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EFFECTS OF PHARMACEUTICAL PROMOTION: A REVIEW AND ASSESSMENT

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ABSTRACT

This review discusses the role of consumer-directed and physician-directed promotion in the pharmaceutical market, based on the classic conceptual framework of whether such promotion is "persuasive" and/or "informative". Implications for public health and welfare partly depend on whether, and to what extent, advertising: 1) raises "selective" or brand-specific demand versus "primary" or industry-wide demand; 2) impacts drug costs; and 3) impacts competition. Empirical evidence from the literature bearing on these effects is surveyed. These studies show that pharmaceutical promotion has both informative and persuasive elements. Consumer advertising is more effective at enlarging the market, educating consumers, inducing physician contact, expanding drug treatment, and promoting adherence among existing users. Physician advertising is primarily persuasive in nature, effectively increasing selective brand demand. Evidence bearing on the effects of promotion on competition and prices is more limited. However, there is no strong evidence that drug promotion deters entry, and there is some suggestive evidence that it may even be mildly pro-competitive. With respect to costs, some studies suggests that consumer advertising may weakly raise the average wholesale price, which is a manufacturer's list price, but there is no strong indication that either consumer- or provider-directed promotion substantially raises retail-level prices. However, this is not to imply that potential promotion-driven substitution from non-advertised to advertised drugs cannot have effects on total drug costs. While most of these effects point to potential welfare improvements as a result of pharmaceutical promotion, there is also evidence that consumer ads may induce overuse and overtreatment in certain cases. Market expansion, overtreatment and shifting brands for non-therapeutic reasons further raise the concern of a sub-optimal patient-drug match at least for some marginal patients. A comprehensive evaluation of the welfare effects of pharmaceutical promotion requires a balanced assessment of these benefits and costs.

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I. Introduction

Between 1980 and 2010, expenditures on prescription (Rx) drugs in the U.S. increased from $53 per person to $831 per person, representing an increase of 1,468% (see Figure 1). Since around 1995 spending on Rx drugs has outpaced the growth in NHE, doubling its share to 10%, and making it one of the fastest growing components of health care costs (see Figure 2). Spending on Rx drugs has leveled off in recent years due to patent expiration on certain major drugs that are not replaced by new on-patent drugs. 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). Since then, promotional spending has declined by about 9% to $29.3 billion in 2010 (SK&A 2012), in part due to patent expiration on some major drugs such as Advair, Prevacid, and Lipitor.

Promotion of prescription drugs is generally limited to drugs on patent. It includes direct-to-consumer advertising (DTCA) on broadcast and print media as well as direct-to-physician promotion (DTPP) through visits by company representatives to physician offices (known as detailing), free samples provided to physicians and advertising in professional journals. While DTPP still comprises most of the promotional budget, the largest relative increase in promotion between 1995 and 2005 resulted from the expansion of DTCA into broadcast media. The share of total promotional spending allocated to DTCA increased from less than one percent in the early 1990s to 8.6% in 1996 to 14.5% in 2003 (see Figure 3), and have remained relatively stable since.

Currently only the U.S. and New Zealand permit advertising directed at consumers. Help-seeking ads, which describe a disease or condition but do not recommend specific drugs,

and "reminder advertising", wherein the advertising states the brand name without making any health claims, are generally permitted in several other countries. The expansion of DTCA in the U.S. was precipitated by the Food and Drug Administration's (FDA) clarification of the rules governing broadcast advertising in August 1997 and August 1999, making it feasible for companies to promote via television and radio advertisements. These new regulations remain a controversial policy and are facing increased scrutiny from Congress and consumer groups. At the heart of the debate is whether pharmaceutical promotion and advertising are welfare-promoting. The pharmaceutical industry claims that both consumer-directed and physician-directed advertising educates patients and providers on potential treatment options, opens up lines of communication between the patient and the physician, and can even increase patient-physician contact or expand appropriate treatment for undertreated conditions, consistent with an 'informative view' of advertising. Some congressional leaders have contended that DTCA raises prescription drug costs, consistent with brand differentiation and a 'persuasive view' of advertising, and requested that the policy be revisited.[1] Some consumer groups maintain that consumers may be harmed by misleading advertising and that the recent expansions in DTCA are responsible for the increases in expenditures on prescription drugs.[2]

Growth in prescription drug spending is broadly driven by increases in utilization and price, and shifts in the composition of drugs being used, all of which may be impacted by marketing. A comprehensive assessment regarding the welfare effects of pharmaceutical advertising and promotion requires information on three broad but related issues: 1) effects on

[1] A popular proposal among critics of DTCA in Congress is to impose a moratorium on advertisements during the first two years of a drug's launch. Original provisions in the bill requiring mandatory moratoriums on the advertising of newly approved prescription drugs were removed, on the grounds of commercial free speech, when the Food and Drug Administration and Revitalization Act was signed into law in 2007.

[2] For instance, Families USA (July 2003) claimed that prescription drug advertising has been disproportionately focused on newer, higher-priced products and linked to an increase in the use of those products. See http://www.familiesusa.org/assets/pdfs/Out_of_Boundsab79.pdf

primary industry-wide vs. selective brand-specific demand; 2) effects on price; and 3) effects on competition. The next section briefly discusses the historical background on pharmaceutical promotion followed by a conceptual framework of advertising and promotion to help guide welfare implications, before turning to the empirical evidence with respect to each of the three issues noted above.

II. Background

U.S. Congress passed the 1938 Federal Food, Drug and Cosmetic Act following the death of 105 patients due to the use of diethylene glycol as a solvent for an antimicrobial sulfanilamide medication.[3] The Act shifted the focus of the Food and Drug Administration (FDA) to serve as a regulatory agency involved with safety and the evaluation of new drugs. The FDA was given authority over the labeling of pharmaceutical products, though the Federal Trade Commission (FTC) retained control over drug advertising. Prior to 1938, DTCA was the primary form of promotion, with patented medications being advertised mostly in newspapers. Following 1938, however, DTCA declined sharply due to the increased practice of requiring prescriptions for certain drugs, while previously most medications were readily available over the counter.

The 1962 Kefauver-Harris Amendments to the Federal Food, Drug and Cosmetic Act shifted jurisdiction on regulating drug promotion from the FTC to the FDA and outlined the basic requirements for acceptable prescription drug marketing. Prescription drug promotional materials cannot be false or misleading, must provide "fair balance" coverage of risks and benefits of using the drug, must provide a "brief summary" of contraindications, side effects, and effectiveness, and must also meet specific guidelines for readability and size of print. For a number of years, the FDA interpreted the "brief summary" provision as requiring the advertiser

[3] See Berndt (2006), Iizuka (2004), and Wilkes, Bell, and Kravitz (2000) for expanded accounts on the historical background and trends surrounding DTCA. Also see Wax (1995) for an account of the sulfanilamide disaster and the subsequent passage of the Federal Food, Drug, and Cosmetic Act.

to provide the detailed information contained in the drug's FDA-approved product labeling, thereby confining consumer-directed advertising to newspapers and magazines.[4]

Expansion of advertising into broadcast media was precipitated by the FDA's clarification of its regulation of consumer-directed advertising, particularly for broadcast advertisements. After a test period, debate, and request for public comment starting in 1995, the FDA approved the broadcast DTCA draft guidance in August 1997.[5] It eliminated the requirement that ads present the entire "brief summary" taken from the product label insert. In August of 1999, the FDA further clarified the risk information requirements. Advertisements needed only to include "major statements" of the risks and benefits of the drug, along with directions to information sources in addition to a physician, such as a toll-free phone number, a website, or a print advertisement. This clarification of the requirements for adequate disclosure removed a major barrier that had initially made television and radio advertising infeasible and had initially relegated advertising directed at consumers to print media only.

While there was no broadcast advertising till 1993, it now comprises the primary form of DTCA – amounting to $2.55 billion in 2005.[6] Between 1996 and 2000, DTCA was the fastest growing component of pharmaceutical promotion, growing at an average annual rate of 33% for gastrointestinal, cholesterol, insomnia, and anti-arthritic/analgesic drugs. In comparison,

[4] There were two conditions under which firms could bypass the "brief summary" provision: 1) if the advertising were "help-seeking" and mentioned only disease symptoms and did not mention any drug name, or 2) if the advertisement is a "reminder" and mentions the drug name or its dosage without specifying what the drug is intended to treat.

[5] Under the regulations, pharmaceutical companies are required to submit all drug advertisements to FDA for review when they are first disseminated to the public. Donohue et al. (2007) show that in the context of regulatory changes requiring legal review before issuing letters, the number of letters sent by the FDA to pharmaceutical manufacturers regarding violations of drug-advertising regulations actually fell from 142 in 1997 to only 21 in 2006, a period when DTCA was increasing at annual double-digit rates. This has led some to suggest that the FDA's oversight of pharmaceutical DTCA has limitations. For instance, some pharmaceutical companies have repeatedly distributed new misleading advertisements for the same drug, and some companies have failed to submit in a timely manner all newly disseminated advertisements to the FDA for review (General Accounting Office 2002).

[6] Some of the earlier broadcast DTCA, prior to the draft guidance, constituted "reminder ads" that mentioned the drug name, though not the indication, and thus bypassed risk-disclosure requirements.

detailing and sampling grew at annual rates of 12-13%, whereas professional journal advertising remained virtually unchanged (Dave and Saffer 2012). While the FDA's shift in guidelines specifically applied to broadcast advertising, there was also an increase in non-broadcast advertising starting in 2000. This may be indirectly related to the FDA's new guidelines which required only "major statements" of the risks and benefits of the drug along with directions to alternate information sources for more complete information. The feasibility of using television and radio advertisements may have raised the marginal product of other non-broadcast forms. Indeed, broadcast ads often direct consumers to concurrent ads in magazines or newspapers for more complete information on the drug's usage and side effects.

