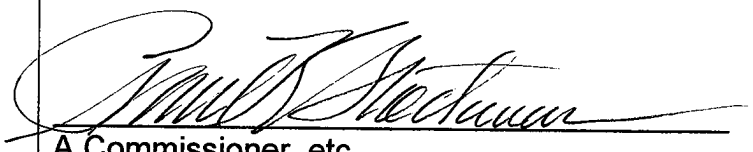
This is **Exhibit D** referred to in the Affidavit of **Julie Donohue** affirmed before me this 22nd day of May, 2007.



A Commissioner, etc.

Effects of Pharmaceutical Promotion on Adherence to the Treatment Guidelines for Depression

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Objectives: We sought to examine the impact of direct-to-consumer advertising (DTCA) and pharmaceutical promotion to physicians on the likelihood that (1) an individual diagnosed with depression received antidepressant medication and that (2) antidepressant medication was used for the appropriate duration.

Research Design and Subjects: A quasiexperimental design was used to examine treatment patterns of 30,621 depressed individuals whose insurance claims were included in the MarketScan database from 1997 through 2000. The main explanatory variables were spending on DTCA, detailing to physicians, and free samples for 6 antidepressant medications.

Results: Individuals diagnosed with depression during periods when class-level antidepressant DTCA spending was highest (cumulative spending more than $18.5 million) had 32% higher relative odds of initiating medication therapy compared with those diagnosed during periods when DTCA spending was lowest ($P < 0.0001$). Free samples of medications dispensed to physicians had no effect on odds of initiating antidepressant use. Class-level DTCA spending on antidepressants had a small positive effect on the duration of antidepressant use, whereas DTCA spending for the specific medication taken by an individual had no effect on treatment duration. Detailing spending at the class or product level had no significant effect on duration of treatment with an antidepressant medication.

Conclusions: Our results suggest that DTCA of antidepressants was associated with an increase in the number of people diagnosed with depression who initiated medication therapy. DTCA was associated with a small increase in the number of individuals treated with antidepressants who received the appropriate duration of therapy. Promotion to physicians was not associated with either the initiation of treatment with an antidepressant or with the duration of therapy.

Key Words: direct-to-consumer advertising, detailing, pharmaceutical promotion, depression, antidepressants

(*Med Care* 2004;42: 1176–1185)

Depression is a highly prevalent condition that results in substantial functional impairment.[1,2] A wide range of effective pharmacologic and psychosocial treatments is available for individuals with depression.[3–6] Yet, according to recent epidemiologic studies, roughly half of individuals with depression receive no treatment.[7] Moreover, those who receive care for depression frequently fail to receive the proper duration of treatment despite its importance for lowering the risk of relapse.[7–12] National treatment guidelines have been developed to improve the quality of care provided to people with depression. In addition, there are numerous initiatives to improve access to depression treatment through public education and screening programs and local efforts to improve the quality of depression treatment in primary care settings.[13–17]

The pharmaceutical industry has a substantial economic interest in the way medications are used for treatment of depression. Newer antidepressant medications have been heavily promoted to physicians through detailing (visits from pharmaceutical sales representatives to physicians), the provision of free samples, educational meetings and events, and advertising in professional journals. Studies of drug marketing suggest that promotion to physicians is effective in influencing drug choice.[18–20]

In recent years, pharmaceutical manufacturers have also marketed antidepressant medications directly to consumers through the mass media. Direct-to-consumer advertising (DTCA) has been criticized for leading to inappropriate use of medications and for unnecessarily driving up drug spending.[21,22] Proponents of DTCA argue that it increases awareness and expands the treatment of underdiagnosed conditions, such as hypercholesterolemia and depression.[23,24] A recent

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study of DTCA found that advertising by individual products increased total sales in the associated therapeutic classes.[25] A study of cholesterol-lowering medications found that DTCA had a small-but-positive impact on adherence to medication therapy.[18] Consumer surveys have shown that DTCA motivates people to discuss previously untreated conditions with their physician.[27–30] Moreover, surveys suggest that a substantial number of people receive prescriptions as a result of seeing an ad for a medication but that the effects of DTCA on patient adherence to medication therapy are unclear.[27–30] Unfortunately, data from surveys are of limited value in gauging the effects of advertising on rates of treatment initiation and continuation because there is no apt "control group" of patients who have not been exposed to DTCA.

We are aware of no previous studies that assessed the impact of DTCA or physician promotion on the quality of care for depression. In this study, we examined the impact of consumer- and physician-directed marketing of antidepressants on (1) the likelihood that someone diagnosed with a new episode of depression received antidepressant medication and (2) whether they received antidepressant medication for the appropriate duration.

METHODS

Overview

The level of spending on promoting antidepressant medications to consumers and physicians has varied by product over time and for the antidepressant class as a whole. This study assessed the association between variation in aggregate monthly spending on pharmaceutical promotion for antidepressants and patterns in the treatment of depression between January 1997 and December 2000.

Data

The dataset used in the analysis consisted of health insurance claims for use of medical services and prescription drugs and marketing data on pharmaceutical promotion. We focused on 6 antidepressants approved by the Food and Drug Administration for the treatment of depression. These medications, which target serotonin, belong to 3 categories of antidepressants called selective serotonin reuptake inhibitors (fluoxetine, sertraline, paroxetine, and citalopram), serotonin norepinephrine reuptake inhibitors (venlafaxine), and serotonin antagonist and reuptake inhibitors (nefazodone). None of the drugs' patents had expired before the end of the study period. Older-generation antidepressants, such as tricyclic antidepressants, were not included because none were marketed directly to consumers.

The medical claims data were obtained from the MarketScan database (The Medstat Group, Ann Arbor, MI). MarketScan contains medical and pharmacy claims for beneficiaries of a group of large self-insured companies. The data set for 1997 through 2000 contain enrollment information and claims records for individuals from 30 large employers located around the United States. The data set also includes information on the benefit designs of the indemnity and managed care plans used by these employers.

We used drug-specific and class-level monthly data on 3 forms of pharmaceutical promotion: DTCA (including print, radio, and television advertising), detailing to physicians, and free samples of drugs left with physicians. We obtained monthly data on DTCA spending from Competitive Media Reporting, which tracks local and national advertising campaigns. Data on monthly spending on detailing to physicians were obtained from Scott-Levin, Inc., an independent medical information company that conducts market research on the pharmaceutical industry. Scott-Levin imputes spending on detailing from a panel of more than 11,000 office-based and hospital-based physicians who track their encounters with pharmaceutical representatives. The panel is geographically representative, includes members of 31 clinical specialties, and accounts for roughly 2% of the US physician population. Monthly data on the units of free samples dispensed to office-based physicians were obtained from IMS Health, another medical information company. IMS Health uses a panel of more than 1200 medical practice staff members who monitor the quantity of the prescription drugs provided by sales representatives in the form of samples.

Study Sample

The unit of analysis for this study was an episode of treatment of depression. We constructed episodes based on the outpatient and prescription drug claims for patients between the ages of 18 and 64. Those patients younger than 18 years of age were eliminated because the depression guidelines used for this study were not applicable to that age group. Patients aged 65 and older were eliminated because outpatient claims data were likely incomplete for Medicare-eligible enrollees.

The index event for an episode of depression was an outpatient visit for one of the following Diagnostic and Statistical Manual Version IV (DSM-IV) diagnoses: major depression current episode (ICD-9 code 296.2x); major depression recurrent episode (ICD-9 code 296.3x); depression not elsewhere classified (ICD-9 code 311x); or dysthymia, anxiety depression, or prolonged depressive reaction (ICD-9 code 300.4x).

