NBER WORKING PAPER SERIES

EFFECTS OF PHYSICIAN-DIRECTED PHARMACEUTICAL PROMOTION ON PRESCRIPTION BEHAVIORS: LONGITUDINAL EVIDENCE

Anusua Datta
Dhaval M. Dave

Working Paper 19592
http://www.nber.org/papers/w19592

NATIONAL BUREAU OF ECONOMIC RESEARCH
1050 Massachusetts Avenue
Cambridge, MA 02138
October 2013

The authors are very grateful to Michael Fitzmaurice, Robert Kaestner, LeighAnn Leung, Yang Wang, and Samuel Zuvekas for helpful comments. We are especially grateful to Sumit Agarwal for the data and his helpful advice. The views expressed herein are those of the authors and do not necessarily reflect the views of the National Bureau of Economic Research.

Effects of Physician-Directed Pharmaceutical Promotion on Prescription Behaviors: Longitudinal Evidence

Anusua Datta and Dhaval M. Dave

NBER Working Paper No. 19592
October 2013
JEL No. D22,I0,M3

ABSTRACT

Spending on prescription drugs (Rx) represents one of the fastest growing components of U.S. healthcare spending, and has coincided with an expansion of pharmaceutical promotional spending. Most (83%) of Rx promotion is directed at physicians in the form of visits by pharmaceutical representatives (known as detailing) and drug samples provided to physicians' offices. Such promotion has come under increased public scrutiny, with critics contending that physician-directed promotion may play a role in raising healthcare costs and may unduly affect physicians' prescribing habits towards more expensive, and possibly less cost-effective, drugs. In this study, we bring longitudinal evidence to bear upon the question of how detailing impacts physicians' prescribing behaviors. Specifically, we examine prescriptions and promotion for a particular drug class based on a nationally-representative sample of 150,000 physicians spanning 24 months. The use of longitudinal physician-level data allows us to tackle some of the empirical concerns in the extant literature, virtually all of which has relied on aggregate national data. We estimate fixed-effects specifications that bypass stable unobserved physician-specific heterogeneity and address potential targeting bias. In addition, we also assess differential effects at both the extensive and intensive margins of prescribing behaviors, and differential effects across physician- and market-level characteristics, questions which have not been explored in prior work. The estimates suggest that detailing has a significant and positive effect on the number of new scripts written for the detailed drug, with an elasticity magnitude of 0.06. This effect is substantially smaller than those in the literature based on aggregate information, suggesting that most of the observed relationship between physician-directed promotion and drug sales is driven by selection bias. Qualitatively consistent with the literature, we find that detailing impacts selective brand-specific demand but does not have any substantial effects on class-level demand. Results also indicate that most of the detailing response may operate at the extensive margin; detailing affects the probability of prescribing the drug more than it affects the number of prescriptions conditional on any prescribing. We draw some implications from these estimates with respect to effects on healthcare costs and public health.

Anusua Datta
Philadelphia University
School of Business Administration
Philadelphia, PA 19144
DattaA@philau.edu

Dhaval M. Dave
Bentley University
Department of Economics
175 Forest Street, AAC 195
Waltham, MA 02452-4705
and NBER
ddave@bentley.edu

I. Introduction

Spending on prescription drugs in the U.S. increased from $40.3 billion in 1990 to $259.1 billion in 2010 (Centers for Medicaid and Medicare Services - CMS 2012), representing an increase of over 540%. Although prescription drug spending is a much smaller proportion of national health expenditures, about 10% in 2010 compared to 31% for hospital care and 21% for physician services, it has been one of the fastest growing components of health care spending. The rising prescription drug expenditures cannot be fully explained by higher prescription (Rx) drug prices, which increased 124% between 1990 and 2010, based on the BLS (Bureau of Labor Statistics 2012) prescription drug price index. Utilization accounts for a large part of the increase.

The growth in the share of prescription drug expenditures has coincided with the growth in pharmaceutical promotion, which increased from $11.4 billion in 1996 to $29.9 billion in 2005 (Donohue et al. 2007) and $32.3 billion in 2008 (SK&A 2011).[1] Promotion of prescription drugs is generally limited to drugs on patent. Such promotion includes direct-to-consumer advertising (DTCA) on broadcast and print media, and direct-to-physician promotion (DTPP) through visits by company representatives to physician offices (known as detailing), product sampling provided to physicians and hospitals, and advertising in professional journals. There are currently about 81,000 pharmaceutical sales representatives in the U.S., and the typical representative "details" about 5-10 physicians a day (www.ZSassociates.com; Weiss

[1] Since 2008, promotional spending has declined by about 13% to $28.1 billion in 2010 (SK&A 2011), in part due to patent expiration on major drugs such as Advair, Prevacid, and Lipitor. Spending in 2011 increased to $29.3 billion (SK&A 2012)

2010).[2] On average, pharmaceutical companies expend over $20,000 annually per physician on marketing efforts that include contact visits, gifts, samples, meals, travel, consultancy fees, and related spending (Weiss 2010). Hence, product detailing and free sampling, which are both complementary direct marketing efforts to providers, constitute the bulk of the pharmaceutical promotional budget, comprising about 83% in 2011 (SK&A 2012).

As pharmaceutical spending continues to escalate and drug safety issues have become more common, such physician-directed outreach efforts have come under mounting public scrutiny.[3] The debate surrounds the conflict of interest between marketing and patient care, that is whether interactions between pharmaceutical representatives and healthcare providers compromise physicians' integrity and impact their prescribing choices. Specifically from the standpoint of public welfare, the issue also centers around whether such practices induce physicians to prescribe more expensive (and/or possibly less effective) drugs in the presence of cheaper and equally-effective alternatives. The pharmaceutical industry acknowledges that detailing practices likely impact physicians' prescribing behaviors, but also contends that such marketing is welfare-enhancing and remains an important source of physician learning. The industry notes that detailers provide valuable information concerning the drug's indications and counterindications, which in turn allows physicians to make better-informed choices.

These concerns have prompted legislative activity and responses at both the state and federal levels, which are aimed at limiting the influence of provider-aimed pharmaceutical

[2] The pharmaceutical sales force has shrunk since 2008 partly due to layoffs and cost-cutting measures and partly due to a shift towards electronic detailing ("e-detailing").

[3] Vioxx spent $208 million on physician detailing (and $256 million on consumer-directed advertising) in 2003, prior to its withdrawal in 2004, which may have played a role in expanding utilization to a point beyond what was necessary based on patient need (Pew Prescription Project 2009). David et al. (2010) find some evidence that increased consumer-directed advertising is associated with an increased reporting of adverse medical events for certain conditions. This suggests that consumer promotion may worsen the average safety profile for the drug.

marketing. An increasing number of states have undertaken academic or counter-detailing in an effort to balance sales-focused information.[4] Such programs utilize clinicians, pharmacists, and nurses to provide objective non-commercial information to physicians anchored on evidence-based research (Pew Prescription Project 2009). The National Resource Center for Academic Detailing, which is funded by the Agency for Healthcare Research and Quality (AHRQ), was created in 2010 to promote counter-detailing measures by adapting AHRQ's evidence-based research for such programs and providing training and logistical support to organizations who are establishing new academic detailing programs.[5] In 1990, the Food and Drug Administration (FDA) enacted regulations that banned "gifts of substantial value" from drug companies to providers (Pomper 2000), though this only shifted the composition of such gifts. The American Medical Association (AMA) has also debated policies relating to detailing and industry "freebies", and has issued ethics guidelines addressing such marketing practices and industry gifts (Weiss 2010). New voluntary pharmaceutical industry guidelines on interactions with providers also went into effect in 2009, partly in an attempt to preempt further state and federal legislative actions. Some states such as Vermont, Massachusetts, and Minnesota have enacted "sunshine laws" that mandate public disclosures of payments to physicians beyond a certain amount (Grande 2010).[6] Similar provisions were debated as part of a federal disclosure bill in 2009 (Physician Payments Sunshine Act). These provisions eventually became part of the Affordable Care Act and now require pharmaceutical companies to report

[4] Currently, DC, MA, ME, NH, NY OR, PA, SC, and VT have some form of academic detailing programs (Hilltop Institute 2009; Pew Prescription Project 2009).
[5] The Independent Drug Education and Outreach Act of 2009 was also introduced in the House and the Senate, proposing to offer federal grants for the development of academic detailing programs.
[6] Minnesota and Vermont actually ban all gifts, and Vermont requires that all free samples of drugs be reported to the State Attorney General's Office. Starting in 2006, New Hampshire has banned the sale of prescription data to commercial entities.

to the Secretary of Health and Human Services any payment or transfer of value to providers (with limited exceptions) or any financial conflict of interest.