Table 1 lists the top 25 consumer-advertised drugs in 2010, which account for about two-thirds of total DTCA -- suggesting a highly skewed distribution in consumer ad spending. Drugs intended to treat chronic conditions such as cardiovascular, mental health, respiratory, and erectile dysfunction conditions tend to be among the most heavily-advertised. Recent years have witnessed a downturn in DTCA (see Figure 2), and total pharmaceutical sales force in the U.S. has been cut by about 30% from its peak. These cuts partly reflect fewer drug launches compared to the late 1990s, and an increasing share of new drugs that are targeted at specialist physicians (for instance, cancer and orphan drugs developed specifically to treat rare conditions). Optimal promotion of such drugs may not include DTCA and, by definition, needs fewer sales reps than the major primary-care drugs of the 1990s.

III. Conceptual Framework

It is often presumed that the average consumer is responsive to advertising and promotion.[7] However, one of the key questions with respect to advertising by firms in markets for healthcare inputs is whether advertising raises "selective" or brand-specific demand versus

[7] This section draws on Bagwell (2007), which provides a comprehensive review of the economics of advertising.

"primary" or industry-wide demand (Borden 1942). The answer to this question has normative implications and relevance for public health. For instance, is advertising by the pharmaceutical industry combative and solely reflective of a market share transfer or does it also convey information and lead to an overall expansion of the market? As a starting point, it is helpful to draw upon three principal views that have emerged with respect to why consumers may respond to advertising: 1) persuasive, 2) informative, and 3) complementary.

Chamberlin (1933) integrates advertising into his theory of monopolistic competition, observing that advertising can help firms to differentiate their products and generate an outward shift in firm-level demand. Advertising impacts demand by altering consumers' tastes and preferences. Under this "persuasion" hypothesis, brand-level demand would not only shift outward in response to advertising but also become relatively less elastic, possibly leading to higher prices. Advertising-induced product differentiation and creation of brand capital may deter entry and enhance the monopolistic power of incumbent firms, especially if these established firms also enjoy scale economies in advertising and production (Kaldor 1950). Thus, under the persuasion view, advertising can have significant anti-competitive effects, a point which was also emphasized by Robinson (1933).

Chamberlin (1933) also pointed to the transfer of information to consumers as another explanation for why consumers respond to advertising. This informative view of advertising took on a formal expression in Ozga (1960) and Stigler (1961). In markets characterized by imperfect information, advertising can effectively reduce search costs by conveying direct or indirect information to consumers regarding the existence, quality, price and other attributes of products. With respect to pharmaceuticals, for instance, advertising may inform individuals of treatment options that they did not know existed and help individuals to diagnose their symptoms

and seek out medical care. As Bagwell (2007) notes, in such markets, advertising emerges as an endogenous response and solution to the information asymmetry. In contrast to the persuasive view, advertising plays a more constructive role under the informative view, and may also have pro-competitive effects. As consumers receive low-cost (relative to incurring search costs) information on products and brands, the firm's demand becomes relatively more elastic and price dispersion in the market is reduced. Advertising can thus promote competition among incumbent firms and facilitate the entry of new firms as well as the introduction of new products.

Nelson (1974) contends that even when advertising does not hold direct information content, it may still signal indirect information regarding product quality and firm attributes. For instance, advertising can signal that a firm is an efficient producer since these firms would benefit the most from expanding demand. Advertising can also enhance the match between products and buyers in markets where consumers have heterogeneous valuations. With respect to prescription drugs, advertising can remind patients to take their medications on time and as prescribed, and contribute to patient adherence. Thus, advertising may help consumers recollect their previous experience with the product and lead to repeat-business. Since this effect is more valuable for firms producing high-quality products, advertising may thus indirectly signal quality even for new consumers.

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 only after consumption. Advertising addresses an informational imbalance for experience goods by providing indirect information content regarding quality, and advertising intensity is thus predicted to be higher for experience goods. In contrast, advertising for search goods (for instance, eyeglasses, consumer electronics, credit

cards) would be focused on providing direct information regarding price, location, availability, and product attributes.[8]

While the persuasive and informative views provide conflicting assessments of the role of advertising, the third view of advertising provides a framework under which advertising is complementary to the advertised product. That is, advertising does not need to exert any direct influence on consumer preferences, and it may or may not possess information content. Within a household production framework, Stigler and Becker (1977) model the advertised product with its associated advertising expenditures as inputs into the production function for each final commodity, implying a complementarity between the advertised product and its advertising. Under this framework, a higher level of prescription drugs advertising can raise demand since the consumer now believes that he can obtain a greater output of the final commodity (health) from a given input of the advertised good (Rx drugs). In a related but separate framework, Becker and Murphy (1993) directly model advertising as an input into the individual's utility function. Advertising raises demand in this framework by increasing the marginal utility of the advertised good.[9]

Both of these paradigms, which impart a complementary role to advertising, also bridge back to the informative view. For instance, if advertising enables consumers to produce information at lower cost (Verma 1980), then consumers can indeed more efficiently convert

[8] Darby and Karni (1973) also find it useful to distinguish a third category of goods that have "credence" attributes, for which the consumer is unable to accurately evaluate quality even post-consumption. This market failure of imperfect information for experience and credence goods also potentially gives firms an incentive to engage in misleading advertising claims (Darby and Karni 1973; Nelson 1974). Where market-based mechanisms are unable to deter deceptive advertising, there is a role for government regulation and publicly-funded dissipative counter-advertising. Posner (1973) notes several mechanisms that may deter misleading advertising claims, including consumer-based incentives to ascertain product claims, reputational loss to sellers who practice deceptive advertising, incentives for rival firms to counteract deceptive advertising, and legal recourse available to consumers. See Cawley, Avery, and Eisenberg (2011) for a study of promotion and deceptive ads for OTC weight-loss products from the context that such products are characterized as credence goods.

[9] Note that this complementarity follows from the fact that there does not exist a separate market for advertising messages – considerable transactions and monitoring costs make it infeasible to separately sell advertising to consumers.

market goods into valued final commodities, as assumed in Stigler and Becker (1977). And, even if advertising in uninformative, it may still play a constructive role since consumers may value it directly, as assumed in Becker and Murphy (1993).

The upshot of this discussion is that no single view of advertising is applicable in every setting. Furthermore, from a public health standpoint, the debate centers around whether advertising reflects a brand-switching process or a market expansion process, especially in relation to the market for health inputs – or in different terms, whether advertising is combative (predatory) or cooperative.[10] Since advertising can affect both selective (brand-centric) as well as primary (market) demand under all three views, the question cannot be resolved based on theory alone and empirical evidence needs to bear upon the specific demand effects of advertising in various markets. With that said, markets for over-the-counter (OTC) and prescription (Rx) medications inputs have some predominant experience attributes. Thus, advertising intensity for the pharmaceutical industry (about 20% of sales) tends to be higher relative to the average industry (4-5%). These views of advertising also highlight potential effects on price, which depend on the extent to which advertising expenditures raise operating costs, affect price elasticity of demand, and allow firms to take advantage of scale economies. The concentration effects of advertising – that is, whether it facilitates entry or whether it augments the monopoly power of established firms – depends on whether advertising is purely persuasive in nature and leads to spurious brand differentiation or whether it redresses imperfect information and makes demand more elastic.

[10] While this is not to suggest that all brand-switching ads are socially wasteful (since some brand-switching may represent a better match of product attributes and consumer demand) and all market expanding ads are good (especially since ads that expand the market for unhealthy inputs such as excessive alcohol consumption or cigarettes, or fast-food, may have adverse internalities as well as externalities), this dichotomy presents a useful starting point to frame some of the effects of advertising.

It should also be noted that these different views of advertising may fit different forms of drug promotion, and the frameworks are not necessarily mutually exclusive. For instance, detailing plays a role in educating providers about newer drugs and their attributes and thus may have information value early in a product's life cycle, whereas later in the life cycle its role is predominantly persuasive, chiefly relegated to delivering samples and reminders. DTCA and detailing, by differentially targeting consumers versus providers, may also "by definition" play different roles in affecting primary versus secondary demand. Thus, there may be a great deal of heterogeneity with respect to how consumer- and physician-directed promotion affects demand, with possible interactions with each other as well as with competition and drug characteristics. Since DTCA (and to some extent detailing) can potentially increase sales without the firm having to offer a lower price or superior quality in trying to get their drug onto a preferential position with the insurer, DTCA may have the ability to undermine the insurer's formulary (Wosińska 2002). Thus, interactions between DTCA effects and the drug's formulary position as well as between DTCA and price are also possible.

IV. Empirical Evidence

To inform on whether promotion impacts primary demand (market expansion) versus selective demand (business stealing and brand-specific demand), econometric studies have estimated the effects of DTCA and DTPP on pharmaceutical sales, patient adherence, the demand for primary care, and, in a few instances, on pharmaceutical prices. Estimating causal effects of advertising and promotion on sales and price is complicated by potential bias due to structural endogeneity or reverse causality; promotion may affect demand, but promotional spending may also be a function of revenues.

In addition, there is potential bias from statistical endogeneity or selection; observed and unobserved heterogeneity across prescription drugs may be driving promotion as well as sales, and prices. In the multi-period optimization framework considered by Bhattacharya and Vogt (2003), the firm simultaneously manages drug price and promotion to determine sales and to 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. As knowledge is costly to acquire, physicians' prescribing patterns tend to be sticky and consumer use may also be sticky especially for chronic conditions. In subsequent periods, promotion can therefore be decreased to lower costs, and price can be raised to increase revenue. Thus, in addition to sales, price, and promotion affecting each other, they are also partly governed by the drug's life cycle and potentially by other drug-specific unobservables, including formulary placement and the implied consumer cost-sharing.

Alluding to such potential selection effects, Iizuka (2004) studies 169 brand-name drugs over 1996-1999, and finds evidence that higher quality drugs (as measured by the FDA's priority rating[11]) are more likely to engage in DTCA. Another determinant of DTCA is a larger potential market size, measured by the prevalence rate (treated or untreated) of certain chronic conditions from the National Health Interview Surveys. DTCA spending also tends to be lower when there is a generic competitor on the market. Thus, advertised drugs are systematically different from non-advertised ones, and some of these differences may also impact sales and price, subsequently confounding the causal relationship between promotion and demand. Some of the

[11] Until 1991, The FDA assigned three quality ratings for new drugs: 'A' and 'B' for those drugs that respectively offer significant and moderate therapeutic gains compared to existing drugs on the market; and 'C' for those drugs that are essentially equivalent, in terms of therapeutic gains, to those on the market. In 1992, these ratings were replaced by 'priority' (previously 'A' and 'B' ratings) and 'standard' (previously 'C' rating).

more sophisticated of the studies address these concerns through instrumental variables and fixed effects.

