

Chapter 9

The United States' Experience with Direct-to-Consumer Advertising of Prescription Drugs: What Have We Learned?

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I. Introduction

Economists have long emphasized that in healthcare, identification of the consumer is ambiguous. Is it the patient, the physician acting as a professional agent on behalf of the patient, or is it the third party payor? In most but not all countries, pharmaceutical manufacturer sales representatives, called “detailers,” are permitted to visit physicians in their offices, and provide them with promotional material.¹ Representatives from pharmaceutical manufacturers also interact with public sector payors such as ministries of health, as well as with private sector payors, such as insurers and self-insured employers in the United States.

Currently only two countries, the U.S. and New Zealand, permit pharmaceutical manufacturers to market directly to consumers, where consumers are defined as potential ordinary patients, and not as healthcare providers. The U.S. also now permits direct-to-consumer advertising (“DTCA”) for prescribed medical devices.² Whether DTCA should be permitted at all, permitted but only with much more stringent regulation, or replaced with public health announcements, are issues on which much has been written, and continue to be controversial in the U.S. and in New Zealand.³ There is also a considerable literature surveying consumer and physicians’ perceptions of DTCA.⁴

Rather than revisiting the various debates, controversies and survey findings, I summarize the accumulated empirical evidence in this chapter: What have we learned to date about the composition, overall size, and impacts of DTCA in the U.S.? More specifically, in assessing the U.S.’ experience with DTCA, I consider four sets of empirical issues: (1) What is

the magnitude of DTCA relative to other forms of pharmaceutical promotion, and relative to sales? (2) Is DTCA widespread, or is it targeted to certain therapeutic areas? More generally, what are the determinants of DTCA targets? (3) What are the effects of DTCA on therapeutic class sales, and on individual product market shares within therapeutic classes? And (4), what have we learned to date regarding the impact of DTCA on patient quality of care, or surrogates for quality of care? Finally, I will also comment briefly on the experience of New Zealand with DTCA, and make several U.S. - New Zealand comparisons.

In sum, these are the major empirical findings to date. Although DTCA has grown rapidly in the U.S., it is a relatively modest component of total prescription drug promotion spending, 13-15% between 2000 and 2003, and a much smaller proportion of sales, 2%. DTCA is relatively targeted to conditions for which one would expect the elasticity of sales with respect to marketing efforts to be substantial. The evidence to date generally suggests that when DTCA has an impact, it is primarily on overall sales at the level of a therapeutic class rather than on individual brand market shares within a class. Finally, there is evidence that DTCA simultaneously mitigates underdiagnosis and undertreatment of depressive disorders, but also encourages ambiguous utilization for patients with marginal illness severity; there is limited evidence that DTCA is associated with greater patient adherence to recommended treatment.

II. Historical Background

Prior to the passage of the U.S. Federal Food, Drug and Cosmetic Act in 1938 that legitimized physicians as “learned intermediaries” and required a physician’s prescription for a pharmacist to dispense a drug to a consumer, DTCA was the overwhelming communications vehicle for promotion.⁵ Following passage of the 1938 legislation, DTCA declined sharply. The 1962 Kefauver-Harris Amendments to the Federal Food, Drug and Cosmetic Act shifted

regulatory jurisdiction from the U.S. Federal Trade Commission (FTC) to the U.S. Food and Drug Administration (FDA), which to this day has responsibilities for regulating prescription drug promotional materials, both for physician- and consumer-oriented promotions.⁶

The 1962 amendments outlined basic requirements for acceptable prescription drug marketing: Prescription drug promotional materials cannot be false or misleading; they must provide a “fair balance” coverage of risks and benefits of using the drug; they must provide a “brief summary” of contraindications, side effects, and effectiveness; and they must also meet specific guidelines for readability and size of print. After some controversy involving the DTCA of an anti-arthritic drug in 1982,⁷ the FDA asked industry to comply with a “voluntary” moratorium during which time the FDA would assess the impact of DTCA on public health. In 1985, the FDA announced that the combination of current regulations and the Kefauver-Harris Amendments was sufficient to enable it to adequately regulate DTCA so as to protect public health, and that hereafter DTCA would be required to meet the same standards and criteria as promotional material aimed at healthcare professionals.

For a number of years, the FDA interpreted the “brief summary” provision as requiring the advertiser to provide the detailed information contained in the drug’s FDA-approved product labeling, thereby confining it to print form, typically in small print. However, under FDA regulatory precedents, there were two conditions under which firms could avoid the “brief summary” in TV advertising. First, if the advertisement were “help-seeking” in that only disease symptoms were mentioned, but no name of any drug was given, and the other was when only the name of the drug was mentioned without specifying its indicated use.⁸

As DTCA began to grow in the mid-1990s, the FDA’s regulatory discretion was tested, and thus in 1997 the FDA felt obliged to clarify its regulation of prescription drug advertising,

particularly for television ads. According to the FDA's 1997 guideline clarifications, instead of requiring the lengthy "brief summary" taken from the product label insert, advertisements now 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 or a web-site.

The level of DTCA has increased considerably since 1994 (Fig. 9.1). The growth trend has been quite steady, and in particular there appears to be no material change in the slope of the trend line following FDA publication of the 1997 clarifying guidelines. After leveling off in 2002, by 2003, total DTCA spending increased to about \$3.2 billion and to \$4.1 billion by 2004, with most of the growth consisting of television advertising.^{9,10}

III. Perspectives from Economic Theory

The theoretical foundations underlying the economics of advertising in general (not just in health care markets) rely in large part on Dorfman and Steiner (1954), who showed that for a profit-maximizing monopolist facing a downward sloping linear demand curve, the optimal advertising expenditure to dollar sales ratio equaled the ratio of two elasticities,

$$\text{\$ Advertising/ \$ Sales} = \varepsilon_{QA}/\varepsilon_{QP} \quad (9.1)$$

where ε_{QA} is the elasticity of quantity demanded with respect to advertising efforts, and ε_{QP} is the elasticity of quantity demanded with respect to price (in absolute value). The advertising sales ratio is therefore particularly large when demand is not very price elastic, and when the advertising elasticity is substantial. When there are several marketing instruments and constant unit promotion costs, under reasonable conditions the optimal ratio of expenditures for any two promotional types (e.g., DTCA and medical journal advertising) equals the ratio of their marketing elasticities.¹¹

The effects of advertising on the welfare of individuals have long been discussed. One strand of literature considers whether marketing is more “persuasive” than “informative,” although the distinction between the two is ambiguous, particularly to those of us who find scientific information to be persuasive.¹² The authors of a widely read industrial organization text summarize this literature by stating that “...the welfare effects of advertising are complex and depend on the type of product and type of advertising, and therefore are generally ambiguous.”¹³ Advertising can provide information to consumers about the availability of products to treat medical conditions, but can also lead to unnecessary and possibly risky utilization of medicines. Further, while brand loyalty may reduce price responsiveness of demand, it can also reduce consumers’ search costs, and provide assurance of quality.¹⁴

IV. DTCA Spending Relative to Other Forms of Drug Promotion

DTCA spending appears to have increased considerably in recent years, but so too have sales. It is also useful to examine DTCA spending relative to other promotional efforts.