Given that the pharmaceutical industry invests most of its promotional budget towards marketing efforts aimed at physicians, and the debate centers on the influence of such outreach, a critical question relates to how physician-directed promotion affects prescribing behavior. Virtually all of the empirical studies that have investigated the effects of pharmaceutical promotion have done so based on aggregate data for a subset of drugs, which inherently limits the prior analyses in a number of ways. Estimates from these studies, most of which rely on national data, are subject to potential bias from unobserved trends and other confounding factors. For instance, addressing targeting bias is a vital issue in identifying plausibly causal effects of advertising. Identification based on national or market-level data cannot bypass the concern that physicians who already have a history of prescribing a particular drug or who have a higher unobserved likelihood of prescribing the drug (for instance due to their patient population or practice type) are more likely to be targeted by detailers. This would impart an upward bias to the estimated effects. While most of these studies have found positive effects of detailing on drug sales, at the very least the magnitude of these effects therefore comes into question. Furthermore, even if detailing plays a causal role in raising drug sales, key gaps remain in this literature with respect to understanding the margin at which detailing exerts its influence. For instance, it remains unclear whether detailing impacts physician prescribing habits at the intensive margin, by influencing the number of prescriptions among physicians who were already prescribing the drug, or at the extensive margin, by influencing physicians who had never prescribed the drug. It is also unclear how these effects

vary across physician and market-level characteristics. As prior studies mainly use aggregate sales and promotion information, they are unable to parse out the effect across these different margins or assess heterogeneity in the response to detailing across physician-level characteristics.

We address these gaps and also add to the weight of the evidence bearing on the impact of direct-to-physician promotion (DTPP) by utilizing a unique nationally-representative longitudinal panel of 149,000 physicians comprising almost 3.6 million physician-month records over 24 months. Specifically, we analyze the impact of detailing and sampling related to Famvir, a branded drug indicated for the treatment of various Herpes infections, on the prescribing behavior of individual physicians. The use of longitudinal physician-level data represents a significant departure from the bulk of the literature, allowing us to estimate physician fixed-effects models to account for targeting bias and other unobserved time-invariant physician heterogeneity, and in the process derive plausibly causal effects of DTPP. In addition, the use of longitudinal physician-level information allows us to study effects at various relevant margins and assess heterogeneity in these effects, which have heretofore remained unexplored.

2. Prior Studies

While pharmaceutical direct-to-consumer advertising (DTCA) has expanded significantly since 1999, when the FDA clarified and relaxed the risk information requirements associated with pharmaceutical promotion, direct-to-physician promotion (DTPP) has historically been and

remains the primary form of promotion used by the pharmaceutical industry.[7] Several econometric studies have examined the impact of such promotion.[8] Berndt et al. (1995), consider the role of detailing and medical journal advertisements as well as DTCA in the market for anti-ulcer drugs. They study the period prior to the shift in FDA guidelines, from September 1977 through December 1994. Based on an IV methodology to account for the simultaneity between marketing, pricing, and demand, they find the strongest demand effect for the stocks of detailing (market share elasticity=0.649) followed by medical journal advertising (0.198). They find the smallest impact for print consumer advertising.

Other studies have also confirmed that the marginal impact of detailing on market share is significantly larger relative to that for consumer-directed advertising. Kalyanaram (2009, 2008) reports market share elasticities of 0.62-0.81 with respect to DTPP compared to 0.12-0.21 with respect to DTCA. Dave and Saffer (2012) also find significantly larger sales-DTPP elasticities (0.51 for detailing and 0.34 for sampling) compared to the sales-DTCA elasticity (0.13). Wosińska (2002) reports that the effect of detailing on market share is about five times higher relative to the effect of DTCA. Ling, Berndt and Kyle (2002), in their study of four heartburn drugs, find a market share-detailing elasticity of 1.68, but do not find any significant own-effects of DTCA. Iizuka and Jin (2007) study the market for three anti-histamines between 1994 through 2001, based on patient-level data from the National Ambulatory Medical Care Survey matched with monthly brand-level advertising data. Based on drug fixed-effects

[7] See Iizuka (2004) and Dave (2012) for expanded accounts on the historical background, trends, and controversies surrounding pharmaceutical promotion.
[8] See Dave (2013) for a more comprehensive survey of the literature on the effects of pharmaceutical promotion aimed at consumers and healthcare providers, in the U.S. and internationally.

models, they find that DTCA has little effect on brand choice compared to DTPP, which has far larger and durable effects.

Rizzo (1999) studies pooled annual data for 46 anti-hypertensive drugs from 1988-1993, and, based on drug-specific fixed effects models, finds that increased current and past detailing efforts reduce the price elasticity and increase sales. The price measure reflects the wholesale price of the drug to drug stores and hospitals. The reduction in the price elasticity may consequently result in higher prices, though Rizzo does not examine the direct link between detailing and price. He concludes that pharmaceutical promotion differentiates products, increases brand loyalty, and inhibits price competition in the pharmaceutical industry.

Mizik and Jacobson (2004) estimate dynamic fixed-effects specifications based on physician-level longitudinal data spanning 24 months for three branded drugs.[9] A notable feature of their study is that they estimate first-differenced specifications to account for unobserved physician-specific characteristics. They find modest effects of detailing, substantially smaller than those reported in studies based on aggregate data, at the contemporaneous and 1-4 months lagged levels. This is consistent with estimates based on aggregate data being potentially biased upwards due to targeting bias and unobserved physician heterogeneity.

Beyond estimating mean effects of DTPP, some studies further assess interactions between the various marketing elements and also consider differential effects of DTPP across various market, physician, and product-level characteristics. Narayanan, Desiraju, and Chintagunta (2004) utilize monthly data on three branded second generation anti-histamines

[9] Due to conditions of anonymity, the drugs or their therapeutic class are not specified in the study.

(and one aggregated measure of all other first-generation and other anti-histamines) spanning April 1993 through March 2002. They find that detailing primarily and positively affects brand share, whereas DTCA has a significant positive effect on both brand shares and class sales. The return on investment (ROI) is much larger for detailing than for DTCA, a feature which they attribute to the fact that detailing allows for a much more targeted promotional effort relative to DTCA. They also find evidence of synergy between the two forms of promotion. For instance, a sales call to a physician's office has a higher marginal impact on brand share when combined with DTCA.[10]

Gonul et al. (2001) utilize information on 1785 patient visits occurring between January 1989 and December 1994 to a panel of 157 physicians to study the effects of pricing and promotional activities on prescription choice within a particular undisclosed therapeutic class. Estimates from multinomial logit specifications suggest that detailing significantly raises the probabililty of prescribing the promoted drug up to a point after which the excessive detailing becomes counter-effective due to diminishing returns. The effect of detailing and sampling is found to be insignificant for physicians with a higher percentage of HMO (health maintenance organizations) patients, which the author conjecture is likely due to the restrictions imposed by HMO drug formularies.[11] They conclude in favor of detailing and sampling being mostly informative and raising the price sensitivity of physicians. Also using a physician-level sample, Manchanda and Chintagunta (2004) confirm the positive but diminishing returns to detailing on prescriptions, with diminishing returns setting in more frequently for detailing targeted towards

[10] They also find that the interaction between detailing and price is negative suggesting that higher levels of detailing raise the price elasticity. This contrasts with the finding in Rizzo (2004) that detailing reduces the price elasticity, albeit for a sample of anti-hypertensive drugs.

[11] The effects of detailing and sampling are negative for Medicare patients, possibly due to confounding with other ailments and drugs prescribed for the patients.

specialists. They find that sampling raises the effectiveness of detailing, and that detailing is most effective when targeted towards specialists followed by primary care physicians. One of the limitations of such physician-level studies is that they typically do not observe competitive detailing efforts or other forms of drug promotion.

Uncertainty regarding the efficacy of the drug and its attributes including the safety profile tends to be high in the early stages of the drug's life cycle. Hence, DTPP may play an informative role in periods immediately following a drug's launch. After some point, DTPP largely takes on a persuasive role by providing samples and reminders. Narayanan et al. (2005) utilize a random coefficients discrete choice model with a Bayesian learning process to test how marketing communication changes over a product's life cycle for prescription anti-histamines. They find that the physician learning effect and the informative role of DTPP generally dominates during the early stages, up to 6-14 months following the drug's launch, whereas the persuasive role dominates in subsequent periods.