Most studies have also estimated an "average" response to promotion and very few studies have considered heterogeneity in the effects with respect to formulary placement, drug characteristics, or advertising medium.

A. Demand Effects

1. Market Expansion vs. Product-level Effects of DTCA

Rosenthal et al. (2003) study brands in five therapeutic classes using an aggregated U.S. monthly time series from August 1996 through December 1999. They employ an instrumental variables (IV) methodology to account for the endogeneity of DTCA and physician promotion. Their results indicate that the primary impact of DTCA lies in expanding the total market size rather than affecting product market share. Specifically, the study finds that, at the level of the therapeutic class, DTCA spending positively impacts sales with an estimated elasticity of 0.10. While they do not report any significant effects of brand-specific DTCA (or detailing) on brand-specific market shares, they do caution that it may be "premature to conclude that DTCA only affects class level sales, and not individual product sales". Specifically, the models estimate only a contemporaneous effect owing to the short span of the time-series, which would be a lower-bound estimate if advertising also has lasting durable effects on sales. The effect of advertising in the prescription drug market may be especially prolonged due to the fact that selling a prescription drug is a multi-stage process, with time lags between advertising exposure, scheduling a physician visit, and obtaining and filling the prescription. Wosińska (2002) shows the importance of the drug formulary in driving DTCA effects (with advertising having a greater effect on demand for drugs that have a preferential position on the insurer's formulary list), and

notes that the inability to differentiate across the formulary status may also explain why Rosenthal et al. (2003) do not find a market share effect of DTCA.

The specifications in Rosenthal et al. (2003) include class fixed effects, but do not control for unobserved heterogeneity across drugs within a class through drug-specific fixed effects. The study uses time to patent expiration, an indicator variable for 1997 (reflecting the FDA's change in policy), and interpolated monthly values of television advertising costs per minute as IVs that can plausibly be excluded from the sales equation. Some studies, however, have shown that the drug's life cycle is an important determinant of sales, advertising, and prices, which suggests that the product's life cycle may not be an appropriate instrument for advertising and promotion (Bhattacharya and Vogt 2003; Dave and Saffer 2012). Nevertheless, Rosenthal et al. (2003) provide one of the earliest and seminal analyses of DTCA following its resurgence in the late 1990s, and several subsequent studies confirm their market-expansion effect of DTCA.

Iizuka and Jin (2005) merge individual-level data from the National Ambulatory Medical Care Surveys over 1995-2000 with monthly DTCA data. Similar to Rosenthal et al. (2003), they use drug-class fixed effects, and so their effect is identified from within-class variation in DTCA over time. They also use an IV procedure, employing the same drug company's DTCA expenditures in other unrelated drug classes as an instrument for DTCA in a particular drug class. Consistent with a market-expansion effect, they find that a higher stock of DTCA spending (which includes current advertising and a depreciated sum of past advertising) is associated with an increased number of physician visits, especially post-1997. Each $28 increase in DTCA leads to an additional physician visit within a year where an Rx drug from the class is prescribed. Liu and Gupta (2011) use monthly-level patient visit data, relating to high cholesterol diagnoses and drug requests, spanning June 2002 through April 2004. They match

local and national-level DTCA expenditures on statins, and estimate IV-based specifications with market-level fixed effects.[12] Their results indicate that DTCA positively impacts the number of visits to physicians by newly-diagnosed patients, and that the effect is larger on drug visits than non-drug visits. Television DTCA has strong effects on underserved populations, such as individuals on Medicaid. Bradford et al. (2006a) further confirm this market expansion effect for DTC advertising of osteoarthritis drugs. Specifically, they analyze monthly clinical information on 57 primary care practices between 2000-2002, merged with brand-specific DTCA on local and network television. Their results also show that ads for Vioxx and Celebrex increased the flow of osteoarthritis patients into physician practices.

Meyerhoefer and Zuvekas (2008) study how DTCA shifts the demand curve for newer-generation anti-depressants, based on data from the 1996-2003 Medical Expenditure Panel Surveys matched with quarterly-level local and national DTCA expenditures. They estimate the class DTCA elasticity to be 0.16, suggesting that consumer ads shift the demand curve outwards and increase the probability that an individual will initiate use of anti-depressants. This effect is particularly strong when out-of-pocket medication costs are low. In support of the information view of advertising, they also find that DTCA rotates the demand curve counter-clockwise and increases the magnitude of the price elasticity of demand. The study does not find any effects of DTCA on the intensive margin – that is, on utilization levels among those already taking anti-depressants.

The market expansion effect suggests that some consumers, whose medical conditions were previously undiagnosed and undertreated, may benefit from the information provided by DTCA; consumers can become aware of new treatments for their symptoms and be incentivized

[12] The study uses as the instrument the monthly average DTCA expenditure in a particular market area across all pharmaceutical firms less expenditure on statins.

to seek out physician care. However, the market expansion effect may also partly reflect inappropriate care or overtreatment. Donohue, Cevasco, and Rosenthal (2007) note that promotional campaigns typically begin within a year of a prescription drug's market entry, and thus advertising may increase the use of drugs with uncertain safety profiles. Pointing to perhaps such an increase in misuse, David et al. (2010) find that higher levels of DTCA lead to increased reporting of adverse medical events for drugs related to certain conditions such as arthritis and depression, whereas detailing reduces the adverse event rate for high cholesterol and allergy drugs. They conclude that the effect of promotion and advertising in improving communication between patients and physicians may be welfare-enhancing if physicians can identify who is the best match for treatment. This is feasible in the case of cholesterol and allergy medications by the existence of simple diagnostic tests. In cases where there is greater uncertainty regarding diagnosis or acceptable standards for care, advertising and promotion may hinder the role of the physician as a mediator between consumer-directed promotion, consumer request, and proper use.

In addition to a market expansion effect, a few studies do find evidence of some DTCA-induced brand-switching. Bradford et al. (2006a), above, find that advertising of Vioxx increased the likelihood that patients received Vioxx but also had a marginal positive impact on Celebrex prescriptions; there was no own-effect from Celebrex ads. They conjecture that this differential effect may be due to the detailing intensity across the drugs (which is unobserved in their study) that may be potentially correlated with the effectiveness of DTCA. Kalyanaram (2009) studies 14 advertised drugs from three therapeutic classes, based on monthly records from 1998 through 1999. He treats DTCA as endogenous, using the lagged market share of the drug and the average cost of consumption of the drug as instrumental variables for DTCA, and finds

that both consumer-directed and provider-directed advertising significantly and positively affect the brand's market share.[13] The estimated market-share elasticity with respect to DTCA is 0.21 and that with respect to DTPP is higher at 0.62. Wosińska (2002), in a study of prescription claims for cholesterol drugs for Blue Shield of California over the period 1996-1999, also finds that current DTCA raises market share. However, this effect is limited to drugs that have preferential status on the insurer's formulary. Thus, it is possible that physicians suggest and prescribe advertised formulary drugs when patients inquire about ads for drugs that are not on the formulary. Specifically, a $1 million increase in consumer advertising is found to increase market share by 0.5% for preferred formulary drugs.

Ling, Berndt, and Kyle (2002) assess whether marketing of Rx heartburn drugs confers future spillover benefits to their OTC versions, consistent with Nelson's (1974) contention that advertising may signal indirect information regarding product quality and firm attributes. Specifically, they study monthly records between January 1988 through June 1999 for Pepcid, Tagamet, Zantac, and Axid, all of which switched from Rx to OTC in 1995-1996. Based on an IV methodology, they find positive effects of DTC marketing of the OTC drugs on own market share with the elasticity becoming larger for later entrants[14], though they do not find such own-effects for DTC marketing of the Rx drugs. However, they do find that DTC marketing of Rx drugs spills over into higher OTC sales for Zantac and Axid (later entrants into the OTC market) but not for Tagamet (an earlier Rx-to-OTC switch).

Dave and Saffer (2012) utilize monthly data on all prescription drugs in four major therapeutic classes from 1994-2005, thereby exploiting the period enveloping the FDA's shift in

[13] The study only considers contemporaneous effects. However, to the extent that DTCA may have lasting effects on market share and also impact the product's price, the IVs may not be orthogonal of the error term in the market share equation.

[14] This is consistent with the Dorfman-Steiner theorem, discussed later. As later entrants typically have a higher marketing intensity (relative to sales), this translates into a higher marketing-demand elasticity, as long as the price elasticity is similar across entrants.

regulations as a natural experiment and exogenous shock to consumer advertising. Similar to Iizuka and Jin (2005), they construct a stock of depreciated DTCA spending over the past year.[15] They employ drug-level fixed effects to account for unobserved time-invariant heterogeneity across drugs and potential selection into DTCA due to unobserved differences in quality and other stable factors. The models further account for various time-varying confounders including physician detailing and sampling, the drug's life cycle, competitive advertising, generic competition, and FDA approval of new indications for the drug and labeling/marketing warnings. This study further underscores the point that it is important to separately analyze the effects of broadcast and non-broadcast DTCA due to differences in their content, growth trends (since the FDA's policy change specifically impacted broadcast DTCA), and potentially differential marginal impacts. They find that broadcast DTCA does significantly impact own-sales and market share with a relatively small elasticity of 0.10., though this response is higher relative to non-broadcast DTCA. This study also finds some evidence that class-level DTCA may raise sales for the non-advertised drugs. Assuming that physicians are prescribing an equally effective drug, this may be a spillover benefit of DTCA in some cases since non-advertised drugs tend to be older and also cost less.