Requiring episodes to originate with an outpatient visit for depression minimizes the chance of including subjects who are using one of the study medications for a condition other than depression.[31,32] An episode was considered terminated when an individual did not have an outpatient visit for depression or a prescription drug claim for one of the study medications for 2 months.

Subjects had to meet a number of additional inclusion criteria. We required patients to be enrolled in a MarketScan health plan for at least 6 months before the start of an episode and at least 6 months after the episode start date to prevent censoring of observations. To ensure correct identification of an episode's start date, a 6-month pretreatment period was imposed during which there could be no indication of diagnosis or treatment of depression. Hence, all episodes began between July 1, 1997, and June 30, 2000. In addition, we required episodes to include a second confirmatory diagnosis of depression for inclusion in the study. We excluded individuals with diagnoses of bipolar disorder or schizophrenia because their treatment is likely to be significantly affected by these comorbidities. We also excluded individuals enrolled in health plans that did not offer prescription drug coverage.

Outcome Measures

We examined 2 outcomes: (1) whether an episode of depression involved the initiation of antidepressant use with one of the study medications within 60 days of the episode start date and (2) if treated with one of the study antidepressants, whether the depressed patient received an appropriate duration of medication treatment consistent with national depression treatment guidelines.

The guidelines for the treatment of major depression state that if medication treatment is chosen, it should be provided until symptoms are alleviated (usually in 10–12 weeks) and then continued for an additional period of 4 to 9 months to prevent relapse.[4–5] To be conservative, our measure of the appropriate duration of therapy was whether the patient filled prescriptions for at least 4 months of treatment with the study drugs within the first 6 months of an episode.

Analysis

We used logistic regression analyses to estimate the impact of promotion on the initiation and duration of medication treatment of depression. In the analysis of whether medication treatment was initiated, the main explanatory variables used were spending on DTCA and units of free samples dispensed to physicians. Total therapeutic class-level spending for both types of promotion was used because initiation of medication therapy could have resulted from promotional spending of any drug in the class. Detailing spending and units of free samples were highly correlated (Spearman correlation coefficient = 0.70). Including both variables in the analysis would have created multicollinearity problems thereby making it infeasible to separate the individual effects of the 2 factors.

Previous studies of drug marketing have found that although the effects of advertising last beyond the period during which marketing expenditures are incurred, these effects diminish over the course of time.[33] Thus, we constructed cumulative measures of spending on advertising to consumers and physician promotion and treated both forms of promotion as depreciating assets. We used promotional spending from the month in which the episode started plus the discounted sum of spending from the previous 6 months. We applied monthly depreciation rates of 0.3% for detailing and 11% for DTCA based on estimates from previous analyses of pharmaceutical promotion.[33] We divided promotional spending into quartiles and calculated odds ratios (ORs) using the lowest quartile as the reference group. Analyses using continuous measures of promotional spending yielded qualitatively similar results but required a restrictive linear form for the promotional effect.

The covariates included were patient age, sex, geographic region, employment status (employed vs. an employee's spouse or dependent, or a retiree), whether the diagnosis coded was major depression (as opposed to dysthymia or other depression), whether the episode was the first in our data collection period, provider specialty (psychiatrist; other physician [primarily primary care providers]; or a therapist, psychologist, or mental health clinic), whether the individual's health plan used capitated payments to reimburse providers, the mean copayment for antidepressant medications in the patient's insurance plan, and the patient's coinsurance rate for outpatient psychiatric services. Given that our analytical strategy relied on temporal variation in promotional spending and treatment patterns, we included linear and quadratic monthly time trends in the analyses to adjust for secular trends in the treatment of depression. We also used an indicator variable for episodes that began in January because a disproportionate share of episodes (14% of total) started in that month.

In the duration of treatment analysis, the main explanatory variables were spending on DTCA and spending on detailing to physicians. Because patients had initiated treatment with a particular brand of antidepressant, we assessed the extent to which their likelihood of receiving the appropriate duration of treatment was associated with promotional spending for the brand they were prescribed as well as that for other drugs in the class. Thus, we included 4 promotional variables in the analysis of treatment duration: spending on detailing for the drug taken (own product detailing), spending on detailing for the other drugs in the class (others' detailing), spending on DTCA for the drug taken (own product DTCA), and spending on DTCA for the other drugs in the class (others' DTCA). We used cumulative promotional expenditures (spending in the month in which the episode started, plus the discounted sum of the previous 6 months' spending).

The same covariates from the analysis of whether drug treatment was initiated were used in the model of treatment duration with 4 exceptions. Because all of the individuals who were included in the treatment duration analysis filled prescriptions for antidepressants, we used actual prescription drug copayment rather than mean copayment by health plan.

We included 3 additional variables: the brand of antidepressant the patient was initially prescribed, whether a medication switch occurred during the first 6 months of the episode, and whether the individual had at least 2 sessions of concomitant psychotherapy.

Because we used data from a large insured population over time, there were potential clustering effects from repeatedly observing the same individuals. To address this problem for both analyses, we used the General Estimating Equations estimator of Liang and Zeger to obtain consistent estimates of standard errors given the non-Gaussian nature of our outcome variables.[34] All analyses were performed using SAS statistical software, version 8.2 (SAS Institute, Cary, NC).

RESULTS

The MarketScan database contained the medical claims for 5,718,683 individuals between 1997 and 2000. We identified our study population from the 62% of individuals in firms that provided the Medstat Group with complete data on medical and pharmacy claims, and insurance benefit design. A total of 30,621 individuals with 36,062 episodes of depression met our study criteria and were included in the analysis of medication treatment initiation. We estimated the impact of drug promotion on the duration of treatment using the subsample of episodes in which medication treatment was initiated (10,490 individuals with 11,306 episodes). Table 1 provides the characteristics of the total sample used in the analysis of treatment initiation and the subsample used in the analysis of treatment duration.

We found that 31% (n = 11,306) of the depressive episodes resulted in a prescription drug claim for an antidepressant within 60 days of the episode start date. Of those receiving medication for depression, 60% (n = 6753) filled at least 4 prescriptions for an antidepressant in the first 6 months of an episode.

Spending on DTCA and Detailing

Figures 1 and 2 show the product-level spending on DTCA and detailing for antidepressants between 1997 and 2000. There was significant variation in spending on both forms of promotion. Two of the drugs (sertraline and citalopram) had zero spending on DTCA during the entire study period. Fluoxetine and paroxetine had the highest levels of spending on DTCA. All of the study drugs had positive expenditures on physician detailing, although there was substantial variation in the levels of spending.

Initiation of Drug Treatment

After controlling for secular trends in the treatment of depression and other factors, we estimated a small positive effect of DTCA spending on the probability that a person received drug treatment given a diagnosis of depression (Table 2). Individuals diagnosed with depression during periods when class-level antidepressant DTCA spending was in the top quartile (cumulative spending of more than $18.5 million) had 32% higher relative odds of initiating medication therapy compared with those diagnosed during periods when DTCA spending was in the bottom quartile (95% confidence interval [CI]1.18–1.48; $P < 0.0001$).

Providing free samples of antidepressant medication to physicians did not appear to significantly increase rates of treatment with antidepressants. We found that individuals who initiated treatment after periods when cumulative free sample spending was in the top quartile (more than 103.9 million units) were no more likely to initiate medication therapy than individuals who were diagnosed during periods of low free sample spending (OR 1.07; 95% CI 0.90–1.27; $P = 0.45$).