In applying the Dorfman – Steiner theorem, it is important to consider that there is likely considerable measurement error in both the numerator and the denominator of equation (9.1). In the numerator, there are at least two potentially offsetting measurement errors. First, in the U.S. free samples are frequently given physicians by the manufacturers’ sales representatives. Such samples accounted for over half of promotional expenditures during 1996-2003 (Table 9.1). In recent years these free samples have increased substantially as a share of total promotion, from about 54% in 1996 to about 63% in 2003.¹⁵ However, the free samples are valued here at their approximate retail price (more specifically, by a list price called average wholesale price, AWP, which industry observers call “Ain’t What’s Paid”); the value of free samples in these promotional figures thus likely considerably overstates their manufacturers’ marginal production

costs. Second, a common U.S. industry practice is to sponsor post-launch studies that monitor actual market utilization of approved products; these expenditures are not included in estimates of pharmaceutical marketing spending, although it could be argued that at least in part they represent marketing research expenditures.

The denominator, dollar sales, also presents serious measurement challenges. What one would want would likely be sales of branded drugs, since generic drugs are marketed very differently from branded drugs. Data on sales of branded drugs by manufacturers are not easily available, in part because a number of firms have both generic and branded products. The U.S. sales data that the Pharmaceutical Research and Manufacturers Association (PhRMA) reports in its annual reports only include sales for its members, and it is not known whether these data include the generic sales of PhRMA member brand companies who have generic subsidiaries (e.g., Novartis with Sandoz). Moreover, while in some cases a pharmaceutical company and a biotechnology company in which it holds a major stake are both members of PhRMA (e.g., Roche in Genentech), other biotechnology companies with approved products on the market are not members of PhRMA (e.g., Vertex, Chiron), but instead belong to another trade organization, the Biotechnology Industry Organization (“BIO”).¹⁶ Sales of such biotech companies are not included in the PhRMA sales figures. Hence, the denominator of the promotion to sales ratio likely understates manufacturers’ sales of branded pharmaceutical and biotechnology therapies, but does include some generic sales.

With these caveats in mind, I now briefly examine various ratios (Table 9.2). Rosenthal, Berndt, Donohue et al. (2002) report that while DTCA increased from 1.2% of total revenues in 1996 to 2.2% in 2000, over this same time period, hospital-based promotion and medical journal advertising decreased from 1.6% to 1.1% of total revenues. Although the DTCA to sales ratio

fell slightly in 2001 and 2002, by 2003, at 2.2% its value is the same as in 2000. These numbers, together with those in Table 9.1 imply that the ratio of hospital-based promotion and medical journal advertising to sales has declined considerably, from 11.0% in 2000 to 4.9% in 2003.¹⁷ Thus, to some extent DTCA appears to be substituting for hospital-based and medical journal advertising.

Finally, while total promotion expenditures over all types of promotional efforts approximately doubled between 1996 and 2001 (Table 9.1), so too did revenues, and thus total promotional intensity remained relatively constant. The total promotion to sales dollar ratio has hovered between 14 and 16% between 1996 and 2002, but it appears to have increased to 17.1% in 2003. This most recent increase may reflect the rising relative importance of free samples provided physicians which in large part (Table 9.1), as noted above, are evaluated at their full retail prices rather than at marginal production costs.¹⁸ The apparent increases might also simply reflect the effects of various measurement errors.

V. Targeting DTCA: Particular Conditions and Drugs

A second empirical issue involves the extent to which DTCA is evenly diffused across or instead is targeted to specific therapeutic classes and drugs. If DTCA is evenly spread across therapeutic classes, this could reflect similar cross-class marketing elasticities of demand. The data suggest quite clearly that DTCA is highly targeted, and perhaps increasingly so. Using 1999 data for 391 major branded drugs, Neslin reported that almost all drugs (95%) were detailed to physicians, but only 18% had positive expenditures on DTCA.¹⁹ Rosenthal, Berndt, Donohue, et al. (2002) report that in 2000, the top 20 DTCA spenders comprised 58.8% of all DTCA spending; this proportion was roughly unchanged in 2001 at 56.4%, but increased to 61.5% in 2003, and to 65.1% in the first six months of 2004.²⁰

Using detailing, DTCA and sales data for drugs in five therapeutic classes (antidepressants, antihistamines, antihyperlipidemics, nasal sprays and proton pump inhibitors), Rosenthal, Berndt, Donohue et al. (2002) found wide ranges in DTCA intensity across therapeutic classes: 0.5% of sales revenues in 1999 for antidepressants, 1.4% for proton pump inhibitors, 1.5% for antihyperlipidemics, 5.8% for antihistamines, and a high of 11.6% for nasal sprays. The corresponding promotion spending/sales ratios for health care professional promotion (excluding DTCA) were all much higher. Moreover, considerable variation also occurred in DTCA intensity within each of the therapeutic classes. For example, in 1999, among antidepressants, only Paxil had some DTCA spending (2.2% of sales), while Celexa, Effexor, Prozac, Serzone and Zoloft had no DTCA spending; among antihistamines, while Astelin and Semprex-D spent nothing on DTCA, for Claritin DTCA spending was 5.0% of sales, and for Zyrtec it was 10.4%.

Then why are some drugs chosen for DTCA promotion while others are not? Based on a detailed assessment of factors affecting DTCA spending across 169 drugs and 21 therapeutic classes during 1996-99, Iizuka (2004) found that about 15% of his drug-year observations contain positive DTCA spending, suggesting relatively targeted DTCA spending, which is consistent with Neslin's (2001) findings. Consistent with Rosenthal, Berndt, Donohue et al. (2002), Iizuka found that as drugs age, their DTCA spending declines. Within the context of the Dorfman-Steiner theorem, this can be interpreted as an age-related decline in the elasticity of sales with respect to advertising, which is plausibly largest early on in the product's life cycle and lower later on as it competes with an increasing number of entrants.

Iizuka (2004) hypothesized that, holding other factors constant, higher quality drugs would be more likely to be targets for DTCA spending. To measure drug quality, Iizuka

employed the FDA's priority rating of a drug at the time of the FDA's initial approval (before 1991) or when the sponsor initially filed for approval (after 1991). Notably, Iizuka reported a positive and statistically significant impact of drug quality on DTCA spending, especially when the high quality drug was also the first or second drug in the therapeutic class. This finding is consistent with literature suggesting advertising elasticities are greater for higher quality products, thereby increasing their advertising to sales ratios.²¹

A particularly interesting analysis involves Iizuka's evaluation of the effect of potential (as opposed to actual) market size on a drug's DTCA spending. Using data from the U.S. National Health Interview Survey on prevalence rates for selected chronic conditions based on annual household and other surveys, Iizuka related potential market size to the primary treatment indication for each drug. This potential market size was the sum of treated plus untreated individuals.