Most of the above-referenced studies (Berndt et al. 1995; Rizzo 1999; Ling, Berndt, and Kyle 2002; Narayanan, Desiraju, and Chintangunta 2004, Narayanan et al. 2005; Kalyanaram 2008, 2009; Dave and Saffer 2012) utilize a national aggregated time series of sales and promotion for varying drug brands. A few studies utilize patient-level data (Wosińska 2002; Iizuka and Jin 2007), though these records are still matched with aggregated national drug-level promotional information. Very little work has exploited longitudinal information on physicians. Gonul et al. (2001) and Manchanda and Chintangunta (2004) are the exceptions, but in essence treat their data as cross-sectional and leave unexploited one of the main advantages of longitudinal data; they do not control for physician fixed effects. In fact, Gonul (2001) cautions

that “prescription behavior patterns might be strongly influenced by factors other than the explanatory variables…” such as “physicians’ unobservable characteristics,” and notes that “ignoring these factors might bias the coefficients of the included explanatory variables (p. 84).

To the best of our knowledge, Mizik and Jacobson (2004) is the sole study to have investigated the effects of physician detailing on prescriptions based on a first-differenced model that purges unobserved physician-specific heterogeneity. The study is notable for this advancement, though in the process of identifying separate effects for contemporaneous and each prior month’s promotion, estimates are limited by collinearity and power concerns. Furthermore, standard errors are not adjusted for autocorrelation within physician practices over time. The identification strategy, which is based on a dynamic panel estimator and utilizes lagged levels as instruments for the first differences, is based on the assumption of no autocorrelation.

Several questions remain unexplored in the literature, even among the very few studies that have used physician- or patient-level data. We address these gaps and add to the weight of the evidence bearing on how DTPP impacts physicians’ prescribing behavior, utilizing nationally-representative longitudinal information on physicians. We take care to fully exploit the advantages afforded by longitudinal information, and estimate physician fixed effects models. In addressing concerns related to targeting bias and unobserved stable physician-specific heterogeneity, the estimates yield plausibly causal effects of detailing. We also provide the first estimates of the effects of detailing at both the intensive and extensive margins of physicians’ prescribing behaviors, and further investigate heterogeneity in the effects based on observed physician characteristics.

3. Data

The data utilized in this study are collected by IMS Health (formerly Verispan), and pertain to monthly records on the number of new scripts written by a nationally-representative sample of 149,247 practicing physicians spanning 24 months (June 1997 – May 1999).[12] Specifically, we study the effects of DTPP for Famvir on the number of new prescriptions written for this drug as well as for other competing drugs in the therapeutic class. Physicians are asked to keep track of the detailing and samples that they receive from sales representatives. Hence, for each physician-month record, we observe two primary (and complementary) forms of DTPP: the total number of visits by pharmaceutical sales representatives directly pertaining to Famvir, and the number of free drug samples for Famvir received by the physician. In addition, the data also contain detailed information on the physician's characteristics, including age, gender, specialty, area of practice (zip code), and practice type (for instance, solo, partnership, small/large/medium group, medical school, hospital, clinic). We match information on the dates of FDA approval and patent expiration for each drug from the FDA's Orange Book.[13]

Famciclovir, which is marketed under the brand name Famvir, was approved by the FDA in June 1994 to treat various herpes viral infections, including herpes zoster (shingles), herpes simplex virus 2 (genital herpes), herpes labialis (cold sores), and also suppress recurring episodes of herpes simplex virus 2.[14] A year after the approval of Famvir, another herpes anti-

[12] This is approximately a 21% sample, as there were about 702,000 practicing physicians (2.6 per 1,000 population) in the U.S. in 1998 (National Center for Health Statistics).
[13] See: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm.
[14] Famvir 500mg was approved in June 1994; Famvir 125mg was approved in December 1995; and Famvir 250mg was approved in April 1996. In August of 2007, the first generic version of Famciclovir (all three doses) was approved. In the physician-level data, these doses are separately observed. We

viral drug, Valcyclovir sold under the brand name Valtrex, was approved (June 1995).[15] The oldest anti-viral medication is Acyclovir, originally sold under the brand name Zovirax. The topical form was approved in 1982, and the oral form was approved in 1985. Generic Acyclovir entered the market in 1997, and was therefore available throughout our sample period.

All three anti-viral drugs are approved for the treatment of recurrent genital herpes episodes and can also be taken in smaller daily doses for prophylactic suppression of the virus and for reduction in the frequency and duration of future outbreaks. However, Famvir and Valtrex are utilized and absorbed more efficiently; hence, they can be taken less frequently or in smaller doses than Acyclovir in treating recurrent episodes and for viral suppression. Both Famvir and Valtrex are more or less equally effective for treating and controlling outbreaks and suppressing recurrence. Clinical research has not found any significant differences in effectiveness between Acyclovir, Famvir, and Valtrex with respect to controlling outbreaks, and between Famvir and Valtrex with respect to suppressing recurrence (Wald et al. 2006). In the case of an initial episode, however, oral Acyclovir or Valtrex may be preferable to Famvir since the efficacy of Famvir for initial episode genital herpes infection has not been firmly established. In 2003, Valtrex also became the only drug to gain FDA approval for reducing the risk of transmission of genital herpes with the use of suppressive therapy and safer sex practices.

In terms of costs associated with episodic use, the retail cost of treating an outbreak is lowest with generic Acyclovir ($30.33), followed by Valtrex ($40.66), and then Famvir ($50.21).

---

combine all doses into a single measure of Famvir prescriptions and Famvir-related detailing and sampling (any dose).

[15] Famvir was originally made by SmithKline Beecham, and Valtrex was made by Glaxo Wellcome. When the firms merged in 2000 to form GlaxoSmithKline, U.S. regulators forced them to sell Famvir to Novartis.

In terms of costs associated with daily suppressive use, the retail cost is again lowest for generic Acyclovir ($1624.24), followed by Valtrex ($2313.52 - $4350.60, depending on dose[16]), and then Famvir ($4200.24).[17]

Table 1 presents means for our key variables across various analyses samples. Over the sample period, about 48.3% of new herpes anti-viral prescriptions were written for the generic Acyclovir. The remainder of the new prescriptions were for the branded drugs: 18.7% for Famvir, 26.4% for Valtrex, and 6.7% for Zovirax. Approximately 43% of physicians were detailed at some point in relation to Famvir. Among those who were detailed during the sample period, the average physician received at least one visit from a pharmaceutical representative every 3 months.

4. Framework

Analytical Framework

The market for prescription drugs is differentiated from other markets both on the demand side and on the supply side due to the involvement of multiple agents. On the demand side, even though the patient is the end-user, the physicians are the primary decision-makers and gatekeepers since the patient cannot legally consume the drug without a prescription from their physician. The physician is also a provider of information on the drug's indications and contraindications to the patient. Furthermore, on the demand side, the insured consumer pays only a fixed copayment or fraction of the full retail price, with the pharmacies reimbursed for the residual cost by the insurance company. On the supply side, the pharmaceutical firm has a

[16] A one-gram daily suppressive dose of Valtrex costs $4350.60, indicated for patients with normal immune function. For most patients, who have 9 or fewer recurrences per year, an alternative suppressive daily dose of 500mg is indicated, with a cost or $2313.52 annually.
[17] See http://www.herpes-coldsores.com/compare-herpes-drugs.htm.

time-limited monopoly for the sale of its patented drugs. The firm can use promotion to physicians, promotion to consumers and pricing as tools for maximizing profits during the monopoly period and subsequent to patent expiration.

It is often presumed that the average consumer is responsive to advertising and promotion.[18] In the context of DTPP, the physician is the "consumer" and it is their behaviors that detailing seeks to impact. Under the persuasive view, advertising can impact demand by altering consumers' tastes and preferences. The informative view of advertising points to the transfer of information to consumers as another explanation for why they respond to advertising messages. Nelson (1970) distinguishes between search goods, wherein the consumer can determine quality prior to purchase though perhaps after incurring some search costs, and experience goods, wherein the consumer can assess quality or attributes only after consumption. Advertising addresses an informational imbalance for experience goods by providing indirect information content regarding attributes, and advertising intensity is thus predicted to be higher for experience goods. A third view of advertising provides a framework under which advertising is complementary to the advertised product, and also bridges back to the informative view. If advertising, for instance, enables consumers to produce information at lower cost, then they can more efficiently convert market goods into valued final commodities (Stigler and Becker 1977). And, even if advertising in uninformative, consumers may value it directly, as assumed in Becker and Murphy (1993).