Individuals in our sample appeared to be sensitive to the out-of-pocket cost of drugs and other forms of treatment of depression. Individuals facing a copay of more than $15.00 for an antidepressant were much less likely to initiate medication therapy than those facing a copay of $5.00 or less (OR 0.70; 95% CI 0.60–0.81; $P < 0.0001$). Individuals enrolled in health plans that paid a higher share of outpatient psychiatric services were less likely to initiate treatment with an antidepressant.

Individuals who were treated primarily by physicians, enrolled in capitated health plans, and treated for major depression were more likely to initiate treatment with an antidepressant during an episode of depression. Women, residents of southern states, and employees (as opposed to retirees or dependents) were also more likely to initiate medication therapy. Older individuals (results not shown) and those seeking care for a second or third episode of depression during our data collection period were less likely to initiate medication therapy for depression.

Appropriate Duration of Treatment

The likelihood that an individual taking antidepressant medication received at least 4 months of treatment was not significantly different across DTCA spending levels for the specific brand of medication taken by the individual (Table 3). When the promotional spending of other antidepressants was taken into account, DTCA had a small positive effect on the duration of treatment once it reached a certain threshold (top quartile spending of $21.8 million or more; OR 1.30; 95% CI 1.06–1.62; $P < 0.05$).

Neither the detailing spending for the drug taken nor the detailing spending for the other drugs in the class had any significant effect on the duration of treatment with an antidepressant medication.

Treatment duration did not necessarily decrease with higher cost sharing for prescription drugs. Individuals who faced copays of $15.00 or more were no more likely to receive the proper duration of care than those facing

TABLE 1. Characteristics of the Study Sample*

	Episodes of Depression Used in Analysis of Treatment Initiation	Subsample of Episodes With Antidepressant Use Used in Analysis of Treatment Duration
No. sample	36,062	11,306
Mean age of patient, years	44	44
Female, %	67.5	70.0
Employee, %	61.1	62.1
Region of the country, %		
North central	35.5	31.7
Northeast	29.9	29.8
South	28.5	32.9
West	6.1	5.6
Depression diagnosis, %†		
Major depression, single episode	18.5	20.1
Major depression, recurrent episode	21.4	23.5
Depression not elsewhere classified	32.4	40.3
Dysthymia, anxiety depression, or prolonged depressive reaction	29.9	16.6
Repeat episode	43.3	12.1
Health plan type, %		
Uses capitated reimbursement		
Health maintenance organization	12.8	16.7
Capitated or partially capitated point-of-service plan	30.3	35.8
Does not use capitated reimbursement		
Comprehensive fee-for-service	34.9	29.8
Noncapitated point-of-service plan	6.1	6.2
Preferred provider organization	15.1	11.0
Other	0.8	0.5
Specialty of the primary treatment provider, %		
Psychiatrist	19.4	22.9
Internal medicine, family practice, general medicine, or other	40.0	52.6
Therapist, psychologist, or mental health clinic	36.5	23.2
Other	4.1	1.3
Copayment for antidepressant prescription, %		
Less than $5.00	24.3	22.3
Between $5.00 and $10.00	10.3	33.2
Between $11.00 and $15.00	29.5	26.4
$15.00 or more	35.9	18.2
Coinsurance for outpatient psychiatric services (percent paid by plan after deductible), %		
50%	3.5	4.8
80%	24.7	23.0
90%	21.9	16.9
100%	49.9	55.3
Medication switch within first 6 months of episode	n/a	23.3

*Percentages may not sum to 100% because of rounding.
†Percentages may exceed 100% because of some individuals having more than 1 depression diagnosis.

copays of less than $5.00. Women, individuals who were older (results not shown), switched medications, were treated primarily by a physician, enrolled in a capitated health plan, and initiated treatment with fluoxetine were more likely to fill at least 4 prescriptions for an antidepressant. Residents of southern states were less likely to receive the proper duration of medication treatment. Individuals being treated for a repeat episode or who had

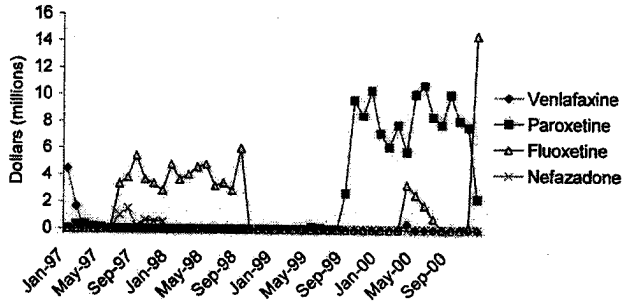

FIGURE 1. Direct-to-consumer advertising spending for antidepressants, 1997–2000. (Sertaline and citalopram had zero spending on direct-to-consumer advertising during this period.)

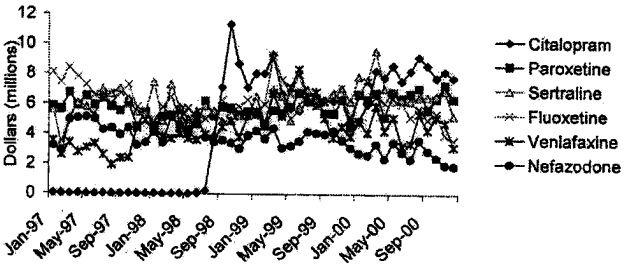

FIGURE 2. Physician detailing spending for antidepressants, 1997–2000.

concomitant use of psychotherapy were no more likely to receive the proper duration of antidepressant treatment (results not shown).

DISCUSSION

One of the chief arguments in support of DTCA of prescription drugs is that it increases the number of individuals who seek care for chronic and disabling conditions such as depression. Our results suggest that periods of high DTCA spending are followed by an increase in the number of individuals diagnosed with depression who initiate medication therapy.

DTCA for antidepressants may increase the number of individuals receiving medication treatment of depression by promoting awareness of the symptoms of depression and the therapies available. Advertising for antidepressants may aid patients in identifying symptoms of depression and activate them to discuss their symptoms with their treatment provider. For conditions like depression, which are associated with social stigma, advertising may reduce negative views associated with treatment. Advertising also may affect treatment choice for those already receiving care for depression. For example, an individual who had received psychotherapy for a previous episode of depression may, upon seeing an antidepressant advertisement, request medication treatment in combination with or in lieu of behavioral treatment. Because our analyses of DTCA were conditional on diagnosis, we were not able to differentiate between these 2 effects.

Increased provision of free samples of antidepressants by pharmaceutical companies did not result in an increase in the number of individuals with depression who initiated drug treatment. Other studies have found that although detailing has little influence on the total number of individuals receiving treatment, it has a substantial effect on medication choice. Similarly, free samples may have a larger impact on medication selection than on the decision to initiate medication treatment. Our analyses were not directed at this issue.

Patients' receipt of treatment of depression for an adequate duration of time may reflect both their willingness to continue with pharmacotherapy and physicians' clinical management. DTCA has been promoted as a useful tool for communication and improving adherence to medication therapy.[23] We found no association between brand-level spending on DTCA and the likelihood that an individual received the appropriate duration of treatment. When the promotional spending of other drugs in the class was taken into account, however, we found that consumer promotion had a small positive impact on treatment duration but only at the highest level of spending.

Nonadherence to prescribed medication therapy is a complex problem resulting from medical, social, behavioral, and economic factors. Multifaceted interventions that involve one-on-one patient follow-up and individualized education have been more successful in prolonging the course of antidepressant therapy than programs involving the distribution of informational leaflets on the use of antidepressants.[35,36]

Pharmaceutical firms have an economic interest in maintaining patients on medication for chronic conditions like depression. Recognizing the high rates of discontinuation of medication therapy among individuals with chronic illnesses, some pharmaceutical firms have tailored their DTCA campaigns toward improving adherence.[37,38] Mass media advertising campaigns may, however, be better suited for bringing patients into treatment than for increasing rates of adherence. Some manufacturers have developed programs that allow patients taking a particular medication to access information, join support groups, and sign up for electronic reminders to refill prescriptions. The effectiveness of these programs at improving adherence has not been evaluated in the medical literature.