Using a variety of model specifications and estimation methods, Iizuka consistently found that while the current treatment population size does not affect DTCA spending by drug, the *potential* market size has a significantly positive impact on DTCA spending. He interpreted this as suggesting that DTCA spending focuses on conditions for which there is undertreatment and unmet needs. This is consistent as well with the notion that when there are significant unmet needs, the advertising elasticity is likely to be larger.

Iizuka also found that DTCA spending is much lower, when a generic competitor to the brand is on the market. Consistent with the Dorfman-Steiner (1954) theorem, Iizuka interpreted the lack of DTCA spending in such situations as reflecting the inability of branded drugs to recoup benefits from DTCA spending when generic competition exists. With mandatory generic substitution policies and the availability of lower-priced generics, generic rather than brand

manufacturers would benefit from such advertising, and thus, in such cases, the advertising elasticity is very small for the branded firm.

VI. Effects of DTCA on Demand

A third issue involves empirical evidence on the effects of DTCA spending on the demand for drugs at the level of the entire therapeutic class, and at the level of individual product market shares within each class.²²

Economists are ultimately interested in the impacts of regulatory policies and firm behavior on consumers' welfare. Given the assumption of consumers rationally acting in their self-interest conditional on available information, there is a widespread belief among economists that, in most markets, if advertising increases the size of the overall market but does not affect any particular product's market share, such advertising is unlikely to be harmful but rather enhances consumer welfare. Advertising must be providing new information that facilitates consumers taking actions on heretofore unmet needs.

However, this sanguine view may not necessarily hold for health care markets in which information is typically incomplete and/or there is asymmetric information between buyers and sellers. While some consumers' medical conditions may be undertreated and may thus benefit from DTCA that focuses on providing information regarding unmet needs, for other consumers DTCA may lead to inappropriate, unnecessary, and perhaps more costly treatments. Hence, if DTCA results in increasing the size of the market being served, in health care, DTCA may or may not be welfare-enhancing. There is a substantial literature on this issue (see, e.g., Kravitz, Epstein, Feldman et al. (2005)).

On the other hand, if advertising only affects market share but not overall market size, then it is frequently viewed as possibly being less benign and perhaps even welfare-reducing; the

literature has categorized such advertising as “persuasive” or “business stealing.” Yet, again there is ambiguity; if such persuasive advertising results in a lower priced product of similar quality capturing market share, or in better matches between the product and the consumer (here, the drug and the patient), then DTCA can be welfare improving.²³ In sum, the effects of advertising on consumer welfare are ambiguous, perhaps even more so in health care than in other contexts.

FDA regulatory efforts attempt to ensure that the content of DTCA is informative and understandable to consumers. Thus of particular interest is whether the empirical evidence supports market size-enhancing impacts of DTCA spending, and/or market share “rivalrous” or “business stealing” impacts. To date, the empirical evidence is reasonably consistent: When DTCA spending has any impact, the primary impact is via increasing market size, rather than affecting individual market shares.

Using aggregate national monthly data on DTCA, retail value of free samples, and on detailing and retail sales for five therapeutic classes, Rosenthal Berndt, Donohue et al. (2003) report that at the level of the therapeutic class, DTCA spending has a statistically significant positive effect on sales, with an average elasticity of around 10%. By comparison, the elasticity of class sales with respect to class level detailing, while statistically significant, is much smaller, about 0.03. However, within each therapeutic class, neither detailing nor DTCA spending affected the market share of individual products. They cautioned, however, that “absence of evidence is not evidence of absence,” in part because marketing researchers have long recognized that the impacts of advertising are long-lived and challenging to identify and estimate reliably.²⁴ Moreover, during 1996-2000, drug manufacturers experimented in targeting

therapeutic classes, and in developing DTCA content and copy. Undoubtedly mistakes were made, and DTC advertisers learned from them.²⁵

Wosinska (2002) examined individual prescription claims data for 1996-99 from Blue Shield of California medical plans. Focusing on cholesterol reducing drugs (statins), she found that while DTC advertising may affect demand for an individual brand positively, it does so only if that brand has a favorable status on the third party payor's formulary. She also found that the marginal impact of DTCA on prescription choice is significantly smaller than the marginal impact of detailing, suggesting that the primary role of DTCA lies in market size expansion.

Calfee, Winston, and Stempki (2002), using national U.S. monthly data on retail prescriptions, also for cholesterol reducing drugs, 1995-2000, found little if any impact from DTCA on the pattern of statin prescriptions dispensed, although they report some evidence suggesting that television advertising reinforced patient compliance with drug therapy.²⁶

Augmenting national data on detailing and DTCA with individual data from the 1994-2000 National Ambulatory Medical Care Survey (NAMCS), Iizuka-Jin (2005a) began by classifying each physician office visit as an Rx visit of class k if it resulted in any prescription in class k; they then classify an office visit as an OTC visit in class k if it resulted in no prescription drug but at least one over-the-counter drug in class k. Combining these categories, they then defined a drug visit as the sum of Rx and OTC visits; if a visit involved a diagnosis but no treatment or a non-drug treatment, it was categorized as a non-drug visit.

Initially examining drug (prescription plus OTC) visits, Iizuka-Jin (2005a) find that DTCA had significantly positive impacts on drug visits, with this effect being about twice as large in years after 1997 than before, which they interpret as implying that DTC became more effective in generating drug visits after the FDA issued its 1997 clarifying guidelines.²⁷ Their

estimates imply that, after 1997, each \$28 increase in DTCA spending yielded one more drug visit within 12 months. Since a single prescription at a retail pharmacy typically costs much more than \$28, and for chronic illnesses is refilled indefinitely, this DTCA represents a substantial return on investment. By contrast, while DTCA spending has a positive and significant impact on the number of non-drug visits, there was no statistically significant difference before and after 1997. When Iizuka-Jin (2005a) disaggregated drug visits into their Rx and OTC components, they found that DTCA influences demand for prescription drug products, but does not affect OTC demand.

Iizuka-Jin (2005b) examined the impact of DTCA spending on choice of drug, i.e., on changing market shares within one particular class, namely, the non-sedating antihistamines.²⁸ Consistent with Rosenthal, Berndt, Donohue et al. (2003) and Wosinska (2002, 2004), Iizuka-Jin (2005b) found that DTCA has little if any impact on the choice of prescription drug within a therapeutic class. This contrasts with the impact of physician-oriented detailing and medical journal advertising, which in most analyses affects demand. Variations in the number of free samples left physicians did not affect brand choice prescriptions.²⁹

Iizuka-Jin (2005b) concluded that the two forms of marketing, detailing and DTCA, play very different roles. DTCA is effective in increasing aggregate demand or category sales and has “public good” spillovers for other products in the same therapeutic class, while detailing and medical journal promotions are more effective at affecting brand choice.