Prior studies, which at times found conflicting evidence on the impact of own-DTCA on own-sales, may have been confounded by aggregating broadcast and non-broadcast forms. In periods predating the FDA's policy shift, virtually all DTCA was relegated to non-broadcast media, whereas starting in 1998 and 1999 advertising in broadcast media became the primary form of DTCA. Therefore, the effect of total DTCA, being a weighted average of the effect of

[15] They assume a monthly depreciation rate of 0.1, which is consistent with 0.1-0.2 range estimated by Iizuka and Jin (2005) and Ling et al. (2002). With a depreciation rate of 0.1, about 72% of the impact of advertising has depreciated by the 12th month. Studies of consumer goods generally find that the effects of past advertising are fully exhausted within a year (Bagwell 2007).

the two separate forms, would be expected to vary depending on the time period under study and the relative composition of total DTCA between non-broadcast and broadcast media.[16]

Directly bypassing the potential endogeneity of advertising, Kravitz et al. (2005) examine how DTCA impacts the prescribing behavior of antidepressants in a randomized control trial (RCT) setting. Standardized patients, mostly professional actors, were randomly assigned to make 298 unannounced visits to family physicians and general internists. The patients made a specific brand request (referring to a DTC advertisement), a general drug request, or no request. Physicians prescribed antidepressants for the patients portraying general depression in 54% of the visits, including 76% of visits where the patients made a general request for a drug, 53% of visits where a specific drug was mentioned, and 31% where no drug was mentioned by the patient. Patients were prescribed Paxil in 27% of the visits where they explicitly mentioned the drug, compared to 4% where there was no request for a drug and 2% where the patients made a general request for a drug. For patients portraying adjustment disorder, where anti-depressants confer little or no benefits, 37% of patients requesting Paxil received a prescription for the drug, compared to 10% of patients who made a general drug request and none for patients who did not request any drugs. This study points to the role of brand-specific DTCA in raising own-demand by leading to a prescription for that brand, as well as in raising overall demand for prescription drugs in the therapeutic class. The authors conclude that DTCA "may have competing effects on

[16] For instance Kalyanaram (2009) finds a small but significant impact of DTCA on own market share, whereas the estimated effects of DTCA on market share are generally insignificant and inconsistent in Rosenthal et al. (2003). While the differing results may partly be driven by methodology and different drug therapeutic classes under study, the difference may also be attributed to the sample period under consideration. Kalyanaram examines data from 1998 and 1999, when broadcast DTCA was becoming more prevalent and overtaking non-broadcast DTCA, whereas the study by Rosenthal et al. also included time periods from 1996 and 1997 when non-broadcast DTCA was still the primary form of consumer-directed advertising. Ling et al. (2002), based on a sample of four heartburn Rx drugs over January 1988 through June 1999, also find that DTC advertising of the Rx brand had no significant impact on own Rx market share. If it is specifically broadcast DTCA that has a larger impact on sales, then it is not surprising that the aggregated effect may be close to zero in studies that consider DTCA during periods prior to the late 1990s.

quality, potentially averting underuse and promoting overuse". A focus group study of 152 primary care physicians, who had participated in this RCT, concluded that patients' request for medication prompted some of the participants to err on the side of overtreatment relative to a careful review of the clinical indications (Tentler et al. 2008).

Observational and survey-based studies suggest that DTCA can educate consumers about health conditions and available treatments, though it may also have the potential to be misleading or uninformative. In a content analysis of 320 distinct consumer-directed ads, Wilkes et al. (2000), for instance, note that the ads tend to minimize the negative features of the drugs, with side-effects often relegated to the end or "buried in the narrative," and over-emphasize "innovativeness" despite many new drugs offering few benefits over existing drugs and having less well-understood safety profiles. However, broadcast ads are required to direct the consumer to other concurrent ads in magazines or newspapers for more complete information on the drug's indications and contraindications. The authors further report that less than 30% of the ads provide valuable sources of information with regards to the specific condition, such as the causes or risk factors, prevalence, clarifications of misconceptions, or supportive treatments through changes in lifestyle, suggesting that the educational quality in these ads is highly variable. However, the study also notes that DTC ads motivate discussions between patients and their physicians, which may involve physicians reeducating the patient with respect to the ad message and their expectations, or the discussion can focus on specific brand-name drugs, trivial complaints, and procurement concerns in which case the discussion may detract from more meaningful conversations regarding the patient's symptoms and full range of treatment options. Thus, DTCA can mediate the patient-physician relationship through such reeducation as well as likely fulfillment of the patient's request for a specific drug.

Hollon (2005) summarizes some of the survey-based evidence and notes that between 25-33% of adults annually have had a discussion with their physician regarding a health issue after having seen an advertisement. While DTCA can stimulate a new diagnosis (about 25% of patients with DTCA visits), potentially leading to treatment of previously under-treated conditions, almost 80% of physicians report that DTCA encourages patients to seek treatments that they may not need (Hollon 2005). Surveys of consumers and primary-care physicians suggest that the majority of drug-specific requests induced by DTCA are fulfilled (Mintzes et al. 2003; Hollon 2005).

2. Effects on Adherence

Additional evidence on the demand effects of DTCA is also provided by econometric studies that examine patient adherence. Consistent with the informative view of advertising, these studies underscore an important health-promoting benefit of DTCA in reminding patients to adhere to their drug therapy as prescribed. For instance, Calfee, Winston and Stempski (2002) utilize a national monthly time-series of statin prescriptions and DTCA, between 1995-2000, and find television advertising expenditures on statins is associated with an increased proportion of existing patients who were successfully treated (existing patients with a high-cholesterol diagnosis whose total cholesterol fell below 200 mg/dL). This effect combines both a drug therapy compliance effect and also a market expansion effect as successfully-treated patients spread the word about the effectiveness of statin drugs and raise demand among untreated or under-treated patients.

Bradford et al. (2006b) merge patient-level data from 88 geographically dispersed primary care practices with national and market-level television advertising expenditures for statin drugs over 1998-2004. They include practice fixed effects in the models, and measure

advertising as dichotomous indicators for whether the DTC ad spending was in the upper quartile at the local and national levels during the month in which the patient commenced statin therapy. They find that national televised DTCA is significantly associated with improvements in the likelihood of attaining cholesterol management goals (by about 6-7% by 6 months), at least among patients with modest LDL-C goals ($\leq$ 160 mg/dL).

Donohue et al. (2004) study claims data for depressed patients between 1997 through 2000 matched with monthly drug-specific and class-level information on DTCA, detailing, and free sampling to physicians. They find that class-level consumer advertising of anti-depressants is associated with an increase in the number of people diagnosed with depression who initiate medication therapy. DTCA is also associated with a small increase in the number of individuals treated with anti-depressants who received the appropriate duration of therapy. They do not find any significant effects of drug-specific DTCA or of drug- or class-specific detailing or sampling on treatment initiation or duration of treatment.[17] However, they note that free samples may have a stronger impact on medication selection at the intensive margin rather than on the decision to initiate medication at the extensive margin. This is also consistent with content analyses of detailing that suggest that such interactions tend to highlight the comparative strengths of one drug over another in the class.

3. Effects of Physician-directed Promotion

In addition to consumer advertising, studies have also examined the impact of promotion aimed at health-care providers, which historically has been the primary form of promotion used by the pharmaceutical industry. Berndt et al. (1995), for instance, consider the role of detailing and medical journal advertisements as well as DTCA in the market for anti-ulcer drugs. They

[17] The study uses aggregate data on promotional spending and accounts for secular trends through a linear and quadratic monthly time trend. The authors caution that there may be unobserved factors that drive the association between DTCA and initiation of anti-depressant medications.

study the period prior to the shift in FDA guidelines, from September 1977 through December 1994. Thus, the DTCA examined in this study is limited and confined only to print media. 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 anti-histamines between 1994 through 2001, based on individual-level data from the National Ambulatory Medical Care Survey matched with monthly brand-level advertising data. Based on fixed-effects models, they find that DTCA has little effect on brand choice compared to DTPP, which has far larger and durable effects.

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 (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.

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.[18] 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 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

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

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.

4. International Evidence

Effects of DTCA

Similar to all industrialized nations except for the U.S. and New Zealand, Canada prohibits direct-to-consumer advertising for prescription medications. However, there is considerable exposure to American-based "illicit" DTCA in Canadian provinces. About 30% of the television viewing of Canadians in English-speaking provinces consists of U.S. satellite and cable TV, which carries consumer-directed Rx drug ads (Mintzes, Morgan, and Wright 2009). Law, Majumdar, and Soumerai (2008) study the impact of such U.S-based ads on Canadian prescribing rates for three drugs (Enbrel for rheumatoid arthritis, Nasonex for allergy symptoms, and Zelnorm for irritable bowel syndrome - IBS - in women) in English-speaking provinces relative to French-speaking Quebec. The study finds only short-lived positive effects for Zelnorm, and no significant effects for the other two drugs. The authors note that Zelnorm is the

only drug approved for its indication in Canada, whereas the other two drugs had competitors in their respective therapeutic classes. IBS is also under-diagnosed and under-treated, in which case DTCA can be informative. However, Zelnorm tends to be measurably effective in only about 1 out of 17 patients, which may explain why the effects of DTCA are short-lived. Insignificant effects of DTCA on the prescribing rates for Enbrel may be because the drug requires a specialist referral and sub-cutaneous injection, which may weaken the pathway from DTCA to drug use in Canada. Thus, similar to studies from the U.S., the impact of DTCA on drug use appears to be variable and dependent on the characteristics of the advertised drug and the medical environment.

Two major shifts in DTCA-related administrative policy occurred in Canada. In 1996, a redefinition of the boundary between 'information dissemination' and 'advertising' by Health Canada provided tacit approval for unbranded disease-oriented "ask your doctor about available treatments" ads. In 2000, manufacturers were allowed to use "reminder ads" that state a brand name but do not mention any indications, or make any therapeutic claims. Though it is not meant to imply a causal effect of the shift in DTCA policy (since many new and significant drugs were also launched over this period), total inflation-adjusted DTCA in Canada increased from under $1.6 million (Canadian $) in 1995 to over $22 million in 2006 (Mintzes, Morgan, and Wright 2009). Similar to the U.S., consumer ads in Canada are highly concentrated on relatively few products for treating chronic conditions (high cholesterol, impotence, depression, cosmetic/acne). While there has been no rigorous study on how such ads have impacted demand and related outcomes to inform on welfare effects, Mintzes, Morgan, and Wright (2009) note that many of the heavily-advertised drugs in Canada have U.S. 'black box' warnings and have been

subject to Health Canada safety advisories. Thus the safety profile of some of the highly consumer-promoted drugs is questionable.