The upshot of this discussion is that there are elements of each view of advertising that apply to physician-directed promotion of Rx drugs, and the frameworks are not necessarily

[18] See Bagwell (2007) for a comprehensive review of the economics of advertising, and Dave (2012) for a review specifically relating to the pharmaceutical market.

mutually exclusive. Prescription drugs, especially new entrants, have some predominant experience attributes, and information provided by pharmaceutical representatives may address some of the uncertainty regarding the mean efficacy and/or counterindications concerning the drug.[19] Thus, detailing plays a role in educating providers about newer drugs and their attributes and may have information value early in a product's life cycle, whereas later in the life cycle its role can be predominantly persuasive and chiefly relegated to delivering samples and reminders.[20]

One of the key questions with respect to advertising by firms in markets for healthcare inputs also relates to whether advertising raises "selective" or brand-specific demand versus "primary" or industry-wide demand (Dave and Kelly 2012). In the context of DTPP, market expansion may be welfare-enhancing if it encourages greater contact between the patient and the physician, expanding treatment to undertreated populations, and, specifically in the case of anti-viral herpes drugs, if it plays a role in reducing transmission and new infections. Selective demand effects, on the other hand, may be welfare-enhancing only if the detailed drug is also the most effective and/or cost-effective treatment available. On the other hand, if detailing raises demand for a drug at the expense of other more cost-effective drugs, then such selective demand effects may be welfare-reducing. Since detailing can affect both selective (brand-centric) as well as primary (market) demand under these views (Dave and Kelly 2012), the

[19] Hence, advertising and other promotion intensity for the pharmaceutical industry tends to be substantially higher relative to the average sector. For instance, the promotion-to-sales ratio for the U.S. pharmaceutical industry is about 15-20%, compared to an all-industry average of 4-5% (Dave 2012).
[20] Physician learning in the presence of uncertainty regarding drug attributes can also occur from feedback received from patients and from peers, and from other forms of pharmaceutical promotion and interactions (for instance, consumer directed ads, seminars/meetings, medical journal articles and advertising, etc.).

question cannot be resolved based on theory alone and empirical evidence needs to bear upon the question.

Methodology

Drawing from this framework, the following demand function relates prescriptions for Famvir to physician-directed promotional efforts for the drug:

$$NRX_{imt} = \exp(\alpha_0 + \lambda_1 DET_{imt} + \lambda_2 SAMP_{imt} + \mu_i B + \omega_m \Omega + \nu_t \Psi + \varepsilon_{imt}) \quad (1)$$

Equation (1) denotes that the number of new prescriptions written for Famvir by the i^{th} physician, in month *m* of year *t*, is a function of the number of Famvir-related visits by pharmaceutical representatives to the i^{th} physician's office during that month and year (detailing denoted by DET) and the number of Famvir samples provided to the physician (SAMP). The parameter of interest is λ_1, which captures the reduced-form impact of physician detailing on prescribing habits operating through all (persuasive and/or learning) channels.

Prescribing habits also depend on observed and unobserved physician attributes (μ) such as age, gender, specialty, type of practice, patient mix, and preferences. All models further include a set of month (ω) and year (ν) indicators in order to capture unobserved seasonal trends and unobserved national trends, for instance relating to shifts in prescription drug coverage, general trends in herpes infections, and other national trends in pharmaceutical promotion directed at consumers.[21] The vector of time-varying variables also includes linear and quadratic effects of the time until patent expiration, which account for the impact of Famvir's life cycle on prescription patterns. The disturbance term is represented by ε.

[21] Initial visits to physicians, related to genital herpes, was generally trending upwards between 1966-2006, but since then has trended downwards (see http://www.cdc.gov/std/Herpes/stats.htm). Over our sample period spanning 1997-1999, such initial visits increased by about 27%.

We estimate this specification using a Poisson regression model for two reasons. First, the discrete nature of the outcome variable as a count of the number of new prescriptions makes the Poisson probability distribution especially suitable. Second, the Poisson framework does not suffer from the 'incidental parameters' problem and can accommodate fixed effects well (Cameron and Trivedi 1998). All standard errors are adjusted for arbitrary correlation within physician cells over time.[22]

Empirical Concerns

We extend the baseline model to address a number of specific issues. One potential concern with identifying the impact of physician-directed advertising relates to the possibility of targeting bias and unobserved physician heterogeneity. Certain physicians, for instance, those who are high prescribers of the drug in question or other competitive drugs or those who have a higher unobserved (to the researcher) likelihood of prescribing the drug, are more likely to be detailed, as are physicians from larger practices, specialties, or market areas with higher potential demand (Fugh-Berman and Ahari 2007; Mizik and Jacobson 2004). Furthermore, the link between DTPP and prescribing habits may be confounded by other unobserved physician-specific characteristics such as inertia in prescribing patterns, brand loyalty, patient mix, tolerance for risk, and preferences towards tradeoffs between efficacy, counterindications, and long-term use for prophylactic purposes.

As shown in Table 1, there are significant differences across physicians who are ever-detailed by Famvir reps (approximately 43% of the physicians in the analysis sample) versus those who are never-detailed (57% of physicians), with respect to the number of new

[22] Since the Poisson framework implicitly assumes that the mean of each count (for state *s* and year *t*) is equal to its variance, this also adjusts the standard errors for over-dispersion (Wooldridge 2001).

prescriptions written for the competing drugs (Valtrex, Zovirax, and generic Acyclovir), age, gender, specialty, and practice type (not reported). In addition, physicians who have not yet been detailed, but will be visited by pharmaceutical representatives at some point in the future (final column in Table 1), also tend to write more scripts for Famvir and other herpes anti-viral medications. This suggests that these physicians, who are targets for detailing, may have a patient population with a relatively higher demand for such drugs to begin with; they also differ from those who are never-detailed with respect to other observable characteristics. This suggests that physicians who see pharmaceutical reps for Famvir are not a random subgroup of healthcare providers; they differ in terms of observable characteristics (selection on observables) that are correlated with Famvir prescriptions, and by extension are also likely to differ in terms of unobservable characteristics (selection on unobservables).

We address this selection by controlling for an extended set of physician-specific attributes, including demographics, specialty and practice type, and the market area in which the physician practices. The latter is accounted for by zip-code level fixed effects, which would also capture any unobserved time-invariant area-specific factors such as stable disease prevalence, area demographics and economic conditions, and provider availability. Comparison of the detailing effects from parsimonious specifications with those that include these extended physician- and area-specific controls can inform the importance of selection on observables, and, by corollary, selection on unobservables. Our next set of specifications fully exploits the longitudinal information and controls for physician-level fixed effects. These account for all observed and unobserved time-invariant physician heterogeneity, for instance factors that may

be correlated with non-random targeting of physicians and other unobservable characteristics such as preferences and stickiness in prescribing habits.

According to prior advertising studies, the impact of advertising messages can linger beyond the time of its presentation (Dave and Kelly 2012). This may be particularly true with respect to physician detailing due to the potential for learning and inertial prescribing patterns. Hence, we construct an alternate detailing measure that includes the current month's detailing plus a decay-weighted sum of detailing over the past six months. Thus, the detailing (and sampling) stock for month *t* is defined as:

$$\text{Detailing Stock} = \Sigma_{i=0 \text{ to } 6}(DET_{t-i})(1-d)^{i}. \quad (2)$$

The decay rate, *d*, is assumed to be 0.2, under which 74% of the impact of detailing would have depreciated by the 6th month.[23] In general, the current month's detailing represents about 20-22% of the detailing stock with the remainder representing decay-weighted promotion from prior months. The detailing stock is also therefore less likely to be a function of the current month's drug sales, ceteris paribus. In addition, we also include quadratic terms for all promotional measures to capture diminishing returns. While detailing and sampling are complementary physician-directed promotional activities and go hand-in-hand, alternate specifications attempt to disentangle their effects – which we are able to do given that the data contain separate information on the visits by the pharmaceutical representatives and the number of Famvir samples which were provided to the physicians' offices.

[23] Results and conclusions are not materially affected with alternate measures of the DTPP stock based on decay rates of 0.1, 0.3 and 0.4 respectively. Prior research on consumer behavior suggests that advertising effects fully depreciate within 6 months to a year, consistent with decay rates of 0.1-0.2 (Bagwell 2007), which have been found to apply to pharmaceutical advertising (Iizuka and Jin 2005; Ling et al. 2002).