The duration of treatment is also driven by physician-determined factors, such as the initial medication choice and the care management provided by the physician. The bulk of antidepressant promotional spending has been aimed at physician detailing (Figs. 1 and 2). The one-on-one nature of detailing may lend itself well to education on the proper duration of antidepressant use. Indeed, experiments have shown "academic detailing" to be highly effective in chang-

TABLE 2. Predictors of Receiving Antidepressant Treatment for an Episode of Depression

	Odds Ratios	95% CI
Total class direct-to-consumer advertising spending		
Less than $2.6 million (reference category)		
$2.6 to $11.2 million	1.19	(1.10–1.28)‡
$11.2 to $18.5 million	1.15	(1.05–1.26)†
More than $18.5 million	1.32	(1.18–1.48)‡
Total class units of free samples dispensed		
Less than 94.4 million units (reference category)		
94.4 to 98.9 million units	1.04	(0.93–1.17)
98.9 to 103.9 million units	1.05	(0.90–1.22)
More than 103.9 million units	1.07	(0.90–1.27)
Prescription drug copayment		
$5.00 or less (reference category)		
$5.01 to $10.00	0.77	(0.66–0.91)†
$10.01 to $15.00	0.63	(0.54–0.73)‡
$15.01 or more	0.70	(0.60–0.81)‡
Coinsurance for outpatient psychiatric services (percent paid by plan)		
50% (reference category)		
80%	0.72	(0.63–0.83)‡
90%	0.73	(0.60–0.89)†
100%	0.77	(0.66–0.89)‡
Provider specialty		
Nonphysician mental health specialist (reference category)		
Psychiatrist	2.37	(2.21–2.54)‡
Nonpsychiatrist physician	3.33	(3.15–3.52)‡
Capitated health plan	1.99	(1.86–2.13)‡
Noncapitated health plan (reference category)		
Major depression diagnosis	1.54	(1.46–1.62)‡
Other depression (reference category)		
Female	1.19	(1.13–1.26)‡
Region		
Northeast	0.73	(0.68–0.78)‡
North central	0.81	(0.75–0.88)‡
West	0.75	(0.67–0.83)‡
South (reference category)		
Employees	1.10	(1.05–1.16)‡
Repeat episodes	0.84	(0.80–0.88)‡
Time trends	included	†

‡Significant at $P < 0.001$ level; †significant at $P < 0.01$ level.

ing prescribing behavior.[39,40] We found no evidence, however, that detailing affected rates of adherence to guideline treatment of depression (Table 3). Studies of the content of detailing visits to physicians suggest that the focus of these interactions is on highlighting the comparative advantages of one drug within a class over another.[41,42]

This study has several limitations. There may be unobserved factors driving the association between DTCA and initiation of medication treatment of depression. We used aggregate data on promotional spending and did not observe an individual's level of exposure to advertising or the frequency of contact between pharmaceutical sales representatives and the physicians in our sample. However, given that the price pharmaceutical firms are charged for advertising is correlated with the number of individuals reached, aggregate spending data should provide a valid measure of exposure. The MarketScan claims represent the health care experience of employees (or their dependents) who work primarily for

TABLE 3. Predictors of the Appropriate Duration of Antidepressant Treatment of Depression

	Odds Ratios	95% CI
Own product direct-to-consumer advertising spending		
Less than $78,300 (reference category)		
$78,300 to $3.4 million	1.03	(0.88–1.20)
$3.4 to $20.2 million	0.93	(0.77–1.14)
More than $20.2 million	1.25	(0.98–1.60)
Others' direct-to-consumer advertising spending		
less than $271,000 (reference category)		
$271,000 to $7.2 million	1.02	(0.89–1.16)
$7.2 to $21.8 million	1.04	(0.88–1.24)
More than $21.8 million	1.30	
Own product detailing spending		
Less than $37.5 million (reference category)		
$37.5 to $40.9 million	0.93	(0.79–1.09)
$40.9 to $44.4 million	0.91	(0.77–1.07)
More than $44.4 million	0.88	(0.73–1.05)
Others' detailing spending		
Less than $150.3 million (reference category)		
$150.3 to $190.1 million	1.16	(0.95–1.43)
$190.1 to $202 million	0.99	(0.77–1.27)
More than $202 million	1.21	(0.91–1.62)
Prescription drug copayment		
Less than $5.01 (reference category)		
$5.01 to $10.00	0.67	(0.58–0.77)‡
$10.01 to $15.00	1.05	(0.91–1.21)
$15.01 or more	0.87	(0.75–1.01)
Medication switch during episode (reference category = no switch)	1.61	(1.46–1.78)‡
Provider specialty		
Psychiatrist	1.22	(1.09–1.38)‡
Nonpsychiatrist physician	1.31	(1.17–1.47)‡
Nonphysician mental health specialist (reference category)		
Major depression diagnosis		
Other depression diagnosis (reference category)	1.01	(0.92–1.10)
Initial drug choice		
Fluoxetine (reference category)		
Sertraline	0.77	(0.65–0.90)†
Paroxetine	0.76	(0.65–0.88)‡
Venlafaxine	0.67	(0.55–0.82)‡
Nefazodone	0.50	(0.39–0.63)‡
Citalopram	0.73	(0.61–0.87)‡
	1.19	(1.08–1.30)‡
Female	1.09	(1.00–1.19)*
Region		
South (reference category)		
Northeast	1.28	(1.16–1.42)‡
North central	1.44	(1.29–1.62)‡
West	1.32	(1.11–1.58)†
Time trends	included	

‡Significant at $P < 0.001$ level; †significant at $P < 0.01$ level; *significant at $P < 0.05$ level.

Fortune 200 companies that offer relatively generous health insurance benefits and may thus not be representative. Other populations, such as the elderly, the uninsured, or those with less generous coverage, may have a differential response to pharmaceutical advertising. We were not able to capture information on antidepressant prescriptions paid out-of-pocket or through dual coverage, although we see no reason why this should bias our findings on promotion.

Our analyses of treatment duration evaluated the effects of brand-specific DTCA spending. This gross measure lumps together the impact of DTCA for a diverse group of medications and may obscure evidence of an impact for individual drugs where the marketing strategies have emphasized quality and length of treatment. Paroxetine's DTCA campaigns focused largely on that product's therapeutic indications for treating anxiety disorders. Our analyses, which were based on individuals diagnosed with depression, may underestimate the effect of DTCA for paroxetine. We used claims data and may underidentify patients with depression by excluding those who have an outpatient visit in which a depression diagnosis is not recorded either because of stigma or for other reasons.[43–45] Claims data also lack information on the severity of illness and potentially important sociodemographic predictors such as education. Finally, the effects of drug marketing are likely to vary depending on the ease of patient self-diagnosis, the degree to which conditions are undertreated, and provider specialty. Thus, the findings from this study may not necessarily be generalizeable to other medication classes.

CONCLUSION

This is one of the first studies to examine the impact of DTCA and physician promotion on quality of care. Our results suggest that advertising antidepressants to consumers may increase the likelihood that an individual with depression initiates medication therapy. Free samples of antidepressants, on the other hand, had no effect on medication use. We found no evidence, however, that pharmaceutical promotion to consumers or physicians has an important impact on the likelihood that therapy would be continued in a way that meets existing guidelines. To the extent that DTCA increases demand for medications, it is important to understand whether the expanded use represents appropriate prescribing. This important issue deserves further investigation.