In sum, studies covering a number of different therapeutic classes suggest that DTCA encourages patients to seek medical help, but these DTCA efforts do not meaningfully interfere with the patient-physician relationship. In spite of considerable DTCA spending, prescription choice is still determined primarily by physicians, once patients come to visit their offices.

Two other recent studies examined DTCA for a specific therapeutic class -- antidepressant drugs, but with very different methodologies. Donohue and Berndt (2004) utilized large employers' retrospective medical claims data on 25,716 individuals who filled prescriptions for antidepressants covered by drug benefit plans, combined with national DTCA and physician detailing data, for 1997-2000. Using an analytical framework that allows for differential substitutability among the four SSRIs, an SNRI (serotonin norepinephrine reuptake inhibitor), and an SARI (serotonin antagonist and reuptake inhibitor), Donohue and Berndt (2004) found no statistically significant effect of DTCA on choice among these six antidepressants, except for individuals diagnosed with anxiety disorders. The authors reported that the effects of DTCA on medication choice were much smaller than those of detailing, which were positively associated with drug choice.

They concluded that the principal impact of DTCA is on motivating individuals to visit their physicians. Even though DTCA may increase the number of persons who visit their doctor and receive medication treatment for chronic conditions such as depression, apparently it has little impact on the choice of medication.

The analyses reviewed thus far are all observational studies using econometric procedures. In contrast, Kravitz, Epstein, Feldman et al. (2005) examined prescribing behavior of antidepressant drugs in a randomized controlled trial setting. Mostly professional actors, middle-aged, white, non-obese women, called "standardized patients," were trained to depict to physicians two types of patients with differing severity of symptoms: one with symptoms of major depression of moderate severity, and the other having an adjustment disorder with depressed mood.

These two patient types were chosen to represent different levels of illness severity. Clinical treatment guidelines recommend quite clearly that the first type of patient presenting with moderate major depression symptoms receive treatment (psychotherapy, antidepressant drugs, or some combination), but for the second type of patient presenting with less severe symptoms the appropriate treatment is equivocal and ambiguous.³⁰

Their experimental design crossed these two patient types presenting to their physician with three types of request by the patient: (1) a patient mentioning a specific brand, saying “I saw this ad on TV the other night. It was about Paxil. Some things about the ad really struck me. I was wondering if you thought Paxil might help,” (2) a patient making a general rather than brand-specific request for a medication, saying “I was watching this TV program about depression the other night. It really got me thinking. I was wondering if you thought a medicine might help me,” and (3) a patient making no medication request and no mention of seeing a TV ad.³¹

Primary care physicians were recruited in four physician networks by mail with telephone follow-up, and were told only that the study would involve seeing two standardized patients several months apart, that each patient would present with a combination of common symptoms, and that the purpose of the study was to assess social influences on practice and the competing demands of primary care. The physician visits were surreptitiously audiotaped. Eighteen standardized patients completed a total of 149 encounters presenting with major depressive disorder, and another 149 with adjustment disorder, with each split approximately evenly among the three patient request types.³²

The authors found that physicians prescribed antidepressants in 54% of visits in which standardized patients portrayed major depression -- 76% in which they made general requests for

medication, 53% in which they made brand-specific requests linked to DTCA, and 31% in which they made no explicit medication request. Only in 11% of major depressive disorder encounters did the physician prescribe Paxil. Hence, for standardized patients presenting with major depressive disorder, general rather than brand-specific DTCA resulted in the greatest proportion receiving an antidepressant prescription. But, if no mention was made of DTCA, only 31% presenting with major depressive disorders received antidepressant therapy, 19% received a mental health referral recommendation, and 25% were advised to return for primary care follow-up within two weeks. Altogether, for those patients presenting with symptoms of major depressive disorder but not mentioning any DTCA, 56% received some form of minimally acceptable initial care (any combination of an antidepressant, mental health referral, or follow-up visit within two weeks), whereas 44% did not. By contrast, among those presenting with symptoms of major depressive disorder, 98% making a general request, and 90% making a brand-specific request, received some form of minimally acceptable initial care. Thus, the experimental evidence indicates that DTCA mitigates undertreatment for standardized patients presenting with major depressive disorder

Antidepressant prescribing was less common (34%) when standardized patients presented with adjustment disorder symptoms. However, here the role of brand-specific DTCA was more powerful. Physicians prescribed an antidepressant for 55% of patient encounters involving a brand-specific request, in 39% of cases in which a general request was made, and only in 10% of cases in which no explicit medication request was made. In about 15% of the adjustment disorder encounters, the physician prescribed Paxil. Hence the experimental evidence also reveals that DTCA encourages medically ambiguous and questionable utilization of antidepressant drugs for patients presenting with adjustment disorder.

Using a different set of statistical procedures, Kravitz, Epstein, and Donaghue et al. (2005) found that prescribing an antidepressant drug was 2.92 times more likely when a standardized patient presented with major depressive rather than adjustment disorder symptoms, and 8.50 and 10.3 times more likely when the patient made a brand-specific or a general medication request, relative to no specific medication request, respectively. Physicians varied systematically in their propensity to prescribe an antidepressant, regardless of the type of patient presenting. But none of the standardized patients was systematically more or less likely than other patients to receive an antidepressant drug prescription.

Several conclusions emerge from this study. First, while patients can be active agents in influencing the treatment they receive, physicians differ systematically in their propensity to prescribe an antidepressant. In this sense, the experimental and non-experimental findings on DTCA affecting overall therapeutic class sales, but not shares within the class, are consistent.

Second, for standardized patients presenting with a brand-specific request for information and either major depressive or adjustment disorder, essentially the same proportion (53% vs. 55%) were prescribed an antidepressant. But when requesting information about antidepressants in general, about twice as many patients presenting with major depressive disorders than those with adjustment disorders were prescribed an antidepressant. This could be interpreted as supporting the notion that brand-specific DTCA contributes to some overtreatment or possibly inappropriate treatment. General disease awareness information presented on television also contributed to marginal treatments, though to a lesser extent than brand-specific DTCA.

Third, only 31% of those patients presenting with major depressive disorder symptoms but making no medication-related request were prescribed an antidepressant, and only 56% received some form of minimally acceptable care, whereas minimally acceptable treatment was

received by 90% making a brand-specific request, and 98% a general request, which supports the notion that DTCA mitigates undertreatment of major depressive disorder.

In sum, the experimental evidence leads one to the conclusion that both undertreatment of depression (in the case of those presenting with major depressive disorder) and overtreatment with antidepressants (for those presenting with adjustment disorder, where, as the authors argue, the prescription of antidepressants “is at the margin of clinical appropriateness”),³³ are likely. DTCA simultaneously mitigates undertreatment of serious illnesses and results in some inappropriate treatment. One caveat, however, is that issues of long-term follow-up and adherence to guideline treatment recommendations were not investigated in this study.