Another potential concern stems from the unique situation of a time limited monopoly. In the multi-period optimization framework considered by Bhattacharya and Vogt (2003), the firm simultaneously manages drug price and promotion to determine sales and maximize profits over the life cycle. The dynamic profit maximizing strategy for a firm is to initially employ a relatively high level of promotion and set a relatively low price to increase current demand by raising consumers' and physicians' stock of knowledge regarding the drug. Since knowledge is costly to acquire, physicians' prescribing patterns can be sticky. In subsequent periods, promotion can therefore be decreased to lower costs and price can be raised to increase revenue. This is not structural but rather correlational or statistical endogeneity since changes in sales and promotion are partly governed by the drug's life cycle. Such bias is bypassed since all models control for life-cycle effects through time-to-patent expiration.

We further extend the analyses to assess effects at the extensive margin, that is whether detailing impacts whether or not the physician prescribes Famvir in any given month, and at the intensive margin, that is whether there are effects on the number of prescriptions conditional on positive prescriptions. We also assess heterogeneity in the detailing effects across several measures of observable physician characteristics.

One limitation in the analyses is that other Famvir-related promotional efforts and competitors' promotional efforts are not observed in the data. This is less of a concern for direct-to-consumer advertising for Famvir and other herpes anti-viral drugs since virtually all DTCA is national in scope and will be captured by the time indicators. DTCA was also very limited in scope over our sample period (June 1997 – May 1999), and did not significantly take off until after the FDA's clarification of its risk requirements in 1999 (Dave and Saffer 2012).

The more relevant concern relates to unobserved detailing efforts undertaken by competing herpes drugs, specifically Valtrex. Since Zovirax had already lost its patent prior to our sample period, it is unlikely to be promoted heavily to consumers or to physicians (Dave 2012). If we assume that detailing across similar drugs in the therapeutic class is competitive and hence positively correlated, then our estimates of the own-detailing effects for Famvir are likely understated. We attempt to indirectly gauge the extent of such bias by investigating cross-effects, that is how detailing related to Famvir impacts prescriptions for Valtrex, Zovirax, and generic Acyclovir.

5. Results

Table 2 presents Poisson regression estimates for the effects of detailing and sampling on new prescriptions for Famvir. All specifications suggest that DTPP significantly and positively impacts physicians' prescribing habits. Furthermore, the effects diminish at higher levels of DTPP as evidenced by the negative quadratic terms and the concavity of the detailing response function. Specification (1) assesses the impact of the current month's detailing efforts and suggests an elasticity magnitude of 0.16. Specification (2) finds that the impact roughly doubles in size (elasticity of 0.33) when the cumulative and persistent effects of past detailing efforts are accounted through the detailing stock. This elasticity magnitude is somewhat lower than prior estimates based on aggregate national data (elasticity estimates ranging from 0.5 to 0.8; see Dave 2013), suggesting that failure to appropriately account for unobserved trends and relying on cross-drug variation in detailing may be imparting a positive bias. The estimates in specification (2), in contrast, are based on cross-physician variation in detailing efforts.

However, even this variation is potentially endogenous due to non-random selection and targeting of physicians.

Specification (3) therefore controls for a set of observed physician-specific characteristics, including age, gender, specialty, and practice type. This further reduces the magnitude of the detailing elasticity by about a third to 0.22, suggesting that there is considerable selection on observables that needs to be addressed when identifying effects of physician promotion. The reduction in the elasticity magnitude is consistent with positive selection, that is observable physician-specific factors which are positively correlated with detailing efforts and which tend to raise the number of scripts written for Famvir. This is also reflective of potential targeting bias, which is predicted to overstate the effects of detailing in naïve regression models. Comparing the elasticity estimates from the basic (model 2) and the extended models (model 3) allows us to evaluate how much of the association between detailing and prescriptions is potentially driven by selection on unobservables. Since the detailing effect is sensitive to the inclusion of the additional physician-specific covariates, which remain unobserved in aggregate studies, it is likely that factors which remain unobserved also play some role in this relationship. Indeed, Altonji et al. (2005) suggest that information on selection on observables can be exploited to assess the extent of selection on unobservables. If we assume that there is at least as much residual positive selection on unobservables as suggested by the inclusion of the physician characteristics, then the causal elasticity of detailing is likely to be substantially lower than 0.22, in the range of 0.11, and possibly even lower than this if there is greater positive selection on unobservables.

Specification (4) further controls for area (zip-code) fixed effects, which in turn does not substantially diminish the elasticity magnitude (0.20). This indicates that any potential targeting is likely driven by physician-specific heterogeneity rather than area-specific heterogeneity. Hence, the next model (specification 5) fully exploits the longitudinal information and controls for physician-level fixed effects to bypass all observed and unobserved stable physician attributes. The positive impact of detailing (evaluated at the observed mean level of detailing) remains statistically significant, though the elasticity is substantially smaller at 0.05.

Detailing is most often complemented with sampling; about 50% of all detailing visits in our sample involve some sampling, Hence, the estimates above should be interpreted as the joint effects of detailing and sampling, which together account for virtually all of the physician-directed promotion efforts. Alternately, it can also be presumed that one of the mechanisms underlying the impact of detailing on prescribing habits is through the provided samples, which may allow doctors to readily prescribe and try out the drug in question for patients. Beyond the first few years of the drug's life cycle, detailing and associated sampling are often utilized to provide reminders to physicians regarding the drug. In specification (6), we separately control for detailing and sampling efforts in order to disentangle the relative importance of each. The detailing elasticity is estimated at 0.04, and the sampling elasticity is estimated at 0.02. Given the complementarity between detailing and the presence of sampling, we interpret the sampling elasticity as mostly reflective of the intensive sampling margin, that is the effects of the quantity of sampling given that some detailing and sampling has occurred.

Prior studies have suggested that consumer-directed advertising has class-level effects and can expand the size of the market (for instance, Dave and Saffer 2012; Iizuka and Jin 2005). However, the effects of detailing have generally been confined to brand-switching or market-share effects, with little or no effects on overall market demand (Dave 2013). Specifications (7) and (8) confirm these prior findings with our micro-level data. In specification (7), we control for total new herpes anti-viral prescriptions as a proxy for class demand. The detailing elasticity is virtually unchanged (0.051), which suggests that the impact on Famvir prescriptions is not capturing an overall impact on market demand; it represents a shift in brand share from other competitor drugs to Famvir. Specification (8) shows more directly that Famvir-related detailing has no substantial impact on overall market demand; the elasticity of *all new herpes anti-viral prescriptions* with respect to Famvir detailing is 0.004. This is consistent with DTPP shifting treatment away from the non-promoted drug towards the promoted drug. However, unlike consumer-directed ads, DTPP cannot induce untreated consumers to visit the doctor, and hence its impact on class-level demand is inherently limited.

Table 3 presents cross-effects in order to assess how detailing of Famvir affects prescriptions for other drugs in the therapeutic class. Models (1), (4), and (7) present estimates for the full sample of physicians across all specialties. The remaining specifications restrict the analyses to those specialties that have relatively high levels of detailing, specifically those specialties where the detailing levels exceed the sample mean (models 2, 5, and 8) and specifically only primary care physicians (models 3, 6, and 9). These latter sample restrictions aim to exclude those specialties which inherently have little or no contact with herpes patients. These estimates suggest that most of the increase in Famvir prescriptions is occurring mostly at

the expense of prescriptions for Valtrex, the newest entry in the class of herpes drugs. There is no significant cross-effect of Famvir detailing on new prescriptions for the generic Acyclovir. This suggests that detailing mostly shifts demand within patented branded drugs – deemed close substitutes – and does not appear to crowd-out the demand for older generics. Estimates also do not suggest any consistent or strong effects for the branded Zovirax (for which the generic version of Acyclovir is available in the market). The latter effect is presumably because the market share for Zovirax over the sample period had declined significantly (approximately standing at 6% of all new prescriptions in the drug class) due to the availability of the generic substitute Acyclovir. Hence, there was not a substantial margin with respect to Zovirax, which could be impacted by a competitor's detailing.

The above results indicate that, though smaller than previously estimated, detailing does have a positive and significant impact on physicians' prescribing habits. In Table 4, we assess whether this effect is being driven by shifts in prescribing habits at the extensive or intensive margins. Specification (1) suggests that the effect on the extensive margin, whether or not to write any Famvir prescriptions in the given month, is relatively large and statistically significant; the "participation" elasticity is estimated at 0.065. Specifications (2) and (3) examine effects on the number of prescriptions, conditional on a positive number of prescriptions. They are estimated using OLS and Poisson, respectively, to assess robustness. The elasticity estimates at this intensive margin are generally similar (0.015-0.019) and substantially smaller than that at the extensive margin. This suggests that detailing is particularly effective in raising the probability that a physician will prescribe Famvir when (s)he

had not done so previously. Among physicians who are already prescribing Famvir, the effect of detailing on additional prescriptions, while significantly positive, is substantially smaller.