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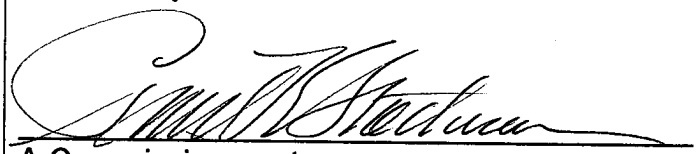
This is **Exhibit E** referred to in the Affidavit of **Julie Donohue** affirmed before me this 22nd day of May, 2007.



A Commissioner, etc.

Consumers' Reports On The Health Effects Of Direct-To-Consumer Drug Advertising

This study found no widespread adverse health affects resulting from drug ads aimed at consumers, but society still needs to weigh in on the consequences of this advertising.

by Joel S. Weissman, David Blumenthal, Alvin J. Silk, Kinga Zapert, Michael Newman, and Robert Leitman

ABSTRACT: We conducted a national telephone survey about health care experiences associated with direct-to-consumer advertising (DTCA) of prescription drugs. Among the 35 percent of our sample who had a physician visit during which DTCA was discussed, 25 percent received a new diagnosis, of which 43 percent were considered high priority according to authoritative sources. More than half also reported actions taken by their physician other than prescribing the advertised drug. Despite concerns about DTCA's negative consequences, we found no differences in health effects between patients who took advertised drugs and those who took other prescription drugs.

UNTIL JUST A FEW YEARS AGO advertising of prescription drugs was aimed almost exclusively at physicians and other health professionals. Although physician drug detailing (in-person visits by drug company representatives) has been criticized for exerting undue influence on prescribing habits, physicians' training and experience equip them, at least in theory, to process and evaluate advertisers' claims and make informed prescribing decisions for their patients.[1] The near-exclusive focus on physicians changed in the late 1990s, when the pharmaceutical industry increased its use of direct-to-consumer advertising (DTCA). Although modest at first, spending on DTCA more than doubled to approximately $2.5 billion in 2000 following the relaxation of regulations from the U.S. Food and Drug Administration (FDA) in 1997.[2]

The practice of DTCA is controversial because it operates at the nexus of health

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care and for-profit enterprise. Views on DTCA center on three effects: cost, communication, and health of the public. Critics claim that DTCA raises health care costs by stimulating consumers to demand newer, more expensive drugs, often with high profit margins.[3] Some members of Congress are so concerned about this possibility that they have suggested limiting Medicare beneficiaries' access to heavily advertised drugs.[4] The pharmaceutical industry rejects arguments that DTCA is inflationary, and while not denying the profit motive, it points out that DTCA serves a patient education function.[5] The industry's argument is that patients are highly motivated to seek the best available treatment for their condition, and they need and deserve more and better information on which to base their judgments. Some patients may be even more informed than their physicians are regarding particular treatments. DTCA critics take a skeptical view of this claim, fearing that pressure from patients erodes physicians' authority and may lead to inappropriate prescribing.[6] Others worry that patients are confused by deceptive advertising and that precious time is wasted during physician office visits to discuss minor conditions or cosmetic issues brought to patients' awareness by ads.[7] Jane Henney, former FDA commissioner, summarized the debate by asking, "Do these advertisements provide consumers with information that empowers them to care for their health, or are they misleading in a way that presents a public health hazard?"[8]

There is scant research on the health effects of DTCA. Prior surveys by the FDA and *Prevention* magazine consider mainly indirect effects of DTCA on health by examining consumers' understanding of advertisements and patient-doctor interactions.[9] Most Americans are aware of DTCA, and huge numbers are having discussions about advertised drugs with their physicians. However, past investigations have not explored the types of conditions that are discussed with physicians during these conversations, the actions that result from discussions about DTCA between doctors and patients, and the effect, if any, on health outcomes.

This paper reports results of a survey of a national sample of consumers who have discussed advertised drugs with their physicians. Our goal was to describe actual health care experiences and outcomes, rather than opinions and attitudes. The underlying assumption was that DTCA stimulates patients to discuss advertised drugs during physician visits and leads to actions taken that result in health-related outcomes. Using patients' reports, our research sought to determine the health-related value (or harm) resulting from these visits. It addressed three questions: (1) What sorts of conditions or problems are discussed during physician visits that include a discussion about an advertised drug? (2) What actions are taken by physicians—including additional tests and treatments—as a result of these visits? (3) Do outcomes of care differ by whether the patient takes the advertised drug that was discussed during the visit or some other drug?

Data And Methods

The data are from a telephone survey designed by a team of researchers from Harvard University/Massachusetts General Hospital and Harris Interactive. The team had full control over the content of the survey, access to the data, and control over interpretation of the results. Telephone interviews with a national probability sample of 3,000 adults were conducted by Harris Interactive between 9 July 2001 and 16 January 2002 using random-digit dialing and random household member selection procedures. Response rates were enhanced in a number of ways. A $10 incentive was offered for completion of the interview (including $2 up front for difficult-to-reach respondents). Where telephone numbers of nonrespondents could be matched with an address (58 percent), letters were mailed explaining the purpose of the survey and encouraging response. A toll-free number was offered so that respondents could complete the survey at a convenient time. Attempts also were made to contact nonrespondents at various times of the day and days of the week. The response rate was 53 percent. Although lower than optimal, this compares favorably with other published data from national consumer surveys.[10]

■ **Questionnaire development.** The survey was designed to gather data on health care experiences resulting from ambulatory visits with physicians. To develop the survey questions, we performed an extensive literature review and then held a focus group run by a professional facilitator in Boston in January 2001. The instrument underwent cognitive testing, was revised based upon our findings, and was pretested on twenty respondents.[11]

Our initial concept was to compare the health care experiences of patients who were aware of DTCA with those of patients who were not. However, research from the FDA as well as our own pretesting showed that exposure to DTCA in the United States is nearly universal. An alternative design was tested that would compare patients who were prompted solely by DTCA to schedule a physician visit with those who had a physician visit that was not prompted by DTCA. This also was rejected, because pretesting suggested that patients schedule appointments with physicians for a variety of reasons, based on multiple sources of information. Very rarely would consumers identify DTCA as the sole reason for scheduling a visit. As a result, we took the perspective that there exists a continuum of visit types ranging from those for which DTCA had no influence on seeing the doctor to those for which DTCA was the principal influence. We focused, therefore, on visits during which DTCA prompted patients to discuss their health, regardless of why the visit was scheduled. Other survey questions elicited the level of DTCA influence on the visit. This study focuses for the most part on the health care experiences that transpired following those visits.

■ **Variables and relevant subpopulations.** The survey was designed to ask questions tailored to subgroups of patients defined by their familiarity with DTCA and by relevant medical events. All respondents, regardless of medical history, were asked about health status, presence of chronic illnesses, and sociodemographic

"DTCA was one of many health information sources influencing patients' decision to discuss a health issue with their physician."

characteristics (sex, race/ethnicity, education, insurance status, and drug coverage).

The major subgroup consisted of respondents who had ever been prompted by a DTC ad to talk to a doctor about an advertised drug or other health issue or concern (35 percent). We refer to these as DTCA discussions or DTCA visits, to distinguish them from visits during which a DTC ad is not discussed. DTCA visits were categorized by whether the patient primarily discussed a drug, a new health concern, or a possible change in treatment for an ongoing concern. Subsequent questions focused on the content of a single DTCA visit, so if patients had more than one, we asked them to choose the one that was most important to their health. Because pretesting suggested that patients' motivation to speak with their physician is multifactorial, respondents also were asked to identify other sources of information that influenced their decision to have the discussion with their doctor and to note which were the most important.