In another study, Weissman, Blumenthal, Silk et al. (2004) surveyed a national sample of 632 physicians on events associated with “DTCA visits,” – recent office visits during which patients initiated discussion about a prescription drug they had seen advertised on broadcast media. Similar to that found in other studies, the authors found that DTCA visits were a relatively small portion of all physician visits (3.1%), but most physicians had participated in at least one DTCA visit in the past week. They summarized their findings as follows:

“Physicians reported mixed feelings about the impact of DTCA on their patients and practices...More than 70 percent felt that DTCA helped educate patients about available treatments; 67% felt that DTCA helped them have better discussions with their patients. However, four out of five doctors believed that DTCA did not provide information in a balanced manner, and a similar number felt that it encouraged patients to seek treatments they did not need. Physicians as a group were more equivocal about other impacts of DTCA, with 46 percent agreeing that it increased patients’ compliance and 32 percent that it made patients less confident in their doctors’ judgment. Overall, 40 percent felt that DTCA had a positive effect on their patients and their practices, 30% felt it had a negative effect, and 30% felt that it had no effect.”³⁴

In 39% of DTCA visits, the physician prescribed the advertised drug, and in 46% of these cases physicians believed it was the most effective drug for the patient, while in 48% of cases, physicians believed it was as effective as other drugs for the patient but they wanted to

accommodate the patient's request; in five percent of cases, other drugs or treatment options may have been more effective for the patient's condition or health problem. When physicians prescribed a drug, most predicted it would result in positive patient outcomes, including improved overall health (76.4%), relief of symptoms (87.4%), reduced severity of illness (76.8%, and better compliance (74.5%). Most DTCA visits (61%) did not result in a prescription for the advertised drug, with the three most common reasons being: a different drug was more appropriate (29.3% of such visits), a less costly equally effective drug was available (25.1%), or another course of non-drug treatment was more appropriate (24.1%).

Finally, physicians reported that 25% of DTCA visits resulted in a new diagnosis. Of these new diagnosis DTCA visits, the ten most common are listed in Figure 9.2. Notice that this list includes both some conditions that are likely to be identified and treated effectively thanks to DTCA advertising, thereby mitigating undertreatment (e.g., depression, anxiety, hypertension and hyperlipidemia), as well as some conditions that have allegedly been targeted for persuasive advertising of certain prescription drugs, even though less expensive alternative treatments are available (e.g., heartburn, allergies, and arthritis).³⁵

VII. DTCA's Effect on Quality of Care

Numerous surveys, e.g., Calfee (2002) and Aikin (2003), have reported that both patients and physicians perceive DTCA to improve adherence to recommended treatment. Yet there is unfortunately relatively little empirical evidence on the magnitude of this compliance effect. More important are impacts of DTCA, if any, on patient outcomes. Two recent studies have provided indirect evidence.

Donohue, Berndt, Rosenthal et al. (2004) examined treatment patterns of 30,521 depressed individuals whose 1997-2000 insurance claims were included in a large retrospective

medical claims database. Two issues were addressed. What are the impacts of DTCA and pharmaceutical promotion to physicians on the likelihood that: (1) an individual diagnosed with depression received antidepressant medication; and (2), conditional on receiving antidepressant therapy, that the antidepressant medication was used for the appropriate duration.

After controlling for secular trends in the treatment of depression and other factors, they observed a small positive and statistically significant effect of DTCA spending on the probability that a person diagnosed with depression received antidepressant drug treatment. Individuals diagnosed with depression during periods when class-level antidepressant DTCA spending was in the top quartile had a 32% higher probability of initiating medication therapy compared to those diagnosed during periods when DTCA spending was in the bottom quartile. Individuals who initiated treatment following periods when cumulative free sample units were in the top quartile were no more likely to initiate antidepressant medication therapy than individuals diagnosed during periods of low free sample spending. Individuals facing a copayment of more than \$15 for an antidepressant were 30% less likely to initiate antidepressant drug therapy than were individuals facing a drug copayment of \$5 or less.

The authors' measure of quality of care was based on the Depression Guideline Panel (1993) recommendations and American Psychiatric Association (2003) guidelines. These state that if antidepressant medication is chosen, it should be provided until symptoms are alleviated (usually in 10-12 weeks) and then continued for an additional period of 4-9 months to prevent relapse. As a conservative measure, and allowing for the possibility that the patient received a free sample (which would not be recorded in the medical claims data base), the authors considered the duration of therapy to be appropriate if the patient filled prescriptions for at least four months of treatment with the study drugs within the first six months of an episode.

Of the 11,306 episodes of treatment involving initiation of drug therapy, 60% filled at least four prescriptions for an antidepressant in the first six months of the episode. Interestingly, DTCA spillovers were observed, not on class sales as discussed above in Section VI, but on patients' adherence to recommended treatment, regardless of which drug treatment they were receiving. Neither the detailing spending for the drug taken, nor the detailing for other drugs in the class, had a statistically significant impact on the probability of receiving appropriate treatment duration. Copayment amount had no statistically significant effect on whether the patient received appropriate treatment duration, but patients seen by psychiatrists were more likely to receive appropriate care than were patients seen by other physicians.³⁶ The authors conclude by noting that to the extent DTCA increases demand for medications, it is important to understand what proportion of the expanded use represents appropriate, medically questionable, or inappropriate prescribing behavior. Their research only begins to address this issue.

Wosinska (2004) examined compliance issues by quantifying number of days between 30-day prescriptions. Based on the Blue Shield of California data described earlier involving patients who began their cholesterol-lowering statin therapy between 1996 and 1999, Wosinska's final data sample consisted of 16,011 patients and 123,736 gaps between prescriptions. Although treatment recommendations typically involve indefinite daily utilization of the hyperlipidemic medication, Wosinska (2004) found that, on average, the number of days between two 30-day prescriptions was 43, corresponding to 13 missed days per cycle.

Defining non-adherence to recommended treatment as the number of missed therapy days, Wosinska (2004) estimated a variety of models using several different estimation methods, which tended to yield qualitatively similar findings. She found that, while DTCA for a single product at initiation of treatment had no statistically significant impact on patient adherence,

category DTCA had a significant beneficial impact. While statistically significant, these effects were relatively small in magnitude.

A most interesting finding occurred when Wosinska examined brand-specific DTCA spending. She found that while DTCA efforts by Zocor and Pravachol appeared to increase adherence, Lipitor's DTCA efforts appear to have had a negative impact. Further analysis suggested that the unexpected finding for Lipitor stemmed from the FDA's requirement that DTCA television advertisements must mention the most common side effects. She reasoned that television advertisements make side effects more salient than does print advertising. Professional actors in the first television ads for Lipitor prominently mentioned side effects of possible liver problems and muscular pain, a task that is usually carried out less prominently and is reserved for unobserved narrators. Discussions Wosinska had with industry analysts suggested that the prominent side effects mentioned in the Lipitor ads may have made patients more anxious, and that it may have affected their adherence.