Unlike most other developed countries, New Zealand had never enacted preemptive legislation to preclude pharmaceutical DTCA (Toop and Mangin 2007), and such ads are implicitly permitted under conditions set by the Medicines Act and the Medicines Regulations (Coney 2002). As in the U.S., consumer-directed advertising grew tremendously in New Zealand during the late-1990s. Anecdotal evidence attests to the effectiveness of DTCA in New Zealand. For instance, a few brief television commercials for the antifungal terbinafine is associated with a doubling of national prescriptions (Toop and Mangin 2007). Glaxo ran a major television campaign in 2002 informing people taking the popular branded beclometasone inhalers that the medicine was to be withdrawn and that they should visit their doctors to ask to switch to fluticasone. Despite some misleading elements in this campaign, it was deemed highly effective and sales of the more expensive fluticasone increased greatly (Toop and Mangin 2007).

Toop et al. (2003) conducted a survey of 1,611 general practitioners (GP) in New Zealand. They find that 90% had experienced DTCA-generated consultations. Furthermore, 79% of the GPs reported that patients frequently inquired about DTC-advertised medications, and 44% of them noted that they had switched to or started treatment with medicines they felt offered little added benefit over drugs they would normally use as a result of DTCA. Only 12% of the respondents believed that DTCA is a useful means of educating consumers about the risks and benefits of prescription drugs, about 16% felt that DTCA helped their patients get necessary medical care at an earlier stage, and 13% reported DTCA improved compliance. This is consistent with evidence from the U.S., which also shows a market expansion effect of DTCA (wherein such ads induce physician visits and adherence with drug therapy) as well as some

welfare-reducing effects through potential over-prescribing and/or prescribing advertised drugs despite little incremental benefits.

Effects of Detailing

Chintagunta and Desiraju (2005) report sales elasticities with respect to detailing and price for three selective serotonin reuptake inhibitor (SSRI) anti-depressants (Prozac, Zoloft, and Paxil) across five markets (U.S., U.K., Germany, Italy, and France), based on quarterly data from 1988-1999. The authors estimate IV models, instrumenting price with current and lagged values of the producer price index for preparations and psychotherapeutics and cost measures from the companies' balance sheets, and instrumenting detailing with the current and lagged values of an index of wages. These estimates indicate that own-detailing has a significant and positive impact on own-sales for all three drugs in all markets. The elasticity magnitudes are generally similar for the other four countries, ranging from 0.17 to 0.59, though several orders of magnitude higher for France (2.32 to 2.43). The authors note that this may be due to a large marginal benefit of SSRI-related detailing in France, since pre-SSRI anti-depressants had not been actively detailed. Cross-detailing elasticities are generally negative and smaller in magnitude, which is consistent with the persuasive view of advertising; detailing primarily affects selective demand and leads to brand-switching.

Berndt, Danzon, and Kruse (2007) present a study of the rate at which new drugs are promoted and diffuse, across three therapeutic classes (anti-hypertensives, anti-depressants, and anti-epileptics) and ten countries. They find that the largest level of detailing occurs for anti-hypertensives, followed by anti-depressants and then by anti-epileptics. Spain has the highest rate of detailing for all three classes, consistent with its high rate of utilization growth of these drugs. U.S. detail counts per capita are close to the median among their sample. Cross-national

differences further indicate that it is not necessarily the case that new drugs in the U.S. are intensely detailed relative to the older drugs. The authors further model the diffusion process through two separate components, including the total drug therapy days per capita and the new-drug expenditure share, and estimate this framework via the Almost Ideal Demand system for the three drug classes. They generally find insignificant or very small detailing elasticities with respect to aggregate utilization for all three classes. This is consistent with the U.S.-based studies which generally find that detailing impacts selective brand-specific demand rather than primary market demand. However, with respect to the new-drug expenditure shares, the results show positive and significant new-detailing elasticities. The cross effect of detailing on older drugs is negative. While the authors caution that the promotion intensity is endogenously determined and would require a simultaneous equations model, their results suggest that detailing can promote the diffusion of newer drugs. This may be health-promoting to the extent that newer medications are more effective in improving health than older medications (Lichtenberg and Virabhak 2007).

5. Summary

A number of robust empirical findings emerge from this literature on the demand effects of pharmaceutical promotion. First, both the econometric as well as survey results indicate positive demand effects of DTCA. Survey results (for instance, Wilkes et al. 2000) indicate that physicians do consider specific drug requests initiated by the patient. While in many cases physicians appear to fulfill these requests (Mintzes et al. 2003), in other cases they take into account acceptable standards of care in prescribing an alternative drug or not prescribing at all (Kravitz et al. 2005). These results are consistent with DTCA having both primary market expansion effects and also selective brand-specific effects.

The econometric literature is able to further pinpoint the relative strength of these two effects. Studies find consistent evidence of a significant class-level market expansion effect of DTCA. Dave and Saffer (2012), for instance, find that class-level DTCA may raise the sales for lower cost, non-advertised drugs. Thus, DTCA may bring a patient to the doctor's office, but in some cases the doctor is prescribing a lower-cost alternative. Consumer-directed promotion raises class-level sales, by encouraging patients to seek medical help, encouraging patient-physician contact, and promoting compliance with prescription drug therapy. This is reflective of the informative view of advertising, wherein DTCA plays at least some role in educating consumers and expanding treatment among those who were previously under-treated. However, at the same time, there is some evidence (Kravitz et al. 2005; David et al. 2010) that the increase in primary demand may partly reflect overtreatment or possibly inappropriate care, especially for conditions where there is greater uncertainty regarding diagnosis and acceptable standards for care. The evidence relating to the effects of own-DTCA on the specific drug's market share is mixed, though some recent studies (Dave and Saffer 2012; Kalyanaram 2009, 2008; Bradford et al. 2006; Wosińska 2002) suggest significant but relatively small elasticity magnitudes. These studies also point to considerable heterogeneity in these own-DTCA effects, depending on whether the drug has a preferential position on the formulary, the level of detailing and other physician-oriented promotion on the drug, other competitors in the therapeutic class, characteristics of the drug, and the composition of DTCA between broadcast and print media. The literature frequently views such 'business-stealing' advertising as less benign, though to the extent that it results in a better match between the consumer and the product it may also confer some welfare benefits (Berndt 2006). On the other hand, since higher-advertised drugs tend to cost more on average, to the extent that such advertising results in a higher-priced product

capturing market share, it may raise healthcare costs and confer negative spillover effects. Though, here too, the effect is ambiguous if price and quality are positively correlated. Overall, stronger market expansion effects combined with weaker and mixed evidence on selective brand-specific demand effects of DTCA suggest that consumer-directed advertising is perhaps more reflective of the informative view of advertising over the persuasive view.

The literature also consistently finds that the effects of physician-directed promotion (DTPP), such as detailing and free sampling, on own-demand are significantly larger relative to consumer-directed promotion. This is consistent with detailing primarily driving market share, whereas DTCA driving class expansion (Wosińska 2002). Detailing, sampling, and medical journal advertising can shift treatment away from non-drug therapy towards the promoted drug but cannot induce untreated consumers to visit the doctor. DTCA, on the other hand, can stimulate contact between untreated patients and physicians (market expansion), and can also perhaps impact prescription choice (brand demand). Thus, DTPP is relatively more reflective of the persuasive view of advertising, at least during the later stages of the drug's life cycle. During the early stages when there is greater uncertainty regarding a newer drug's attributes, DTPP may also bridge an informational gap and educate physicians regarding the drug's availability, effectiveness, and safety profile.[19]

B. Price Effects

1. Empirical Studies

Advertising by pharmaceutical manufacturers does not contain price information. Furthermore, since patients only pay the pharmacy their copayment, which differs across health

[19] To this end, by inducing physicians to treat more patients with drug therapy, DTPP may also potentially expand the number of treated patients conditional on the number of visits though this effect has not been directly studied in the literature.

plans, pharmacies also have no incentives to advertise prices for Rx drugs.[20] In the context of manufacturer non-price advertising, promotion may nevertheless affect price through various processes. First, the increase in operating costs due to higher promotional spending may be shifted to consumers in the form of higher prices. Second, promotion may increase demand and/or reduce the absolute magnitude of the demand-price elasticity, in turn raising price. This is consistent with the persuasive view of advertising, wherein advertising-induced product differentiation and creation of brand capital may enhance firms' monopolistic power. Under the persuasive view where the shift makes demand relatively more inelastic, advertising raises price as long as there are no strong economies of scale in production to counteract the inelastic demand.[21] Iwasaki et al. (2008) show, for instance, that in an oligopoly situation advertising will raise prices if it raises product demand, makes demand less elastic, and does not substantially lower marginal costs. Brekke and Kuhn (2006) similarly show that in a duopoly case with differentiated (branded) drugs, detailing, DTCA, and price are complementary strategies for the firm. Allowing DTCA induces greater detailing and leads to higher prices.[22]

In contrast to the persuasive view, manufacturers' advertising targeted towards consumers (and physicians) may lower price if such promotion reduces search costs for consumers (and physicians) by communicating direct or indirect information regarding the existence, quality, price and other product attributes, and subsequently makes demand more elastic (Encinosa et al. 2011). With respect to the pharmaceutical marketplace, the consumer can

[20] Pharmacies do advertise price information regarding OTC drugs, and sometimes their waiving of patient copays for generic drugs.

[21] Marginal production costs for the Rx industry tend to be constant as most of the costs are fixed and tied up in research and development.

[22] Iwasaki et al. (2008) also show that a set of sufficient conditions for higher Nash equilibrium prices include the firm's own advertising and price being complements and advertising raising the rival firm's marginal returns to its own advertising and price. Erdem et al. (2008) study four categories of consumer goods that can be characterized as experience goods and generally find that advertising raises the marginal willingness to pay. Prescription drugs are best characterized as experience goods since the consumer generally needs to buy and consume the product in order to judge its quality and attributes (Berndt 2006).

also be interpreted as the pharmacy benefit managers (PBM) who negotiate discounts and rebates with drug manufacturers on behalf of the insurers. Steiner (1973) presents a dual-stage model wherein consumer advertising can affect both the manufacturer's and the retailer's margin. Manufacturers' consumer-directed advertising provides information and raises consumer demand for the brand, which may facilitate competition between retailers on the advertised brand and subsequently lower retail margins while raising manufacturer prices.[23]

The empirical evidence on the effects of advertising and promotion on price is more limited relative to the evidence on demand. This paucity of research partly derives from the difficulty in obtaining measures of net Rx drug prices due to the presence of third-party payers and unobserved rebates from drug manufacturers to third-party payers.