Respondents were then asked to report the condition or problem discussed during the visit, and whether the condition had ever been confirmed ("Did a doctor or other medical professional ever tell you that you had [the marker condition]?"). This is similar to the approach used by the Agency for Healthcare Research and Quality (AHRQ) in its Medical Expenditure Panel Survey (MEPS).[12] These conditions were reviewed by a physician and coded into a "reason for visit" using the classification system employed by the National Ambulatory Medical Care Survey (NAMCS).[13] A few conditions either were too general (for example, "infections") or merely mentioned a particular drug (for example, "Viagra") and so were not forced into a NAMCS category. Furthermore, to address whether DTCA resulted in the diagnosis of or treatment for conditions of public health interest, we identified the fifteen "high priority" conditions listed by AHRQ and adopted by the Institute of Medicine (IOM) in its report *Crossing the Quality Chasm.*[14]

A series of questions addressed actions taken as a result of the DTCA visit. We asked whether the physician wrote a prescription for the advertised drug or another prescription drug, or recommended an over-the-counter (OTC) drug. We inquired whether the physician made a referral to a specialist, suggested a change in diet or exercise, ordered a laboratory test, or suggested limitations in smoking or drinking.

A second subgroup included all respondents who had a DTCA visit, were prescribed a drug, and took the drug as prescribed (21 percent). They were asked a series of health-related quality-of-life questions, including reported presence of side effects, and improvement/worsening of overall health, symptoms, and laboratory results. Finally, among respondents who reported switching medications to treat their conditions (5 percent), we asked which drug had worse side effects (com-

paring the "old" drug to the "new" drug) and which drug was easier or more difficult to remember to take (compliance). If one drug had no side effects and the other did, we assumed that the drug with side effects was worse.

■ **Analysis.** The primary purpose of the analysis was to describe the experiences of patients who reported having a DTCA visit. However, because patients are subject to multiple influences in making health care decisions, we attempted to isolate further the influence of DTCA. We did this in two ways: (1) We compared patients for whom DTCA was one of the two most important sources of information that influenced them to have the health discussion with their doctor versus all other patients (high versus low DTCA influence); and (2) among patients who were prescribed drugs and took them, we compared patients who received the DTCA drug versus all other patients.

Because they may be at higher risk for poor outcomes, we compared patients in fair or poor health with all other patients. We also compared patients with and without high-priority diagnoses. Bivariate differences were tested using the chi-square statistic. We then adjusted the responses by direct standardization, employing logistic regression models. The predicted logits were retransformed to percentages. This approach assigns each person the attribute of interest—for example, fair/poor health status—but all other characteristics are assumed to be at the sample mean. Statistical inferences were based on the results of the underlying logistic regressions. Initial runs included all of the variables in Exhibit 1, but since health status and insurance coverage for drugs were the only variables that were consistently significant ($p < .05$), the percentages are adjusted only for those variables. However, because none of the results changed by more than a percentage point or two, we present only the unadjusted results.

Analyses were performed with SPSS. To account for nonresponse, all responses were weighted so as to represent a national sample.[15] To account for possible recall bias, we repeated the analyses for just those respondents who had a DTCA discussion in the three months before the interview.

Study Results

Our sample included 76 percent white, non-Hispanics; 39 percent college graduates; and 88 percent adults with health insurance (Exhibit 1). The study procedures resulted in a sample that closely resembled national data in terms of regional representation, health status, and recent ambulatory visits. There was a slight underrepresentation of younger, minority, less educated, and uninsured adults.

■ **Effects of DTC ads.** Approximately 86 percent of all consumers saw or heard a DTC ad in the last year. About 35 percent of all respondents were prompted by an ad to have a discussion about an advertised drug or other health concern during a visit with a physician (DTCA visit). Nearly two-fifths of patients having a DTCA visit talked about a prescription drug, about one in five discussed a new concern, and about one-third talked about a possible change in treatment for an ongoing condi-

EXHIBIT 1
Description Of Study Sample, Survey On Direct-To-Consumer Advertising Of Prescription Drugs, 2001–02

	Number of respondents[a] (unweighted)	Percent distribution	
		Unweighted	Weighted
All	3,000	100.0%	100.0%
U.S. region			
New England	163	5.4	5.3
Mid-Atlantic	521	17.4	17.2
Southeast	672	22.4	22.5
South Central	296	9.9	10.0
Midwest	515	17.2	16.8
Plains	234	7.8	7.8
Mountain	191	6.4	6.7
West	408	13.6	13.7
Age			
18–34	834	27.8	32.0
35–64	1,591	53.0	51.3
65+	575	19.2	16.7
Race/ethnicity			
White, non-Hispanic	2,280	76.0	71.8
Black, non-Hispanic	287	9.6	11.5
Hispanic	241	8.0	10.5
Asian	58	1.9	1.7
Unknown/other	134	4.5	4.5
Education			
Less than high school	259	8.6	11.0
High school or some college	1,566	52.2	65.4
College grad	1,161	38.7	23.1
Unknown	14	0.5	0.4
Insurance status			
Insured	2,629	87.6	83.1
Uninsured	362	12.1	16.6
Insurance provides some drug coverage			
Yes	2,231	91.6	91.2
No	203	8.3	8.8
Health status			
Excellent/good/very good	2,509	83.6	82.8
Fair/poor	478	15.9	16.7
Saw doctor in past 3 months			
Yes	1,610	53.7	52.1
No	1,374	45.8	47.3

SOURCE: Authors' survey of experiences with direct-to-consumer advertising (DTCA) of prescription drugs, 2001–02.
NOTES: Percentages may not total to 100 due to missing data or rounding.
[a]Number of valid responses in each category.

tion (Exhibit 2). DTCA was one of many health information sources influencing patients' decision to discuss a health issue with their physician. Other than DTCA, 51 percent of patients were influenced by friends/family, 40 percent by broadcast media, 34 percent by print media, 33 percent by pamphlets in doctors' offices, 33 percent by another doctor, 16 percent by the Internet, and 17 percent by a pharmacist. Of persons with a DTCA visit, about 45 percent (n = 474) were (by our definition)

EXHIBIT 2
Characteristics Of DTCA Visits With Physicians, By Patient's Health Status And Influence Of Advertising, 2001–02

		Patient's health status (N = 1,035)		DTCA influence (N = 1,022)	
	All (N = 1,039)	Excellent/good (n = 837)	Fair/poor (n = 198)	High (n = 474)	Low (n = 548)
Type of discussion reported[a]					
About prescription drug	37.4%	40.8%	26.1%	41.9%	34.6%
About new health concern	21.9	23.8	19.6	20.0	25.9
About change for ongoing concern	35.6	30.8	45.2	34.5	32.1
Other	5.0	4.5	9.0	3.6	7.4
Conditions and diagnoses[b]					
Existing condition	46.4	42.4	63.4	48.4	44.9
New diagnosis/condition	24.7	26.5	17.3	21.4	27.8
Condition not confirmed by physician or health care worker	20.1	22.5	10.9	22.0	18.5
Missing/unknown	8.8	8.7	8.4	8.2	8.8

SOURCE: Authors' survey of experiences with direct-to-consumer advertising (DTCA) of prescription drugs, 2001–02.
NOTE: DTCA visits are defined as visits with a physician during which a DTCA-prompted discussion occurred about an advertised drug or other health concern.
[a] For type of DTCA discussion reported, differences were significant ($p < .01$ using the chi-square test) for patient's health status and DTCA influence.
[b] Existing conditions are conditions, identified by the respondent, that were discussed during the DTCA visit, for which respondents received confirmation (were ever told by physician or other health care worker that they had the condition), and were reported to exist prior to the visit. New diagnoses/conditions are confirmed conditions that the patient did not know existed or had not been diagnosed prior to the visit, as reported by the respondent. For conditions and diagnoses, differences were significant ($p < .01$ using the chi-square test) for patient's health status.

highly influenced by DTCA to have the discussion with their physician, and 19 percent (n = 198) were in fair/poor health. People in good health or who were highly influenced by DTCA were more likely than others to have a DTCA discussion about a particular prescription drug rather than about new or ongoing health concerns ($p < .01$).

