx and Celebrex had positive effects on the flow of osteoarthritis patients into physician practices. Advertising of both drugs generated an effect similar to that hypothesized by Keith and by Masson and Rubin, where increases in the potential ad exposure were associated with increases in patient flow.18 This effect, however, was somewhat attenuated for Celebrex advertising.

Once patients arrived at the physician’s office, it was clear that DTC advertising tended to change the rate at which COX-2 inhibitors were prescribed. The effect of Vioxx DTC ads was consistently positive, increasing the proportion of visits at which a prescription was written for Vioxx. Vioxx DTC ads might also have had a positive effect on Celebrex prescribing rates, although the effect was only marginally significant for current-month local DTCA ds. More national Celebrex DTC advertising was associated with higher rates of Vioxx prescribing but was not associated with significant changes in prescribing for Celebrex.

- **“Detailing” versus advertising.** There are a number of possible explanations for the lack of an own-effect from Celebrex DTC advertising. For example, data from IMS Health indicate that Pfizer devoted relatively more effort in 2000 to direct-to-physician marketing for Celebrex in the form of visits by pharmaceutical representatives, who provided samples (known in the industry as detailing) than Merck did on behalf of Vioxx. It is possible that this relative emphasis on detailing is reflected in the relative ineffectiveness of DTC advertising at generating prescriptions. It is also possible that since Merck advertised relatively more heavily on behalf of Vioxx early in the life cycle of the drugs, the class-level effects were exhausted early on, leaving little room for Celebrex advertising to increase the number of prescriptions. In the end, we did not have sufficient data to untangle why Vioxx advertising had a broader class effect and an own-effect, while Celebrex DTC advertising seems to only have exhibited class effects for prescribing.

- **Study limitations.** Despite the importance of our study, it has limitations. First, without monthly data for pharmaceutical detailing, we were unable to account directly for the impact and interaction of detailing. Such physician-based marketing remains a larger component of pharmaceutical marketing efforts than DTC advertising.19 It is possible that DTC advertising and detailing were coordinated; if so, the DTC advertising effects measured here might have included some detailing effect. Personal communication with drug company representatives, however, suggested that since both Vioxx and Celebrex were important products to their manufacturers, the reps discussed these products at every opportunity. This implies that there would be little correlation between the levels of detailing and local or national variation in advertising, which in turn would minimize the potential for bias in the results. Second, practices also generally have a supply of drug samples on hand to give to patients when they write a prescription. The availability of samples might influence which product is prescribed. Again, personal communication with physicians and drug reps suggested that most physicians would typically have had a stock of samples of both drugs on hand, which implies that the potential for omitted variables bias is limited. Also, the practice-level fixed effects included in the models capture any general tendency to favor one drug over another.

In summary, DTC advertising for COX-2 inhibitors appears to have affected physician practices and patients. Pfizer’s and Merck’s DTC advertising had positive net effects in moving people toward more contact with their physicians. Once patients had contact with physicians, Merck’s DTC advertising for Vioxx tended to stimulate Vioxx prescriptions and might have had a marginally important effect on Celebrex prescribing; however, Pfizer’s DTC advertising for Celebrex seems to only have affected (in a positive way) prescribing for Vioxx.
This paper was funded by grants from the Agency for Healthcare Research and Quality (R01 HS01326-01) and from the National Heart, Lung, and Blood Institute (R01 HL077941-01). The authors thank Ruth Jenkins for assistance in extracting clinical data from the PPRNet system, and Olena Verbenko and Michael Kunz for assistance in constructing the analysis data sets.

NOTES


10. We explored alternative measures of DTC advertising. In one, we included current-month and six-month cumulative lagged ad measures. The six-month lagged measures were not significant, and the current-month effects were unchanged. In a second, we included current-month and one- and two-month lagged measures. The parameters on the current-month DTC ads were largely unchanged, but the significance level on all measures was lower as a result of collinearity between the three monthly measures included in the same model.


12. The regression results are available as online exhibits. See Online Supplemental Exhibit 1 at http://content.healthaffairs.org/cgi/content/full/25/4/1371/DC1.

13. See Online Supplemental Exhibit 2, ibid.

14. See Online Supplemental Exhibit 3, ibid.

15. See Notes 13 and 14.

16. Mukherjee et al., “Risk of Cardiovascular Events.” This article had a significant effect in models where we estimated the DTC effect nonlinearly, but it had an insignificant effect in the linear models we present here. Since this was not a major focus of the paper, we presented the more straightforward linear models here.

17. Topol, “Failing the Public Health.”