Tables 5 and 6 assess whether, and the extent to which, the detailing response is heterogeneous across physician characteristics and across quintiles of market volume, respectively. In Table 5, we find somewhat larger detailing elasticity estimates among metropolitan statistical areas (MSA) which had a larger penetration of managed care insurance plans relative to those that had a smaller share of managed care plans (0.063 versus 0.048). Physicians in such areas tend to operate in larger practices. Furthermore, managed care plans tend to focus on treatment through prescription drugs and early interventions in an effort to reduce costs down the line; hence, use of all anti-viral drugs (possibly for suppressive efforts) is higher in such areas, and this may afford detailing a greater opportunity to impact selective brand-specific demand. Effects are also slightly larger among male physicians (model 3) relative to female physicians (model 4).

Effects are also higher for those physicians whose patients are privately insured (model 5). The latter effect is validating in that, if physicians are mindful of the cost to the consumer then they are likely to prescribe a more expensive, branded drug if the consumer has prescription drug insurance. Hence, one would expect detailing to have stronger effects among physicians who cater to patients with prescription drug insurance.

In the final three specifications, we discount some of the physician specialties that may be unrelated to the use of herpes drug in order to check for a stronger association, in the spirit of a dose-response check. Specification (6) restricts the sample to those physicians who were ever-detailed, for whom the detailing response is expectedly relatively larger (elasticity of

0.075). This sample may be excluding specialties which may have limited contact with herpes patients or this may also potentially reflect another sort of non-random targeting; these physicians may have been targeted since their expected response is greater. On the other hand, omitting the never-detailed physicians from the analysis may be ignoring an important source of variation that was helpful in controlling for unobserved trends conditional on no detailing; hence, the effect among those who are ever-detailed could be potentially over-stated.

In model (7), we limit the analyses to primary care physicians since they are most likely to have first provider contact with herpes patients and hence treat and prescribe herpes medications, and in model (8) we limit the analyses to all specialties where the mean level of detailing within specialty exceeds the mean level of detailing over all specialties. Note that in this latter sample restriction, we are not selecting on physicians (as was done in model 6, with respect to ever-detailed physicians) but rather bypassing entire specialties (such as cardiologists, gastroenterologists, pediatricians, etc.) that are not likely to treat/prescribe herpes medications and are not being detailed to. It is validating that the detailing elasticity is larger (0.06 and 0.07, respectively) for these groups as expected.

Table 6 estimates models across quintiles based on the market volume of all prescriptions written for herpes anti-viral drugs. The effects of detailing are expectedly and monotonically largest across the higher quintiles of market volume. That is, the impact of detailing on new prescriptions for Famvir is higher in markets that have a higher demand for such medications and which present a potential opportunity for pharmaceutical representatives to effectively shift prescribing habits from competitor drugs to Famvir.

We assess the robustness of these estimates to further checks.[24] The estimates are not sensitive if negative binomial specifications are utilized in lieu of the Poisson models. The above estimates aggregate the two doses of Famvir (125mg and 500mg) and their respective detailing. We also assessed the effects of dose-specific Famvir detailing on new prescriptions for each specific dose. While the effects of detailing are significant and positive for both doses, the estimated detailing elasticity for Famvir 125mg was significantly higher (0.07) relative to that for Famvir 500mg (0.05).[25] Famvir 125mg entered the market about 18 months after Famvir 500mg; thus, the differences in the response magnitudes across these two doses may be related to the differential role that detailing plays over the drug's life cycle. For the newer entrant Famvir 125mg, detailing is primarily aimed at educating providers about the new dosing and its attributes, whereas for the older drug Famvir 500mg, detailing may be chiefly concerned with delivering samples and reminders.[26]

6. Discussion

Pharmaceutical efforts aimed at physicians remain a controversial issue, as it is often contended that such promotion may play a role in raising healthcare costs and unduly affect physicians' prescribing habits towards more expensive, and possibly less cost-effective, drugs. A key input necessary for assessing these contentions concerns whether, and the extent to which, direct-to-physician promotion such as detailing and sampling impacts physicians' prescribing behaviors. Heretofore, this question has been mostly addressed based on aggregate national data, which substantially hinders the interpretation of these prior estimates

[24] Results are available upon request.
[25] These estimates are derived from the fully-specified model (similar to model 5 in Table 2) with physician fixed effects. Full results are available upon request.
[26] The larger positive detailing response for Famvir 125mg is also partly due to the substitution effect as detailing of the newer dose may crowd out prescriptions for the older dose.

as credibly causal due to potential bias from non-random targeting and unobserved physician heterogeneity. Furthermore, several questions regarding variation in the detailing response across various margins and physician characteristics remain unexplored.

We address these gaps and provide virtually the first longitudinal study bearing on the effects of detailing and sampling, fully exploiting the longitudinal physician-level records to bypass time-invariant physician-level heterogeneity and targeting. These estimates suggest that detailing (and to a lesser extent, the quantity of sampling) imparts a significant and positive effect on the number of new prescriptions written for the detailed drug. However, the elasticity estimate of around 0.05 to 0.07 is substantially lower than that reported in prior studies based on aggregate data, suggesting that most of the observed association between detailing and drug sales reflects unobserved selection.[27] We also provide the first evidence in terms of disentangling this effect between the extensive and intensive margins, and in doing so find that the detailing response is substantially higher at the extensive margin (elasticity of 0.07) than at the intensive margin (0.02). These effects are not uniformly distributed across physicians and markets, and tend to differ based on certain observable physician characteristics (such as gender, specialty, and insurance status of patients) and market-level characteristics (such as prevalence of managed care plans and market volume of class-level prescriptions).

Our estimates based on micro-level evidence are qualitatively consistent with prior studies in that we also do not uncover substantial effects of detailing on class-level demand.

[27] Even at these low elasticity magnitudes, detailing is potentially profitable. The average cost of a detailing visit is about $150 (http://www.marketingpower.com/ResourceLibrary/Publications/MarketingHealthServices/2004/24/1/MHSSpr04Davidson.pdf) and the retail cost of daily Famvir use for suppression is about $4200. A back-of-the-envelope calculation, based on a detailing elasticity estimate of 0.06, suggests that a $1 increase in detailing can potentially generate additional revenues of $2.14 (assuming a new Famvir prescription for suppressive use for a year).

This suggestively limits any welfare-enhancing effects of detailing since if detailing were to raise class-level demand then this may be indicative of expanding treatment to untreated or undertreated patients.[28] We find that Famvir-related detailing raises new prescriptions for Famvir, mostly at the expense of prescriptions for Valtrex. We do not find any evidence that such detailing reduces new prescriptions for generic Acyclovir.

Famvir is generally more costly relative to Valtrex, with respect to both episodic use as well as suppressive use. There is also little evidence to suggest that Famvir is any more effective than Valtrex in treating outbreaks or suppressing outbreaks; furthermore, Valtrex is generally superior to Famvir in treating the initial herpes episode, and Valtrex is the only drug indicated for reducing transmission to non-infected partners. Hence, Famvir appears to be less cost-effective relative to the other drugs, and at least for the average patient, detailing-induced shift in prescriptions towards Famvir and away from alternate drugs may not be welfare-enhancing. While there is no crowd-out of the generic alternative, such shifts within patented drugs may nevertheless contribute to somewhat higher costs, ceteris paribus.

Between 1996 and 2010, promotional spending on detailing and sampling increased from $9.8 billion (Donohue et al. 2007) to $21.3 billion (SK&A 2011). Our estimates suggest that this would increase the demand for the promoted drugs by between 6-7%. Since virtually all of this represents selective demand effects, there would be no substantial increase on total utilization of prescription drugs. However, if the detailed drug costs more (as was the case with Famvir), then the detailing-induced increase in selective demand may contribute to higher overall prescription drug spending. To place the potential increase in spending in perspective,

[28] Consumer ads for prescription drugs, in contrast, have been found to positively affect class-level demand, and this is sometimes interpreted as welfare-improving (Dave 2012; Iizuka and Jin 2005).

we extrapolate the effects of Famvir. The 6-7% increase in demand for Famvir, driven by the observed 113% increase in detailing and sampling overall between 1996-2010, would raise spending by about 5.0-5.5%.[29]

We note the caveat that the case of herpes anti-viral drugs may not generalize to the overall prescription drug market. However, it should also be noted that the herpes anti-viral drug class is typical of many other drug classes in many respects: 1) it contains branded and generic alternatives; 2) there are no clear efficacy advantages of one drug over the others; 3) the condition is highly prevalent with 1 out of 4 adults being afflicted; 4) most adults remain untreated. Mindful of external validity limitations, the estimates for Famvir-related detailing underscore the possibility that such detailing of more expensive drugs may shift prescribing habits towards such drugs with little clinical improvements, though with effect magnitudes considerably smaller than previously estimated.