About half of patients with DTCA visits had previously been diagnosed with the condition discussed during the visit, and nearly one in four were given new diagnoses. New and existing conditions are listed in the exhibit only if they were confirmed by a health professional (according to the respondent). The five most common existing conditions were allergies (13 percent), arthritis (10 percent), high cholesterol (7 percent), diabetes (7 percent), and asthma (5 percent). The most common new diagnoses were allergies (9 percent); diseases of the esophagus, duodenum, and stomach (including gastroesophageal reflux disease, or GERD) (8 percent); high cholesterol (6 percent); arthritis (6 percent); hypertension (6 percent); diabetes (5 percent); and depression (5 percent). Approximately 43 percent of new diagnoses and 51 percent of existing diagnoses were "high priority" conditions according to AHRQ/IOM criteria (data not shown). Notably, 8.8 percent of patients did not specify a condition discussed during the visit, and an additional 20.1 percent of conditions were not confirmed—that is, the patient did

not recall being told by a doctor or other health professional that he or she had the condition reported in the survey.[16]

■ **Physicians' actions.** Exhibits 3 and 4 refer to actions taken by physicians as a result of the DTCA visit. Nearly three-quarters of respondents with a DTCA visit received a drug prescription; 43 percent of DTCA visits resulted in a prescription for the advertised drug. Other actions taken included referrals to specialists, lifestyle changes, recommendations for OTC drugs, lab tests, and reductions in smoking/drinking.

Nearly all respondents (95 percent) with a DTCA visit reported at least one action taken. Even after we excluded prescriptions for the DTCA drug, 53 percent still resulted in at least one action taken by the physician. People in fair/poor health and with high-priority conditions generally had more actions taken on their behalf, but they did not differ significantly from their healthier counterparts in terms of the likelihood of receiving a DTCA drug. Patients with unconfirmed

EXHIBIT 3
Reported Actions Taken By Physicians Resulting From DTCA Visits, By Patient's Health Status And Diagnosis/Condition Type, 2001–02

		Health status (N = 952)		Diagnosis/condition type[a] (N = 949)		
Action	All (N = 953)[b]	Excellent/ good (n = 770)	Fair/poor (n = 182)	Existing (n = 481)	New (n = 271)	Not confirmed (n = 197)
Prescribed any drug	72.9%	71.0%	81.1%	81.1%	80.0%	45.7%
Prescribed DTCA drug	43.3	43.5	42.9	49.1	44.7	28.8
Referred to specialist	32.6	27.5	53.5	35.8	35.7	21.2
Suggested lifestyle change	52.0	49.2	63.9	51.7	58.3	45.7
Recommended OTC drug	19.1	19.8	16.2	18.3	20.4	18.7
Ordered lab test	57.3	52.8	76.2	58.0	66.3	44.7
Suggested quit smoking/ drinking	33.9	30.7	47.3	35.2	35.0	30.0
Patients reporting any action taken	95.2	95.1	95.1	96.3	99.2	87.1
Patients reporting any action taken other than prescription for DTCA drug[c]	55.8	55.3	57.6	50.8	57.1	66.5
No action taken	4.8	4.9	4.9	3.7	0.8	12.9

SOURCE: Authors' survey of experiences with direct-to-consumer advertising (DTCA) of prescription drugs, 2001–02.

NOTES: DTCA visits are defined as visits with a physician during which a DTCA-prompted discussion occurred about an advertised drug or other health concern. OTC is over-the-counter. For health status, differences were significant ($p < .01$ using the chi-square test) for prescribed any drug, referred to specialist, suggested lifestyle change, ordered lab test, and suggested quit smoking/drinking. For diagnosis/condition type, differences were significant ($p < .05$ using the chi-square test) for prescribed any drug, prescribed DTCA drug, referred to specialist, suggested lifestyle change, ordered lab test, patients reporting any action taken, patients reporting any action taken other than prescription for DTCA drug, and no action taken.

[a] Existing conditions are conditions, identified by the respondent, that were discussed during the DTCA visit, for which respondents received confirmation (were ever told by physician or other health care worker that they had the condition) and were reported to exist prior to the visit. New diagnoses/conditions are confirmed conditions that the patient did not know existed or had not been diagnosed prior to the visit, as reported by the respondent.

[b] Excludes patients who could not identify any condition or reason for visit.

[c] To calculate this number, we divided the number of respondents who were not prescribed a DTCA drug but reported at least one other action taken on their behalf by the number of patients with a DTCA visit.

EXHIBIT 4
Reported Actions Taken By Physicians Resulting From DTCA Visits, By Priority Of Condition And Influence Of Advertising, 2001–02

Action	All (N = 953)[a]	High-priority condition[b] (N = 752)		DTCA influence (N = 940)	
		Priority (n = 374)	All other (n = 378)	High (n = 436)	Low (n = 504)
Prescribed any drug	72.9%	81.4%	79.8%	71.4%	73.8%
Prescribed DTCA drug	43.3	47.4	47.8	46.9	40.6
Referred to specialist	32.6	40.1	31.8	24.6	38.6
Suggested lifestyle change	52.0	66.0	42.7	45.2	57.3
Recommended OTC drug	19.1	14.4	23.6	19.9	18.4
Ordered lab test	57.3	72.1	50.4	50.4	62.3
Suggested quit smoking/drinking	33.9	42.0	28.7	31.5	35.9
Patients reporting any action taken	95.2	97.7	96.9	94.3	95.7
Patients reporting any action taken other than prescription for DTCA drug[c]	55.8	52.7	50.5	51.3	59.1
No action taken	4.8	2.3	3.1	5.7	4.3

SOURCE: Authors' survey of experiences with direct-to-consumer advertising (DTCA) of prescription drugs, 2001–02.

NOTES: DTCA visits are defined as visits with a physician during which a DTCA-prompted discussion occurred about an advertised drug or other health concern. OTC is over-the-counter. For high-priority condition, differences were significant ($p < .05$ using the chi-square test) for referred to specialist, suggested lifestyle change, recommended OTC drug, ordered lab test, and suggested quit smoking/drinking. For DTCA influence, differences were significant ($p < .05$ using the chi-square test) for referred to specialist, suggested lifestyle change, ordered lab test, and patients reporting any action taken other than prescription for DTCA drug.

[a] Excludes patients who could not identify any condition or reason for visit.

[b] Cancer, diabetes, emphysema, high cholesterol, HIV/AIDS, hypertension, ischemic heart disease, stroke, arthritis, asthma, gall bladder disease, stomach ulcer, back problems, Alzheimer's disease and other dementias, and depression and anxiety disorders, as listed in Institute of Medicine, *Crossing the Quality Chasm: A New Health System for the Twenty-first Century* (Washington: National Academies Press, 2001); and the Medical Expenditure Panel Survey (MEPS) HC-006R: 1996 Medical Conditions.