Rizzo (1999) studies 46 anti-hypertensive drugs and, based on drug-specific fixed effects models, finds that increased current and past detailing efforts reduce the price elasticity. 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. The study is based on pooled annual data from 1988 to 1993, which predates the DTCA policy shift, and only considers promotion to physicians. He concludes that pharmaceutical promotion differentiates products, increases brand loyalty, and inhibits price competition in the pharmaceutical industry. Rizzo's results contrast with Narayanan, Desiraju, and Chintagunta (2004) who find a negative interaction between detailing and price suggesting that detailing may raise the price elasticity, albeit for a different sample of drugs (anti-histamines) and a more recent time period (1993-2002).

[23] It should be noted however that lower retail margins combined with higher manufacturer prices does not necessarily imply lower retail prices. If the increase in manufacturer prices is not large enough, and consumer price sensitivity increases sufficiently, then retail prices may fall. See Steiner (1993) for some evidence on the inverse association between advertising and retail margins, and the inverse association between manufacturer and retail margins.

Capella et al. (2009) study national monthly-level data from 2001-2005 for drugs in five therapeutic classes to estimate the effects of DTCA and DTPP on the price elasticity of demand (with respect to the average wholesale price). Similar to Rizzo (1999), they construct a depreciated stock of each promotional measure and estimate drug-level fixed effects models. For four of the five classes, they do not find any significant effects of DTCA on the price elasticity; only for drugs intended to treat an overactive bladder do they find a small, statistically significant decrease in the price elasticity. With respect to product sampling, they find that for three of the five classes, such promotion reduces the price elasticity. They conclude that there is no strong evidence that consumers pay higher prices as a result of DTC advertising.

Law et al. (2009) examine quarterly-level pharmacy data for Plavix (an anti-platelet drug used to prevent stroke and heart attack in at-risk patients) from 27 Medicaid programs over 1999-2005. Plavix initiated DTCA in 2001. Based on an interrupted time-series analysis, the study finds that, while there was no change in the preexisting trend in demand, there was a sustained increase in total Medicaid-reimbursed pharmacy cost per unit of $0.40 (11.8%) after the expansion in DTCA. They note that the extra reimbursement from Medicaid likely reflects an increase in the manufacturer's price.

Saffer and Dave (2012), utilizing a larger sample of all Rx drugs in four therapeutic classes, also find that DTCA raises the average wholesale price (prices paid by pharmacies), though the estimated elasticity is of a relatively small magnitude (0.04). They estimate drug-level fixed effects models and exploit presumably exogenous variation in DTCA driven by the FDA's policy shift in the late 1990s. Consistent with the positive impact on price, this study also finds suggestive evidence that the consumer price response became relatively more inelastic during the period when DTCA was expanding. Simulations indicate that expansions in broadcast

DTCA over 1994-2005 accounted for about 19% of the overall growth in prescription drug spending (assuming that movements in the average wholesale and retail prices are proportional)[24], with less than a third of this impact being driven by higher prices and the remainder due to higher demand.

Kopp and Sheffet (1997) provide an early study of the effects of DTCA on retail gross margins, testing the dual-stage theory of Steiner (1973). They construct the brand gross margin ratio, which measures the percentage by which a particular drug's retail margin is higher or lower relative to the class average, based on the average wholesale price and a pharmacy survey of retail prices. They then compare this brand gross margin ratio for 13 DTC-advertised brands with the remainder of 120 top-selling drugs that were not DTC-advertised over 1986-1992 (control group). Since non-DTC advertised drugs are systematically different from those that are advertised (Iizuka and Jin 2004), trends in the control group may not be a valid counterfactual. DTCA during this period, which pre-dated the FDA's policy shift, was relatively small and confined to print media. In support of Steiner's model, the study finds that retail margins for the advertised drugs fell relative to the non-advertised drugs.

Encinosa et al. (2011) examine data on 17 million prescription drug claims for 177 drugs in 19 therapeutic classes, between 2001-2002. They study both the average wholesale price and the transacted retail price, which is the total reimbursement that the pharmacy receives from the insurers and any patient copayment. The authors estimate drug-level fixed effects models and find that an increase in DTCA (from 0 to the sample mean) reduced average transacted prices by 1.8%, decreased price dispersion by 3.7%, and reduced pharmacy profit margins by 1.5% (consistent with Kopp and Sheffet 1997). The reduced price dispersion is interpreted as a sign of

[24] Reimbursement amounts are typically based on the AWP minus some percentage that varies across drugs and periods. Thus the AWP is a list price which typically exceeds real prices of drugs, though correlated with the actual transactions prices.

increased price shopping by the insurers' pharmacy benefit managers. Since the authors do not have information on DTPP, models do not control for physician-directed promotion. However, similar to Dave and Saffer (2012), they also find positive effects on the average wholesale price though this effect becomes insignificant once they control for market fixed effects. Thus, DTCA spending induces insurers to engage in more aggressive price negotiations with pharmacies, resulting in lower retail profit margins and lower retail prices.

2. Limitations

One challenge faced by all of these empirical studies concerns the simultaneity between advertising and pricing decisions. For instance, as noted earlier, in the model developed by Bhattacharya and Vogt (2003), price and promotion are jointly determined over the drug's life cycle such that the dynamic profit maximizing strategy for the firm is to initially employ a relatively high level of promotion and to set a relatively low price.

This trajectory of higher prices and lower advertising over the drug's life cycle is also consistent with the Dorfman-Steiner (Dorfman and Steiner 1954) condition for optimal advertising:

$$Advertising / Sales = \varepsilon_{QA} / \varepsilon_{QP}$$

The optimal advertising-to-sales ratio is a positive function of the elasticity of sales with respect to advertising (ε_{QA}) and is inversely related to the elasticity of sales with respect to price (ε_{QP}), both expressed in absolute magnitudes. Thus, the decline in advertising over the drug's life cycle is consistent with an age-related decline in the sales-advertising elasticity (Berndt 2006). It is also consistent with an increase in the price elasticity as the drug ages and newer drugs enter the therapeutic class. A positive association between advertising and price inelasticity may thus reflect causality in both directions – if persuasive in nature, advertising may make demand more

inelastic, but ceteris paribus more inelastic demand also leads to a higher optimal level of advertising. While many of these studies attempt to address this simultaneity through additional controls for the drug's life cycle, drug-level fixed effects, exploiting the natural experiment afforded by the FDA's shift in regulations, and other means, the results should be interpreted in the context of the limitations noted.

Another limitation in this strand of the literature relates to the measurement of drug prices in the empirical studies. None of the price measures include rebates negotiated between pharmacy benefit managers (PBM) and other payers (for instance, state Medicaid agencies) from the drug manufacturers, since information on these rebate arrangements is confidential. Various sources estimate these rebates at between 2-35% of drug sales prices (Dave and Saffer 2012). This rebate does not affect the price paid by a retail pharmacy to the wholesaler, or the price paid by the PBM to the pharmacy. It is a separate transaction between the PBM and the manufacturer, and affects the net transaction price. Manufacturers of brand-name drugs that treat conditions for which alternative drugs are available have a strong incentive to grant discounts to the PBM in return for preferential positioning of their drug on the formulary. If generic equivalents are available, the manufacturer may also grant a discount to make the price of its brand-name product more competitive. Thus movements in the list average wholesale price (AWP) or the observed transacted retail price may not be reflective of movement in the net transaction price. The growth in restrictive formularies over the period when DTCA was expanding suggests that the size of the negotiated rebates may also have expanded, leading to a decrease in the net transaction price. However, the key issue is whether and to what extent is the size of the rebate correlated with DTCA. If DTCA is targeted to raise consumer demand, provide new information, and provide for better positioning on the formulary, then DTCA may also be

associated with higher rebates leading to an over-estimate of the positive effects of DTCA on the net transaction price. In this case, given that the estimated price elasticity is low, it is possible that transaction prices net of rebates may have remained unchanged or even declined. If DTCA raises market power, and reduces the rebates to PBMs, then the estimated elasticity of the net transaction price with respect to DTCA is biased downwards.

3. Summary

These limitations notwithstanding, the above studies do point to a few relatively consistent findings. First, DTCA may have a positive though small effect on the list average wholesale price (AWP) (Saffer and Dave 2012; Encinosa et al. 2011; Law et al. 2009), consistent with DTCA-induced market power. Second, there is suggestive evidence that DTCA may have also reduced pharmacy retail margins (Encinosa et al. 2011; Kopp and Sheffet 1997). Both of these sets of findings are also consistent with Steiner's (1973) dual-stage model, wherein manufacturer advertising provides information, helps differentiate brands, raises consumer demand for the product, facilitates price-based competition (and price negotiations in the case of Rx drugs), and subsequently lowers retail margins while raising manufacturer prices. Evidence is weakly indicative that certain forms of promotion may lower the price elasticity (Dave and Saffer 2012; Capella et al. 2009; Rizzo 1999). Even then there is no strong evidence that DTCA or DTPP causes substantially higher retail level prices.

C. Effects on Entry and Innovation

The above studies suggest that consumer-directed pharmaceutical promotion has information content, conveying potential treatment options to consumers and expanding the market for drug therapy, at least for certain conditions. Under this informative view, advertising can have pro-competitive effects. To some extent, this can also apply to DTPP which has

information value during the early phases of the drug's life cycle. As consumers (and insurer representatives - PBMs) receive low-cost (relative to incurring search costs) information on products, the demand can become relatively more elastic and price dispersion in the market is reduced. Advertising can thus promote competition among incumbent firms and facilitate the entry of new firms as well as the introduction of new products. At the same time, some of the studies also point to persuasive effects of DTCA and DTPP. Such promotion-induced product differentiation and creation of brand capital may have anti-competitive effects by enhancing the monopolistic power of firms and deterring entry.[25] However, anti-competitive effects on generics, at least in the U.S. market, may be muted since pharmacists can substitute generics even if the physician writes a script for the branded drug.[26]

Further evidence is gleaned from studies that have directly investigated the effects of advertising on the entry of generic and branded substitutes in the pharmaceutical markets. Since advertising and entry decisions may be based on observed and unobserved market characteristics, identifying causal effects of promotion remains a challenge, though some of these studies have attempted to address the endogeneity bias via IV-based methods.