As evidence, Wosinska reported that past television DTCA spending by Lipitor, but not more recent current DTCA Lipitor spending, had reduced adherence. Because past advertising was defined as the level of expenditure in 30 to 60 days prior to the prescription, her findings are consistent with a side effects hypothesis; if patients react to the side-effect warnings with a temporary suspension of therapy of at least a few days, then the level of advertising in the prior (rather than the current) month would have had an impact on adherence.

The issues raised by Wosinska (2004) regarding prominence of side effects warnings in television DTCA and their impact on patient adherence to guideline treatment are complex and undoubtedly of concern not only to advertisers and regulators, but also to patients and their

physicians. Her findings are best viewed as preliminary, but clearly worthy of additional research.

Finally, the consistency across various studies in the finding of spillovers of DTCA to other brands with little or no impact on own-brand is striking. As advertisers learn from their mistakes and become more sophisticated, the results for own-brand DTCA may change. Controversies on whether DTCA and, for that matter, other forms of advertising, are informative and market-expanding versus persuasive and market share stealing, are likely to continue for some time.

VIII. New Zealand's Experience with DTCA

The legislative history of DTCA in New Zealand is very different from that of the U.S. When New Zealand enacted statutes concerning the content of promotional material in its 1981 Medicines Act and its 1984 Medicines Regulation, it did not even consider the possibility of consumer-directed promotions, but only envisaged rather technical information promotions to health care providers and payors.³⁷ Thus, since it seemed to be impossible, DTCA was not explicitly prohibited in New Zealand.

The apparent success of DTCA in the U.S. is likely to be one reason why pharmaceutical firms pursued DTCA in New Zealand, particularly since it was not explicitly forbidden there. Also contributing to the introduction of DTCA in New Zealand was passage of its Bill of Rights Act in 1990, which explicitly protected freedom of speech, including commercial free speech. Pharmaceutical companies were quick to perceive this statute as being analogous to the First Amendment of the U.S. Constitution, which has been interpreted as generally protecting commercial free speech.³⁸

A major difference between the U.S. and New Zealand regulatory environment is that in New Zealand, DTCA is self-regulated through the Therapeutic Advertising Pre-vetting System (TAPS), and its Advertising Standards Complaint Board (ASCB). The ASCB consists of four public representatives and four members from the advertising industry. It investigates advertising content of both prescription and over-the-counter medications when triggered by a formal written complaint. Although the ASCB is not empowered to impose punitive measures on errant advertisers, decisions have achieved almost total compliance since the media refuse to accept any advertisement the ASCB has ruled errant (Hoek, Gendall, and Caffee 2002).³⁹

DTCA advertising began in New Zealand in the early 1990s, and by the end of the decade it became widespread.⁴⁰ Not surprisingly, DTCA has generated considerable controversy in New Zealand, with many of the arguments and issues being similar to those in the U.S.⁴¹

Complaints have been voiced in New Zealand about the industry failing to regulate itself adequately. While both New Zealand and U.S. regulations require provision of specific information, the absence of a comparable “fair balance” criterion in New Zealand has meant that advertisements in New Zealand have tended to emphasize a product’s benefits, devoting less time and space to risks and side-effects. Critics point to comparisons between consumer survey responses in the U.S. and New Zealand as indicative of inadequate self-regulation and lack of fair balance in New Zealand.⁴²

Although various self-regulating and legislative efforts to control or even ban DTCA have been considered since the late 1990s, matters became more complicated when in December 2003, as part of a broader initiative to harmonize trade, New Zealand and Australia signed a treaty to establish a single binational agency to regulate medical therapeutic products, the Joint Therapeutics Agency. As of 2005, Australia did not allow DTCA, although it permitted disease

state awareness advertisements in which no brand name is mentioned.⁴³ Thus there is conflicting policy in Australia and New Zealand that needs to be reconciled at the binational Joint Therapeutics Agency.

Although Annette King, New Zealand Labour Party's Minister of Health, publicly stated her opposition to DTCA and used the argument that such a policy would ensure harmonized practices between Australia and New Zealand, at that time the New Zealand government was a minority government, relying for support from a "Greens" party in order to continue to rule. Because the binational Joint Therapeutics Agency would regulate complementary medicines (e.g., herbal remedies) which were previously largely unregulated in New Zealand, the Greens declined to support the proposed legislation, leaving the government without the majority required to pass the bill into law.⁴⁴ As of late 2005, the future of DTCA in New Zealand was unclear.

IX. Concluding Remarks

Even though advertising has long been controversial in many industries, commercial advertising in the context of healthcare goods and services has been particularly contentious, and even more so when it is directed at consumers rather than at health care providers or insurers. In this chapter, I have summarized the accumulated empirical evidence on the size, composition and impacts of DTCA in the United States. I have also briefly discussed New Zealand's experience with DTCA.

In terms of size, in the United States DTCA has grown rapidly, but as a share of the total promotional arsenal, it is still relatively small, 13-15% during 2000-03; as a percentage of sales, it was even smaller (2%). DTCA was also relatively concentrated, and apparently increasingly so, with the top 20 drugs in terms of DTCA expenditures accounting for about 65% of all DTCA

spending in the first half of 2004. The evidence suggests that DTCA is targeted particularly at those conditions for which the potential market is large relative to the actual market, and at “high quality” drugs, i.e., drugs to which the FDA assigned a “priority” status.