[29] As noted earlier, costs for Famvir therapy are about 25% higher in relation to Valtrex, and about 67-159% higher in relation to generic Acyclovir (depending on episodic or ongoing suppressive use). Most (about 70%) of the shift towards Famvir comes from a reduction in Valtrex prescriptions.

References

Accela Communications website, http://www.accelacommunications.com/PDFs/ACI_eDetail_BestPractices.pdf, Accessed October 29, 2012.

Altonji, J.G., Elder, T.E., and Taber, C.R., "Selection on observed and unobserved variables: assessing the effectiveness of catholic schools," *Journal of Political Economy*, 113(1): 151-184, 2005.

Bagwell, K., "The Economic Analysis of Advertising," in M. Armstrong and R. Porter, eds., *Handbook of Industrial Organization,* Volume III (Amsterdam: North-Holland, 2007).

Becker, G.S. and Murphy, K.M., "A simple theory of advertising as a good or bad," *Quarterly Journal of Economics*, 108:941–964, 1993.

Berndt, E., Bui, L., Reiley, D., and Urban, G., "Information, Marketing and Pricing in the US Antiulcer Drug Market," *American Economic Review*, 85(2):100-105, 1995.

Bhattacharya, J. and Vogt, G. "A Simple Model of Pharmaceutical Price Dynamics," *The Journal of Law and Economics*, 46(2):599–626, 2003.

Bureau of Labor Statistics website, http://www.bls.gov/cpi/data.htm, Accessed October 7, 2012.

Cameron C, Trivedi P. *Regression Analysis of Count Data*. Cambridge University Press: Cambridge, 1998.

Centers for Medicare and Medicaid Services website, http://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/index.html, Accessed October 7, 2012.

Dave, D., and Kelly, I., "Advertising," in: Anthony Culyer (Ed.), Encyclopedia *of Health Economics*, Elsevier Inc., Amsterdam, 2012, Forthcoming.

Dave, D., "Effects of Pharmaceutical Promotion: A Review and Assessment," *NBER Working Paper Series* No. 18830, National Bureau of Economic Research, Cambridge, MA, February 2013.

Dave, D. and Saffer, D., "Impact of Direct-to-Consumer Advertising on Pharmaceutical Prices and Demand," *Southern Economic Journal*, 79(1): 97-126, 2012.

David, G., Markowitz, S., and Richards-Shubik, S., "The Effects of Pharmaceutical Marketing and Promotion on Adverse Drug Events and Regulation," *American Economic Journal: Economic Policy*, 2(4):1-25, 2010.

Donohue, J.M., Cevasco, M., and Rosenthal, M.B., "A Decade of Direct-to-Consumer Advertising of Prescription Drugs," *The New England Journal of Medicine*, 357(7):673-668, 2007.

Fugh-Berman, A., and Ahari, S., "Following the Script: How Drug Reps Make Friends and Influence Doctors," PLoS Medicine, 4(4):621-625, 2007.

Gonul, F., Carter, F., Petrova, E., and Srinivasan, K. "Promotion of prescription drugs and its impact on physicians' choice behavior," *Journal of Marketing*, 65(3): 79-90, 2001.

Grande, D., "Limiting the Influence of Pharmaceutical Industry Gifts on Physicians: Self-Regulation or Government Intervention," *Journal of General Internal Medicine*, 25(1): 79:83, 2010.

Hilltop Institute, "Academic Detailing: A Review of the Literature and States' Approaches," University of Maryland-Baltimore County, 2009.

Iizuka, T, "What explains the use of direct to consumer advertising of prescription drugs?," *Journal of Industrial Economics*, 52(3):349-379, 2004.

Iizuka, T., and Jin, G.Z, "The Effect of Prescription Drug Advertising on Doctor Visits," *Journal of Economics and Management Strategy*, 14 (3):701-727, 2005.

Iizuka, T., and Jin, G.Z., "Direct to Consumer Advertising and Prescription Choice," *Journal of Industrial Economics*, 55 (4):771, 2007.

Kalyanaram, G. "The Order of Entry Effect in Prescription (Rx) and Over-the-counter (OTC) Pharmaceutical Drugs," *International Journal of Pharmaceutical and Healthcare Marketing*, 2(1):35-46, 2008.

Kalyanaram, G. "The Endogenous Modeling of the Effect of Direct Advertising to Consumers (DTCA) in Prescription Drugs," *International Journal of Pharmaceutical and Healthcare Marketing*, 3(2): 137-148, 2009.

Ling, D.C., Berndt, E.R., and Kyle, M.K. "Deregulating Direct-to-Consumer marketing of prescription drugs: Effects on prescription and over-the-counter product sales," *Journal of Law and Economics*, 45:691-723, 2002.

Manchanda and Chintagunta. "Responsiveness of Physician Prescription Behavior to Salesforce Effort: An Individual Level Analysis," *Marketing Letters*, 15(2/3):129-145, 2004.

McLachlan, G. and Peel, D., *Finite Mixture Models*, John Wiley and Sons:New York, 2000.

Mizik, N., and Jacobson, R., "Are Physicians 'Easy Marks'? Quantifying the Effects of Detailing and Sampling on New Prescriptions," *Management Science*, 50(12): 1704-1715, 2004.

Narayanan, S., Desiraju, R., and Chintagunta, P. "Return on investment implications for pharmaceutical promotional expenditures: the role of marketing-mix interactions," *Journal of Marketing*, 68(4): 90-105, 2004.

Narayanan, S., Manchanda, P., and Chintagunta, P. "Temporal differences in the role of marketing communication in new product categories," *Journal of Marketing Research*, 42: 278-290, 2005.

Nelson, P., "Information and consumer behavior," *Journal of Political Economy*, 78:311–329, 1970.

Pew Prescription Project, "Academic Detailing: Evidence-Based Prescribing Information," *Pew Prescription Project Fact Sheet*, April 2 2009.

Pomper, S., "Drug Rush," *Washington Monthly*, May 2000.

Rizzo, J., "Advertising and Competition in the Ethical Pharmaceutical Industry: The case of Hypertensive Drugs," *Journal of Law and Economics*, 42(1),89-116, 1999.

SK&A. "2010 U.S. Pharma Company Promotion Spending," *Cegedim Strategic Data Report*, http://www.skainfo.com/, January 2011.

SK&A. "2011 U.S. Pharma Company Promotion Spending," *Cegedim Strategic Data Report*, http://www.skainfo.com/, February 2012.

Stigler, G.J. and Becker, G.S. "De gustibus non est disputandum," *American Economic Review*, 67:76–90, 1977.

Wald, A., Selke, S., Warren, T. et al. "Comparative efficacy of famciclovir and valacyclovir for suppression of recurrent genital herpes and viral shedding," *Sexually Transmitted Diseases*, 33(9): 529-533, 2006.

Weiss, J., "Medical Marketing in the United States: A Prescription for Reform," *The George Washington Law Review*, 79(1): 260-292, 2010.

Wooldridge J. *Econometric Analysis of Cross Section and Panel Data*. MIT Press: Cambridge, 2001.

Wosińska, M. “Just what the patient ordered? Direct-to-consumer advertising and the demand for pharmaceutical products,” *Harvard Business School Marketing Research Papers No. 02-04*, 2002.