Hurwitz and Caves (1988) study 29 drug markets between 1978 and 1983, and estimate both OLS and IV models. They find that provider-directed promotion by incumbent firms preserves their market share against generic entrants. The study period generally predates the shift towards default generic substitution and the cessation of promotion upon the generic entry. Thus, subsequent studies find little evidence that Rx promotion deters generic substitutes,

[25] Königbauer (2007) presents a model in which over-investment of physician-directed advertising can deter generic market entry by creating excess brand capital. However, the model also predicts that since advertising induces vertical product differentiation, some advertising is a necessary prerequisite for generic market entry. Without advertising and differentiation, generic market entry would be deterred due to strong Bertrand competition.
[26] For this reason, promotion generally slows as patent expiry approaches and ceases entirely once generics enter.

Scott Morton (2000), for instance, investigates the role of pre-patent expiry brand-level DTPP in impacting post-expiry generic entry. In models that treat promotion as exogenous, she finds that journal advertising has a small negative effect on the number of generic entrants whereas detailing expenditures positively affect the number of entrants. However, promotion is likely to be endogenous, reflecting the same market conditions that affect entry; strong markets attract both more advertising and more entrants. Thus, the study also estimates IV-based models, using as instruments the drug's life cycle, an indicator for whether the firm has other forms of the same drug still under patent protection, and the number of physicians that would be expected to prescribe the drug. In these models, brand advertising does not present any significant or substantial barrier to entry by generic firms.

Ellison and Ellison (2011) examine whether the incumbent firms' DTPP (and other strategic factors) is motivated by an entry-deterrence strategy. In their model, advertising raises consumers' valuation both for the branded and the generic drug. The model predicts lower levels of advertising with entry-deterrence motivation among intermediately-sized markets, relative to advertising with no deterrent motive; firms in such markets would reduce their promotion to make their market less attractive to potential entrants. Furthermore, advertising monotonically decreases with market size in the model without an entry-deterrent motive, but the relationship in non-monotonic and convex in the model with an entry-deterrent motive. The authors study these predictions for a panel of drugs that lost their U.S. patent protection between 1986 and 1992 and find only weak evidence of strategic entry deterrence with respect to detailing and journal advertising. Due to various changes in the pharmaceutical marketplace, including a greater shift towards default generic substitution for branded drugs especially since the mid

1990s and the advent of DTCA, the conclusions from this study may not apply to current market conditions.

Studies have also considered how pharmaceutical promotion impacts the entry of other branded products in the class. Leffler (1981) examines a sample of 51 new drugs introduced between 1968 and 1977. He finds that DTPP of existing products in a therapeutic class is associated with greater success of new products (measured as the market share of new products in their second year post-introduction). The study acknowledges that entry and advertising incentives may be simultaneously determined, and cautions that "no causal relationship is implied." However, it also notes that the positive correlation is contrary to a simple entry-barrier hypothesis. The study also concludes that the success of new drugs generated by pharmaceutical promotion is presumably pro-competitive since new product entry is associated with lower prices of established drugs (relative to the overall drug price index). This study predates drug insurance, and thus conclusions may not hold in today's market conditions. Furthermore, since new product entry decisions are now taken several years prior to launch due to a lengthy R&D process, the results from this study should be interpreted as effects on diffusion or uptake rather than entry effects.

Kwong and Norton (2007) study the lagged effects of DTCA and DTPP on pharmaceutical innovation in eight drug markets, as measured by the total number of investigational products entering into clinical development in a given market, over 1995-2001. Based on negative binomial specifications, they find that detailing may have a significant positive effect on the number of new products entering into clinical development, with markets for chronic disease with high levels of detailing being more attractive to pharmaceutical firms. Other types of advertising were not found to impact product entry however. They note that this

may be due to the unique role of detailing in affecting brand-specific demand and enhancing product differentiation. The authors also acknowledge that their results may be subject to endogeneity and omitted variables bias, though they are not able to implement IV-based corrections or control for drug-class fixed effects due to the limited sample size.

V. Conclusion

Pharmaceutical promotion, and in particular DTCA, has emerged as a marketing force in the U.S. healthcare system. While the debate surrounding such promotion is unlikely to be resolved anytime soon, pharmaceutical promotion should be evaluated both in terms of its costs as well as its benefits. Welfare implications can be indirectly gleaned from the extent to which such promotion affects demand, competition, and prices.

Several studies have suggested that consumer-directed advertising provides some information content regarding treatment options, induces physician contact, and expands treatment, at least for certain under-treated or chronic conditions such as depression and high cholesterol. Thus, the benefits of DTCA derive from improved health due to increases in the number of individuals using prescription drugs and increased adherence with drug therapy. Detecting and treating health conditions at an earlier stage, through primary care, may also be more cost-effective relative to treatment at a later stage through acute care. Avery et al. (2008) find that some disadvantaged groups such as Blacks and those with lower education and income levels are exposed to more pharmaceutical DTC ads. Many health conditions are especially under-treated for these disadvantaged groups; for instance, Blacks are significantly less likely to receive prescription drug treatment for high cholesterol. Thus, if such DTC ads provide useful information and induce patients to visit their doctors, then the potential educational benefits of consumer-directed advertising may help to reduce health-related disparities.

There is limited direct evidence on the competitive effects of pharmaceutical promotion. Though, the few studies that have been conducted seem to indicate that, if anything, promotion aimed at providers can facilitate entry of other products in the drug class and also positively impact the number of new products entering into clinical development. These studies do not find any strong evidence that promotion by incumbent firms deters generic entry. Thus, this strand of the literature concludes that marketing activities for established products may be mildly pro-competitive. These results are consistent with the informative-view of advertising, and studies that show advertising-induced market expansion effects generally interpret these findings as welfare-improving.

One of the costs of DTCA and DTPP includes potentially higher drug prices and increased use of more expensive drugs in place of equally effective lower-priced drugs.[27] For instance, higher drug and health care expenditures can raise insurance premiums, increasing taxpayer and individual costs, and may lead to a larger prevalence of uninsured. Cost-ineffective treatments also impose opportunity costs for public and private resources. Here too, the evidence is very limited and hampered by measurement error in drug prices. However, the few studies in this area suggest that promotion may have a small positive effect on the average wholesale price and reduce retail pharmacy margins. There is no strong evidence that DTCA or other forms of promotion substantially raise retail-level drug prices.

However, evidence from physician surveys and a randomized control study (Kravitz et al. 2005) does suggest that there may be some DTCA-induced overuse and overtreatment, especially in cases where there are no structured clinical guidelines for treatment. For instance,

[27] While there is no direct study of this latter effect in the literature, see Kravitz et al. (2005). This study points to the role of brand-specific DTCA in raising own-demand by leading to a prescription for that brand, as well as in raising overall demand for prescription drugs in the therapeutic class (consistent with several other reviewed observational studies utilized aggregate data). Thus, there is some indirect evidence that DTCA can potentially avert both underuse and promote overuse, and to the extent that advertised drugs tend to be more expensive, DTCA can shift demand towards these more expensive drugs.

in the study by Kravitz et al. (2005), among patients portraying adjustment disorder, where anti-depressants confer very little or no benefits, 37% of patients requesting Paxil received a prescription for the drug, compared to none for patients who did not request any drugs.

While there is certainly an element of improved adherence and expanded treatment underlying the market expansion effects of DTCA, the fact that physicians prescribe a certain drug in response to patients' request suggests that there is also a persuasive brand-switching component to DTCA. Econometric studies find some evidence that DTCA affects selective demand, which is often viewed as less benign relative to promotion that affects primary demand. However, these brand-specific effects generally tend to be small in magnitude. In contrast, both U.S.-based and international studies consistently find that the brand-switching effects are far stronger for physician-aimed promotion.

Market expansion, overtreatment and shifting brands for non-therapeutic reasons also raise the concern of a sub-optimal patient-drug match for some marginal patients. As shown in David et al. (2010), increased levels of DTCA are associated with increased reporting of adverse medical events for certain conditions. This suggests that promotion-driven market expansion and brand-switching could also carry the risk that the drug is prescribed inappropriately and worsen the average safety profile for the drug. Since newer drugs generally tend to be more heavily promoted, especially in terms of consumer-directed ads, a popular proposal among critics of DTCA in Congress is to impose a moratorium on such ads during the first two years of a drug's launch.[28] This would give the FDA, providers, and patients time to learn about any new safety issues after the drug enters the market. Though, the benefits of such a proposal also need

[28] A group of leading pharmaceutical manufacturers (Merck, Schering-Plough, Johnson & Johnson and Pfizer) have agreed to a voluntary six-month moratorium on DTCA for new drugs, in an attempt to educate doctors and health professionals first about the new drugs before trying to reach consumers directly.

to be balanced against the need to convey information regarding the existence of new drug therapies, which may be especially important in the early stages of a drug's launch. Thus, optimal use of DTCA may require further structured guidelines (Almasi et al. 2006).

In summary, pharmaceutical promotion has effects which can be health-promoting and welfare-enhancing, but may also have adverse effects through potential overtreatment, cost-ineffective substitutions, and potential misuse (David et al. 2010). In cases where physicians can effectively perform their role as mediators the concern about promotion-induced inappropriate use is mitigated. However, for conditions where the diagnosis or risks may be difficult to assess, there may be a need for greater oversight and investment in post-marketing surveillance by the pharmaceutical firms.