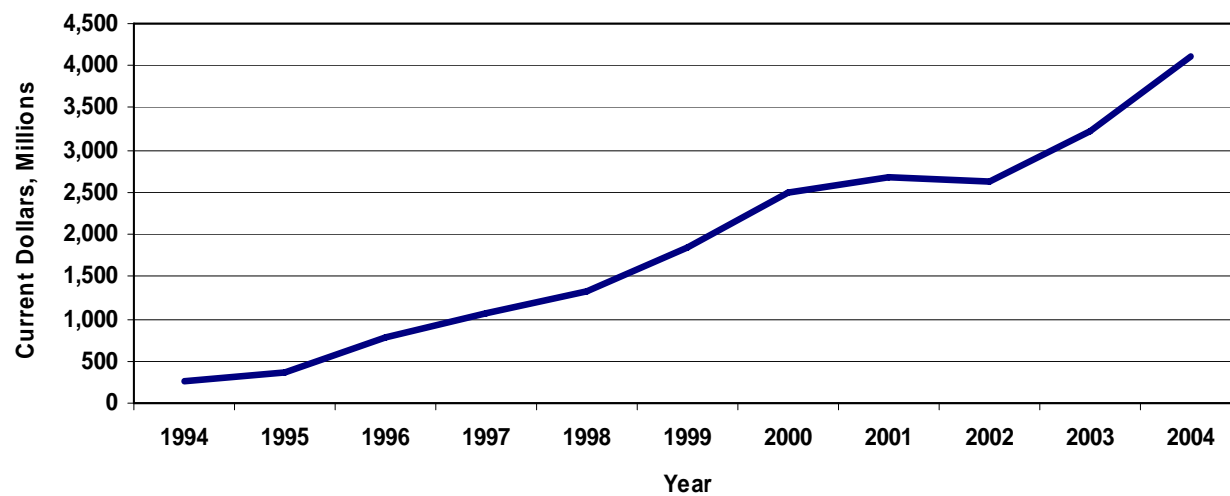
Both non-experimental and experimental studies reveal that while DTCA increases the size of the overall sales of a particular therapeutic class, brand-specific DTCA does not appear to have a statistically significant impact on the share of any particular brand within the therapeutic class. By increasing the size of therapeutic class sales but not affecting shares within the class, DTCA has ambiguous effects on consumer welfare. In particular, there is some experimental evidence suggesting that in the case of antidepressants, DTCA mitigates undertreatment of the condition, but it also appears to encourage marginal and possibly inappropriate treatment. Which of these effects dominates is at this point unclear, but it is reasonable to assume that the direction and size of the net impact varies across therapeutic classes and drugs. There is also some preliminary non-experimental evidence suggesting that consumers’ adherence to treatment is affected considerably by perceived safety risks, particularly when emphasized in television advertisements.

Finally, New Zealand’s experience with DTCA is in some respects similar to that of the U.S., but the self-regulatory environment in New Zealand that to this point has not required “fair balance” in advertisements as is required by the FDA in the U.S., has resulted in ads that compare favorably with the U.S. in terms of communicating benefits of drugs, but rather unfavorably when communicating risks and information on who should not be taking the medicines. Whether DTCA will continue or be banned in New Zealand is currently unclear.

In sum, the evidence to date suggests that as an instrument promoting public health, DTCA has considerable potential, particularly in mitigating undertreatment of important

illnesses, e.g., major depressive disorder. It can also result in questionable and inappropriate utilization, not only possibly exposing patients to health risks, but also contributing to increased health care costs. As with other forms of advertising, DTCA both informs and persuades. Its effects on consumer welfare are complex and ambiguous. Regulating the communication content of advertisements and other promotions that attempt to balance information on risks and benefits is inherently very difficult and challenging.

Fig. 9.1 Trend in Direct to Consumer Advertising Spending, 1994-2004



Source: IMS Health and Competitive Media Reports

Table 9.1 Composition of Prescription Drug Promotion Expenditures

	<i>1996</i>	<i>2001</i>	<i>2002</i>	<i>2003</i>
Physician office detailing %	26.8	25.2	25.1	17.2
Hospital detailing %	6.0	3.7%	4.1	3.2
Retail value of free samples %	53.5	54.9	56.2	63.4
Medical journal advertising %	5.0	2.2	2.1	1.7
Direct-to-consumer advertising %	8.6	14.1	12.5	14.5
Total %	99.9	100.1	100.0	100.0
Total promotion expenditures (in million dollar, mid 2000)	9,764	18,617	20,379	24,460

Fig. 9.2 Ten Most Common New Diagnoses Identified from DTCA Visits

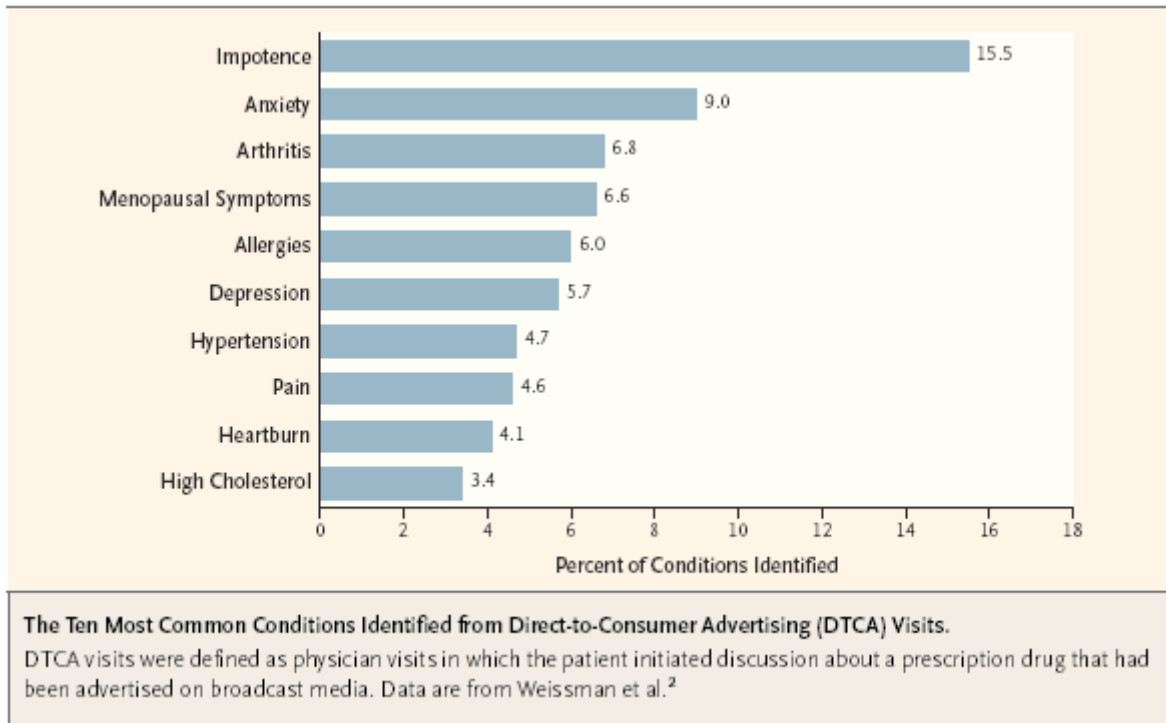


Table 9. 2 Promotion as a Percent (%) of Sales, 1996-2003

	<i>1996</i>	<i>1997</i>	<i>1998</i>	<i>1999</i>	<i>2000</i>	<i>2001</i>	<i>2002</i>	<i>2003</i>
Physician promotion	12.9	13.8	13.7	11.9	11.4	12.5	13.3	14.9
Consumer promotion	1.2	1.5%	1.6	1.8	2.2	2.1	1.9	2.2
Total promotion/sales ratio	14.2	15.3	15.3	13.7	14.0	14.6	15.2	17.1

Sources: IMS Health and PhRMA; sales are PhRMA member only

ENDNOTES

¹ For an interesting history of detailing in the United States, see Greene (2004)

² See Berndt (2005) and the references cited therein.