[c] To calculate this number, we divided the number of respondents who were not prescribed a DTCA drug but reported at least one other action taken on their behalf by the number of patients with a DTCA visit.

conditions were less likely to have actions taken, and patients with new conditions were slightly more likely than others were to receive a lifestyle recommendation. People who were highly influenced by DTCA were no more likely than others were to be prescribed the advertised drug but were less likely than others were to be referred to a specialist, have a lab test ordered, or have a lifestyle change suggested ($p < .001$).

■ **Health-related outcomes.** About four out of five patients who received a prescription drug and took it as prescribed reported that they felt much better or somewhat better overall after taking the drug, and similar numbers reported that their symptoms improved. Among persons who underwent lab tests, 84 percent reported that their test results improved. These health-related quality-of-life outcomes generally did not vary by type of drug prescribed (DTCA versus other) ($p < .05$). Among patients who switched prescription drugs for the same condition (5 percent of all consumers), 28 percent said that the new drug was easier to take or remember to take, 8 percent said that it was more difficult, and 64 percent said that it was about

"Some of the new diagnoses that were discovered as a result of these visits are often underdiagnosed and undertreated."

the same. None of these effects varied significantly by whether the patient switched to a DTCA or to another drug (all $p < .05$), and no clinically notable differences occurred between patients with new or existing diagnoses. However, those who switched to a DTCA drug were less likely than others who switched were to report that side effects of the new drug were worse (8 percent versus 22 percent) (overall $p = .041$).[17]

Because patient reports are subject to recall bias, we repeated the analyses for people who had a DTCA visit in the three months before the interview (n = 257, or 25 percent of all DTCA visits). Virtually all of the figures were within a few percentage points of the results for the full sample, although fewer differences were statistically significant because of the smaller sample sizes.

Discussion

■ **Effects on consumers.** This study provides a new perspective on the health consequences of DTCA visits, as perceived by patients. As a marketing tool, DTCA is clearly effective when one considers the large number of people who are aware of the ads, and the number who discuss the ads with their physicians and who eventually receive the advertised drug. But marketing theory also suggests that consumers can gain extra benefits not limited to the advertised drug, by obtaining supplementary information about their health.[18] Prior consumer surveys suggest some of these spillover effects, including raised awareness of new conditions, attentiveness to side effects, increased information seeking, and education about nondrug treatments.[19] These benefits may be countered by the potential for harm resulting from possibly deceptive advertising, or overuse that may result from targeting relatively healthy people or by "medicalizing" nonmedical problems.[20]

■ **Reassuring findings.** Our data add to the literature on health effects by addressing the study questions raised earlier and are reassuring on several counts. First, we found that a sizable portion of patients with DTCA visits reported seeing physicians for clinically important conditions and that many visits resulted in new diagnoses. Some of the most common new diagnoses that were discovered as a result of these visits—high cholesterol, hypertension, diabetes, and depression—are often underdiagnosed and undertreated in the general population.[21] Very few visits were for cosmetic or lifestyle problems.

Second, we found that DTCA visits resulted in health care actions taken on behalf of patients that went beyond the expected prescribing of drugs, both advertised and not. Third, given concerns over the possible adverse health consequences of DTCA, our study is notable for what it does not show. We failed to find large negative health consequences for patients on a number of health-related as-

pects, including symptom relief, improved laboratory results, and ease of taking the drug, and for the most part found no difference by whether the patient took the drug that was advertised or some other drug. There seemed, in fact, to be a small advantage in relief of side effects among patients who switched their medications to the advertised drug after their visit, although the number of respondents was small. At a minimum, therefore, we did not detect widespread adverse effects of DTCA based on self-reported health status.

■ **Methodological issues.** The data from our study and the focus groups that preceded the survey raise at least two methodological questions about researchers' ability to attribute specific motives to patients' behavior. First, consumers rely on a multitude of information sources, and the process leading from an ad to a prescription is complex. Many intervening steps often must occur, including scheduling a physician visit, taking and interpreting laboratory tests (for example, for allergies or high blood cholesterol), and perhaps trying lifestyle changes first.[22]

Second, people who are interested in making informed decisions about their health may be more likely to exhibit better health habits than others are, thus confounding the effect of public education. Research on mass communications and advertising has long recognized that even when exposure is widespread, perception and retention are usually motivated—that is, selective. For example, Republicans are more likely than Democrats are to pay attention to advertisements for Republican candidates.[23] Thus, we expect prior interest in one's health to be correlated with attention to and recall of DTC advertising.

■ **Study limitations.** This investigation has certain other limitations that may affect its interpretation and generalizability. The basic study design provides descriptive, cross-sectional data. We did not collect information on outcomes for patients who had physician encounters without a DTCA-prompted discussion. However, as noted above, DTCA awareness is widespread, and so it is unlikely that any cross-sectional study in this country would be able to isolate its effects so completely. Second, even though we had a large national sample, it was still too small to allow for rigorous control of underlying clinical conditions other than overall health status. Future studies restricted to specific conditions might obtain different results.

Third, the generally positive health outcomes we found may be subject to placebo effects or recall bias, although on the latter issue our reanalysis using three-month data suggests otherwise. Furthermore, the duration of experience with new drugs may not have been long enough to identify side effects, and retrospective assessments of outcomes can be biased, although they also can be valid reflections of patients' beliefs.[24] Fourth, future studies should include some measure of appropriateness of treatments.

Fifth, it is difficult to assess the magnitude of our findings without additional context. For example, we found that 8 percent of all adults received a new diagnosis from a health care professional as a result of a visit during which a DTCA-prompted discussion took place. This represents approximately sixteen million

people—a very large number. But given the multitude of health care influences, it would be difficult to ascribe all of that benefit to DTCA. Sixth, we did not measure health outcomes for people not receiving a prescription drug, although in our study this represented only 27 percent of people with DTCA visits.

Seventh, documented positive effects in our study may be attributable to either the physician-patient interaction, to the dispensing of pharmaceuticals, or both. Eighth, the response rate was less than optimal. Although prior research on survey methods has demonstrated that response rates even lower than 50 percent can provide valid estimates of consumer opinion, these results may not apply to reports of health care experiences.[25]

■ **Areas not addressed.** Finally, some of the criticisms of DTCA are economic or ethical and were not addressed by this study. We cannot comment on whether patients were receiving drugs that were more expensive than necessary, or whether consumers were misled by DTC ads. Surveys of consumers also cannot address whether DTCA adds costs to the health care system, and if it does, whether its benefits are worthwhile.

DESPITE THESE LIMITATIONS, our study reports on data heretofore unavailable on patients' experiences with DTCA. Our results suggest that DTCA is a potentially powerful source of consumer health information with effects that include, but also transcend, promoting the use of advertised drugs. DTCA appears to affect patients' behavior, resulting in more physician visits that detect treatable disease but also precipitating a variety of other health actions whose consequences remain to be understood. The advent of DTCA coincides with a general trend toward consumerism, with expectations on the part of patients that their physicians will interpret health information for them and help them judge its value.[26] It is telling, perhaps, that physicians belonging to the National Medical Association, whose members tend to treat more disadvantaged patients, perceive that DTCA benefits their patients by increasing awareness and improving doctor-patient communication.[27]

In conclusion, there seem to be no widespread adverse health effects from these visits, on balance. From a societal standpoint, a definitive judgment on the consequences of DTCA awaits further study and reflection. One important question is whether other sources of health information could achieve DTCA's educational benefits at less cost and with fewer undesirable consequences. To answer this question would require that public and nonprofit agencies launch comparable efforts to educate the public about their health and that those efforts be systematically studied. For now, however, DTCA constitutes an influential purveyor of health information for the general public, one whose power and prominence on our health care scene may be unmatched by any other factor.

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