Table 1
Sample Means

Sample	All	Ever Detailed	Never Detailed	Ever Detailed Periods prior to Positive Detailing
New prescriptions of Famvir	0.1828	0.3640	0.0463	0.1571
	(0.7880)	(1.1173)	(0.3242)	(0.6561)
New prescriptions of Valtrex	0.2579	0.4671	0.1004	0.2924
	(1.1310)	(1.5603)	(0.5929)	(1.1244)
New prescriptions of Zovirax	0.0651	0.1127	0.0292	0.1054
	(0.3967)	(0.5294)	(0.2486)	(0.5197)
New prescriptions of generic Acyclovir	0.4718	0.7762	0.2427	0.5396
	(1.3816)	(1.8080)	(0.8732)	(1.4578)
Ever Detailed: Dichotomous indicator for whether the physician had ever received Famvir-related detailing	0.4295 (0.4950)	_	_	_
Any Detailing: Dichotomous indicator for whether the physician had received any Famvir-related detailing over sample period	0.4055 (0.4910)	0.9442 (0.2296)	_	0.7837 (0.4118)
Number of Famvir-related detailing visits by pharmaceutical sales representatives	0.1436 (0.5528)	0.3343 (0.8047)	_	_
Number of Famvir samples received by physician	0.8991 (5.0907)	2.0710 (7.5590)	0.0168 (0.7709)	0.3423 (3.2795)
Physician age	47.8 (13.2)	46.5 (13.1)	48.9 (13.1)	45.0 (14.1)
Physician gender: Male	0.7858 (0.4103)	0.7744 (0.4180)	0.7943 (0.4042)	0.7399 (0.4387)
Specialty: Dermatology	0.0281 (0.1652)	0.0496 (0.2171)	0.0119 (0.1084)	0.0352 (0.1843)
Specialty: Emergency medicine	0.0506 (0.2191)	0.0245 (0.1547)	0.0702 (0.2555)	0.0368 (0.1883)
Specialty: Obstetrician-Gynecology	0.0846 (0.2782)	0.0906 (0.2871)	0.0800 (0.2713)	0.1255 (0.3313)
Specialty: Other	0.4527 (0.4978)	0.2330 (0.4227)	0.6182 (0.4858)	0.3474 (0.4762)
Specialty: Primary Care	0.3841 (0.4864)	0.6023 (0.4894)	0.2197 (0.4141)	0.4550 (0.4980)
Observations	3,563,448	1,530,600	2,032,848	395,040

Notes: Means are reported for the sample period spanning 6/1997 - 5/1999, with standard deviations reported in parentheses. Number of observations listed is the maximum observations. For some variations, number of observations is slightly lower due to missing information. All differences are statistically significant at the 5% level.

Table 2
Effects of DTPP on Prescriptions
Poisson Regression

Model	1	2	3	4	5	6	7	8
Outcome	New Prescriptions for Famvir							New Prescriptions for Drug Class
Current Detailing	1.16804***							
	(0.01046)							
Current Detailing Square	-0.14670***							
	(0.00326)							
Current Detailing Elasticity	[0.16166]							
Detailing Stock		0.64331***	0.44126***	0.38376***	0.05177***	0.04121***	0.05350***	0.00793***
		(0.00852)	(0.00738)	(0.00861)	(0.00305)	(0.00327)	(0.00316)	(0.00135)
Detailing Stock Square		-0.03729***	-0.02378***	-0.01840***	-0.00181***	-0.00143***	-0.00210***	-0.00038***
		(0.00115)	(0.00088)	(0.00091)	(0.00023)	(0.00023)	(0.00031)	(0.00011)
Detailing Stock Elasticity		[0.32607]	[0.21902]	[0.20266]	[0.05030]	[0.04006]	[0.05146]	[0.00432]
Sampling Stock						0.00250***		
						(0.00033)		
Sampling Stock Square						-0.00001***		
						(0.00000)		
Sampling Stock Elasticity						[0.01714]		
Month & Year Indicators	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Physician Characteristics	No	No	Yes	Yes	No	No	No	No
Zip-code Indicators	No	No	No	Yes	No	No	No	No
Physician Indicators	No	No	No	No	Yes	Yes	Yes	Yes
Class Demand	No	No	No	No	No	No	Yes	No
Observations	3563448	2672586	2498490	2313396	977202	977202	977202	2060442

Notes: Coefficient estimates from Poisson regression models are reported. Standard errors are clustered at the physician-level, and reported in parentheses. Elasticity estimates, evaluated at the sample means, are reported in brackets. Physician characteristics include: age, age-squared, male, indicators for specialty, and indicators for practice type. Class Demand represents total new prescriptions for all herpes anti-viral drugs. Asterisks denote statistical significance as follows: *** p-value≤0.01; ** 0.01<p-value≤0.05; ***0.05<p-value≤0.10.

Table 3
Cross-Effects of Famvir Detailing on Prescriptions
Poisson Regression

Model	1	2	3	4	5	6	7	8	9
Outcome	New Prescriptions for Valtrex			New Prescriptions for Generic Acyclovir			New Prescriptions for Branded Acyclovir (Zovirax)		
Sample	All Specialties	Specialties with detailing levels > Mean	Primary Care Physicians	All Specialities	Specialties with detailing levels > Mean	Primary Care Physicians	All Specialities	Specialties with detailing levels > Mean	Primary Care Physicians
Detailing Stock	-0.01231***	-0.0129***	-0.00907**	-0.00001	0.000534	0.00242	0.01042**	.0064529	-0.00045
	(0.00275)	(0.00307)	(0.00392)	(0.00197)	(0.00212)	(0.00228)	(0.00525)	(0.0058328)	(0.00671)
Detailing Stock Square	0.00033	0.000332	0.00028	-0.00017	-0.000189	-0.00025	-0.00069	-.0005419	-0.00043
	(0.00024)	(0.000252)	(0.00033)	(0.00015)	(0.000160)	(0.00017)	(0.00044)	(0.0004612)	(0.00053)
Detailing Stock Elasticity	[-0.01061]	[-0.01718]	[-0.01119]	[-0.00015]	[0.00010]	[0.00209]	[0.01002]	[0.00783]	[-0.00283]
Month Indicators	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year Indicators	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Physician Indicators	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	1091124	589968	528534	1767024	806886	734436	557010	322308	279450

Notes: Coefficient estimates from Poisson regression models are reported. Standard errors are clustered at the physician-level, and reported in parentheses. Elasticity estimates, evaluated at the sample means, are reported in brackets. Physician characteristics include: age, age-squared, male, indicators for specialty, and indicators for practice type. Asterisks denote statistical significance as follows: *** p-value≤0.01; ** 0.01<p-value≤0.05; ***0.05<p-value≤0.10.

Table 4
Effects of Detailing Stock on Prescriptions
Intensive vs. Extensive Margin

Model	1	2	3
Outcome	Any New Famvir Prescriptions (NRX)	Number of New Famvir Prescriptions conditional on NRX>0	
Estimation	OLS	OLS	Poisson
Detailing Stock	0.01118***	0.01851***	0.00774***
	(0.00054)	(0.00537)	(0.00206)
Detailing Stock Square	-0.00035***	0.00008	-0.00006
	(0.00005)	(0.00046)	(0.00016)
Detailing Stock Elasticity	[0.06495]	[0.01881]	[0.01461]
Month Indicators	Yes	Yes	Yes
Year Indicators	Yes	Yes	Yes
Physician Indicators	Yes	Yes	Yes
Observations	2498490	218702	200520

Notes: See Table 2

Table 5
Effects of Detailing Stock on Prescriptions – Poisson Regression
Assessing Heterogeneous Effects

Model	1	2	3	4	5	6	7	8
Sample	Non-Managed Care MSA	Managed Care MSA	Males	Females	Private Insured Patients	Ever-Detailed Physicians	Primary Care Physicians	Specialties with Detailing Levels > Mean
Detailing Stock	0.04927***	0.06730***	0.05053***	0.05662***	0.06785***	0.05047***	0.04422***	0.0491***
	(0.00333)	(0.00771)	(0.00332)	(0.00759)	(0.00675)	(0.00306)	(0.00367)	(0.00330)
Detailing Stock Square	-0.00162***	-0.00291***	-0.00168***	-0.00253***	-0.00241***	-0.00176***	-0.00163***	-0.00165***
	(0.00025)	(0.00063)	(0.00025)	(0.00057)	(0.00059)	(0.00023)	(0.00028)	(0.000241)
Detailing Stock Elasticity	[0.04829]	[0.06291]	[0.05098]	[0.04578]	[0.05561]	[0.07523]	[0.05784]	[0.06810]
Month Indicators	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year Indicators	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Physician Indicators	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	803484	173718	794304	182898	309186	606492	511002	581850

Notes: See Table 2

Table 6
Effects of Detailing Stock on Prescriptions – Poisson Regression
Effects based on Market Volume

Model	1	2	3	4	5
Sample	Market Volume Quintile 1	Market Volume Quintile 2	Market Volume Quintile 3	Market Volume Quintile 4	Market Volume Quintile 5
Detailing Stock	0.10428***	0.04645***	0.04298***	0.04413***	0.04122***
	(0.00931)	(0.00683)	(0.00606)	(0.00626)	(0.00783)
Detailing Stock Square	-0.00441***	-0.00138**	-0.00159***	-0.00124***	-0.00109**
	(0.00105)	(0.00062)	(0.00045)	(0.00040)	(0.00055)
Detailing Stock Elasticity	[0.05193]	[0.05380]	[0.06318]	[0.08244]	[0.09926]
Month & Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Physician Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	493794	195606	129078	82494	43704

Notes: See Table 2