³ See, for example, in the context of the United States, Angell (2004), Avorn (2003,2004), Batchlor-Laouri (2003), Berndt (2005), Calfee (2002,2003), Dubois (2003), and Gahart et al. (2003); recently the U.S. Pharmaceutical Research and Manufacturers of America issued guideline principles for its members regarding DTCA; see PhRMA (2005). For a discussion of policy debates in New Zealand, and a comparison of the United States and New Zealand controversies, see Hoek, Gendall and Calfee (2004).

⁴ For a review of this literature and principal findings, see Aikin (2003) and Calfee (2002); the most recent survey is that by Weissman et al. (2004), who provide extensive references.

⁵ For discussion, see Temin (1980).

⁶ See Pines (1999), Calfee (2002) and Donohue (2003) for more detailed historical discussion of the marketing of prescription drugs to physicians and consumers.

⁷ Hollon (1999).

⁸ For a discussion of DTCA on antiulcer drugs, see Ling, Berndt and Kyle (2002).

⁹ Rosenthal et al. (2002) report DTCA spending by media through 2001, the last year for which data are publicly available.

¹⁰ Data from Nielsen Monitor-Plus.

¹¹ Palda (1969).

¹² In the context of prescription pharmaceuticals, see, for example, Hurwitz and Caves (1988), Leffler (1981) and Vernon (1981).

¹³ Carlton-Perloff (1994), p. 625.

¹⁴ For empirical evidence on consumers' search costs for acute vs. chronic medications, and impacts on retail pricing of drugs, see Sorenson (2000). Bagwell (2001) provides a useful collection of economics articles dealing with the theoretical foundations and empirical analyses of advertising as information vs. persuasion, and the relationships among advertising, product quality and market structure.

¹⁵ Data from IMS Health, accessed online at <http://www.imshealth.com/ims>. Nominal figures converted to 2000 dollars using the implicit GDP price deflator.

¹⁶ A list of current PhRMA member companies can be obtained by accessing their website, <http://www.phrma.org>.

¹⁷ Data from IMS Health, Competitive Media Reports, and PhRMA.

¹⁸ For a discussion of what one should expect regarding promotional intensity in pharmaceuticals compared to that in other industries, and for some empirical comparisons, see Berndt (2001,2002).

¹⁹ Scott A. Neslin (2001). Also see Wittink (2002).

²⁰ The 2000 and 2003 data are from IMS Health and Competitive Media Reports, while that for 2004 is from Nielsen Monitor-Plus.

²¹ This line of reasoning is typically attributed to Nelson (1970, 1974), who argues that when a product is of high quality, the value to its manufacturer of informing potential buyers of its availability and attributes is also high.

²² A corresponding literature has emerged that surveys patients' and physicians' perceptions of DTCA, and how it has affected relationships between physicians and patients. These surveys are discussed in detail in, among others, Aikin (2003) and Calfee (2002). The most recent of these is that by Weissman et al. (2004), who also reference earlier Prevention magazine and FDA surveys.

²³ See Berndt, Bhattacharjya, Mishol et al. (2003) for further discussion.

²⁴ For discussion, see, for example, Berndt, Kyle and Ling (2003).

²⁵ Unfortunately, the evidence on this is based on the author's informal conversations with industry personnel, and is not in the public domain.

²⁶ Calfee, Winston and Stempski (2003), p. 673.

²⁷ Iizuka and Jim (2005a) distinguish between the accumulated stock of DTCA, and the current period DTCA efforts. This is done by specifying a DTCA stock having a constant geometric rate of depreciation, which they estimate along with other parameters using nonlinear estimation methods. They estimate the monthly depreciation rate to be about 3%, which is about 33% on an annual basis.

²⁸ Iizuka-Jin (2005b) was originally the latter portion of Iizuka-Jin (2003).

²⁹ Stocks of detailing and medical journal advertising depreciate much more slowly than does the DTCA stock. When a price term is interacted with DTCA stock, the resulting coefficient estimate is positive but statistically insignificant, indicating that DTCA does not significantly reduce price sensitivity

³⁰ Kravitz et al. (2005), pp. 1995-1996.

³¹ Kravitz et al. (2005), p. 1997.

³² Kravitz et al. (2005), pp. 1996-1998.

³³ Kravitz et al. (2005), p. 2000.

³⁴ Weissman et al. (2004), p. W4-224.

³⁵ For further discussion, see Weissman et al. (2004) and Berndt (2005).

³⁶ For a further decomposition, see Pomerantz et al. (2004) who find that patients seen by psychiatrists were most likely to receive appropriate treatment duration, patients seen by primary care and internal medicine physicians were less likely to receive appropriate treatment duration, and that patients seen by specialists other than psychiatrists, primary care physicians or internists were least likely to receive appropriate treatment duration.

³⁷ Some of the material here is taken from Hoek, Gendall and Calfee, as well as from informal correspondence with Janet Hoek at Massey University.

³⁸ An influential legal precedent in the United States is the case *Central Hudson Gas & Electric vs. Public Service Commission*, which was considered by the U.S. Supreme Court in 1997. The Supreme Court Justices ruled that the First Amendment protects consumers' "right to receive information", but that regulations affecting commercial free speech do not violate the First Amendment if: (i) the regulated speech concerns an illegal activity; (ii) the speech is misleading; or (iii) the government's interest in restricting the speech is substantial, the regulation in question directly advances the government's interest, and that the regulation is no more extensive than necessary to serve the government's interest. Additional Court rulings invalidated state laws prohibiting price advertising prescription drugs and of alcohol, and laws banning newsracks for primarily commercial publications, such as real estate guides. For further information, see "Government Regulation of Commercial Speech. The issue: How far may government go in regulating speech that proposes an economic transaction?", available online at <http://www.law.umkc.edu/faculty/projects/ftrials/conlaw/commercial.htm>, last accessed May 2, 2005.

³⁹ Hoek, Gendall and Calfee (2002), p. 204.

⁴⁰ See New Zealand Ministry of Health (2000).

⁴¹ In addition to Hoek, Gendall and Calfee (2002), see Toop et al. (2003) (a report from faculty at various Schools of Medicine in New Zealand arguing for the banning of DTCA) and Saunders (2003) (a report commissioned by the Advertising Standards Authority, supporting continued self-regulation of DTCA).

⁴² Hoek, Gendall and Calfee (2002), Table 3, p. 214.

⁴³ Hoek, Gendall and Calfee (2002), pp. 206-209.

⁴⁴ Much of the information in this paragraph emanates from email correspondence with Professor Janet Hoek, J.A.Hoek@massey.ac.nz. Additional information is available from the website of the Joint Therapeutics Agency, <http://www.jtaproject.com>, the Advertising Standards Authority, <http://www.asa.co.nz>, and the website of the Researched Medicines Industry ("RMI", analogous to PhRMA in the United States, although not all pharmaceutical companies are members of RMI), <http://www.rmianz.co.nz>.