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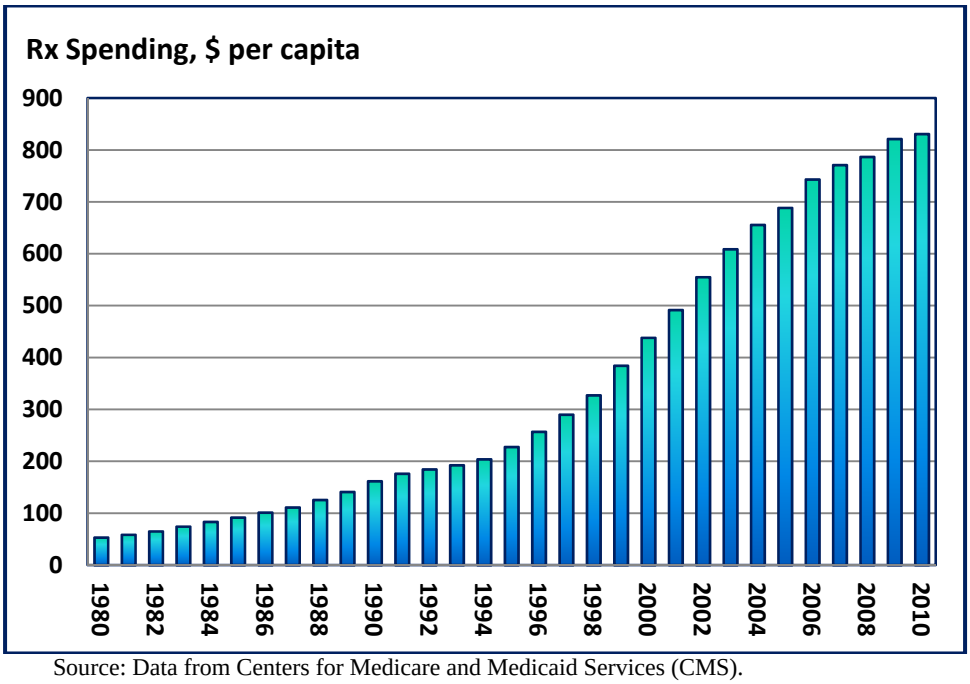
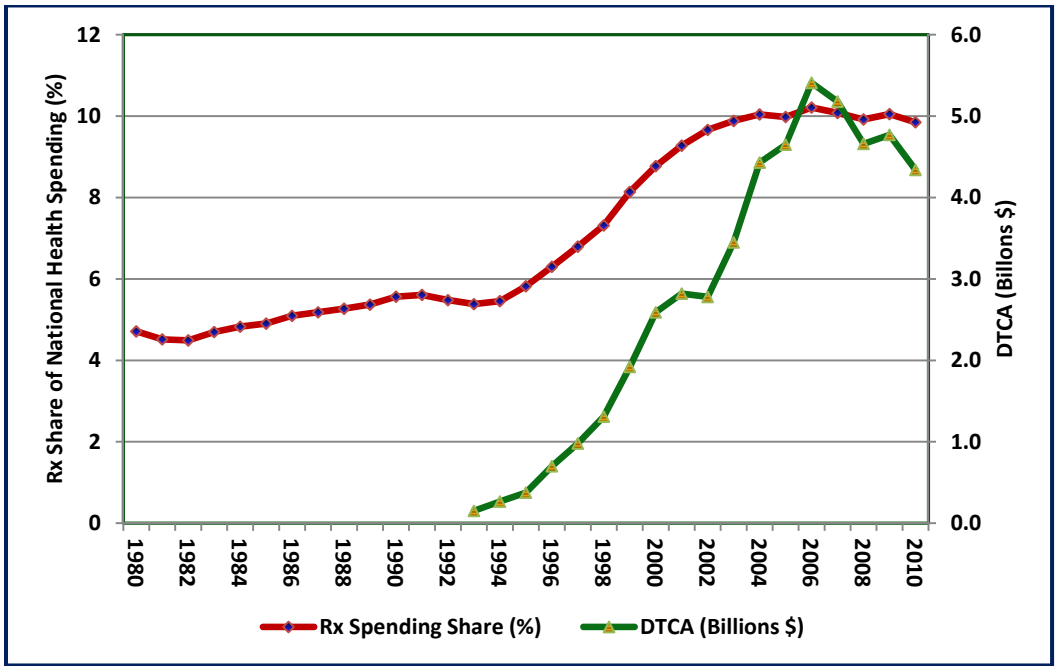
Figure 1
Prescription Drug Spending in the U.S.



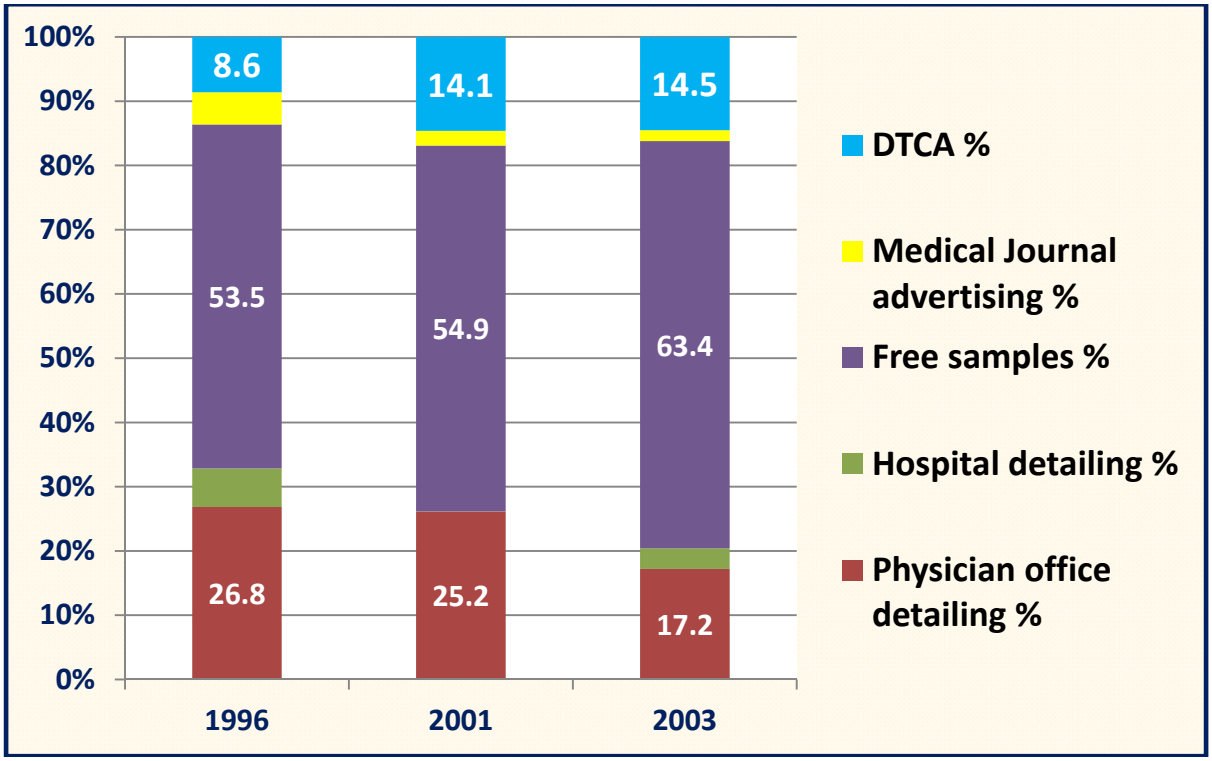
Source: Data from Centers for Medicare and Medicaid Services (CMS).

Figure 2
Rx Spending Share of National Health Expenditures & Direct-to-Consumer Advertising



Source: Data from CMS, Dave and Saffer (2012), Frank et al. (2002) and Bulik (2011)

Figure 3
Components of Pharmaceutical Promotion



Source: Donohue et al. (2007) and authors' calculations from data used in Dave and Saffer (2012). Sampling is valued based on the average wholesale price (AWP), a manufacturer's list price, and thus exceeds value based on production costs.

Table 1
25 Prescription Drugs with Highest DTCA in 2010 (millions $)

Rank	Pharmaceutical	Marketer	2010	2009	Primary Condition(s)
1	Lipitor	Pfizer	$272.0	$247.1	High cholesterol
2	Cialis	Eli Lilly & Co.	$220.6	$179.2	Erectile dysfunction
3	Cymbalta	Eli Lilly & Co.	$206.0	$182.7	Mental health; depression
4	Advair	GlaxoSmithKline	$200.5	$183.3	Asthma; respiratory
5	Abilify	Bristol-Myers Squibb Co.	$155.7	$205.7	Mental health; depression
6	Symbicort	AstraZeneca	$152.2	$136.2	Asthma; COPD; respiratory
7	Pristiq	Pfizer	$127.4	$124.4	Mental health; depression
8	Plavix	Bristol-Myers Squibb Co.	$127.3	$149.9	Blood; thinner
9	Chantix	Pfizer	$122.2	$155.8	Smoking
10	Lyrica	Pfizer	$112.2	$162.2	Diabetes; fibromyalgia
11	Toviaz	Pfizer	$109.5	$56.5	Bladder control
12	Viagra	Pfizer	$99.9	$128.0	Erectile dysfunction
13	Crestor	AstraZeneca	$95.1	$129.4	High cholesterol
14	Boniva	Roche Holding	$85.2	$81.6	Osteoporosis
15	Lovaza	GlaxoSmithKline	$80.7	$6.4	High cholesterol
16	Seroquel	AstraZeneca	$80.6	$64.2	Mental health; depression
17	Enbrel	Amgen/Pfizer	$71.5	$85.3	Arthritis; psoriasis
18	Spiriva HandiHaler	Boehringer Ingelheim	$70.7	$77.6	COPD; respiratory
19	Singulair	Merck & Co.	$70.3	$78.1	Asthma; allergy; respiratory
20	Simponi	Johnson & Johnson	$70.1	$5.9	Arthritis
21	Januvia	Merck & Co.	$64.6	$27.6	Diabetes
22	Restasis	Allergan	$58.0	$41.0	Chronic dry eye
23	Vyvanse	Shire	$58.0	$84.6	ADHD
24	Trilipix	Abbott Laboratories	$56.3	$43.7	High cholesterol
25	Lunesta	Dainippon Sumitomo Pharma Co.	$54.1	$19.4	Sleep disorder
		Total	$2,820.7	$2,655.8	

Source: Bulik, B.S. "Pharmaceutical Marketing," *Ad Age Insights White Paper*, October 17 2011.