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Article in *Journal of Pharmaceutical Marketing & Management* · December 2011

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Factors That Influence Physicians' Prescribing of Pharmaceuticals: A Literature Review

Andrew S. Gallan

ABSTRACT. The prescribing of pharmaceuticals by health care providers is influenced by many factors. The significance of these factors is an important consideration to public health advocates and government agencies, health insurance companies, pharmaceutical firms, physician and provider associations, medical ethics researchers, patient consumers, and other stakeholders in health care. Better understanding of the factors that motivate physician prescribing can bring about more efficient use of health care resources through the improved dissemination of information and more informed decision making. This paper attempts to provide a sound and inclusive review of the influences upon physician

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The author thanks Debra Stephens, PhD, Associate Professor, University of Portland, Cheryl Jarvis, PhD, Assistant Professor, Arizona State University, the two anonymous *JPMM* reviewers, and the Editor for assistance in preparation of this manuscript. No financial support was received for the preparation of this article.

Journal of Pharmaceutical Marketing & Management, Vol. 16(4) 2004

Available online at <http://www.haworthpress.com/web/JPMM>

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doi:10.1300/J058v16n04_02

prescribing patterns in the extant literature. This review identifies several factors as being highly influential upon physician prescribing: peer influence, financial and managed care considerations, pharmaceutical representatives and drug samples, and direct-to-consumer advertising. To date, several key areas have not been well researched; these include the perceived price of a drug, the role of new technology, and the impact of physician experience. Based upon the literature review, a theoretical model of individual physician prescribing in the outpatient setting is proposed. Further research might be directed toward determining the influence of each factor upon physician prescribing and testing the overall model and interactions among its individual components. *[Article copies available for a fee from The Haworth Document Delivery Service: 1-800-HAWORTH. E-mail address: <docdelivery@haworthpress.com> Website: <http://www.HaworthPress.com> © 2004 by The Haworth Press, Inc. All rights reserved.]*

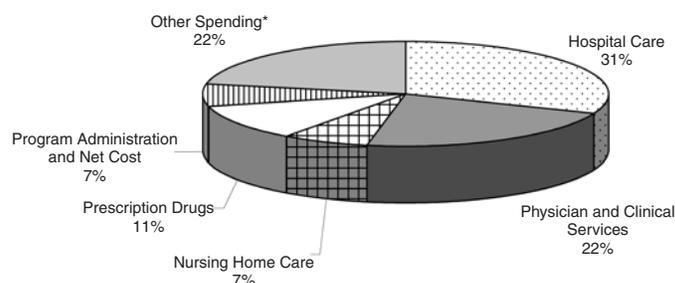
KEYWORDS. Physician prescribing, direct-to-consumer (DTC) advertising, peer influence, academic detailing, drug samples, physician gifts, continuing medical education (CME)

INTRODUCTION

In recent years, total health care costs in America have increased as a percentage of GDP and are expected to do so for the foreseeable future (1). Although still a relatively small part of total US health care expenditures, prescription drugs are one of the most rapidly growing components (Figure 1) (2). It is estimated that by 2008 drug sales in the US will approach \$250 billion (3). As a result, many attempts have been made to control these costs, such as implementing managed care formularies, shifting financial risk to patients, pushing for reimportation from pharmacies outside the US, and restricting the ways pharmaceutical companies may promote their products.

Increased use has affected the growth in prescription drug spending more than rising prices (4). Some of the factors that can lead to increased use include the aging of the American population, the increased prevalence of chronic diseases and obesity, improved diagnosis of treatable illness, improved and novel therapeutic agents, and consumer awareness and the advent of direct-to-consumer advertising of pharmaceuticals (5). Some of the increased use has also been a result of improved awareness and reduced stigma of common ailments. For instance, in the 1990s, the development and promotion of SSRIs significantly increased diagnosis and treatment of depression (6).

FIGURE 1. 2002 US Health Care Expenditures.



Source: CMS, Office of the Actuary, National Health Statistics Group, 2004.

*Includes dentist services, other professional services, home health, durable medical products, OTC medicines and sundries, public health, research, and construction.

One key downside of physician-pharmaceutical representative interaction has been the inaccuracy of information that may be communicated to physicians and their relative lack of awareness of it (7, 8). Physician prescribing has been near the center of a hotly contested issue—the rising costs of and the seeming decreasing control of these health care costs. Attempts have been made recently to inspect and influence health care providers’ prescribing patterns.

It is estimated that \$30 billion was spent on promotion and marketing by pharmaceutical companies in 2003, including \$5.8 billion on sales representatives and \$11.5 billion on drug samples (9, 10). Between 1996 and 2000, “the proportion of drug revenues spent on all promotional efforts remained fairly constant,” although the mix of spending was gradually changing (11). In 2000, Harvard researchers found, nearly \$2.5 billion was spent on direct-to-consumer advertising (DTCA) alone, “rising from 9 percent in 1996 to about 16 percent in 2000” (12). In 2001, DTCA spending totaled \$2.8 billion (13). Currently, however, the vast majority of promotional spending by pharmaceutical companies has been on sales representatives and samples (10).

This article will review the literature on the impact of marketing efforts by pharmaceutical companies, as well as the impact of economic forces, perceptions of pricing, physician peer-to-peer influence, and the influence and potential for technology to change decision making in the medical field.

LITERATURE REVIEW

Overview

Focus

The focus of this paper is on factors that influence the prescribing, predominantly by primary care physicians, of orally administered drugs in the outpatient setting in the United States. The US is the single largest national market for pharmaceuticals in the world (14). The factors that motivate physicians to prescribe injectable pharmaceuticals within hospitals, long-term care facilities, and other settings may be significantly different than those found in this paper.

It is quite possible that sources of information may not be sources of influence (15). The quantitative effects of diverse factors on prescribing were thus reported where available to differentiate between information and influence.

Comprehensive quantitative analysis of factors that influence physician prescribing is relatively new. Although meaningful efforts have been made since the early 1980s to assess this issue, the converging forces of increasing pharmaceutical costs and increasing public awareness of the issues have brought mounting attention to the importance of various effects on drug prescribing.

Methodology for the Review

A search of existing literature, primarily through MEDLINE and ABI/Inform, shows a few academic and government-sponsored studies, consultants' surveys, and foundation studies that focus on this subject. Criteria for inclusion in this literature review included the following:

- Studies were limited to the effects of various factors on prescribing in the outpatient setting in the United States, in line with the previously described focus of this review. Articles that assess effects in other contexts and other markets were included only where their contribution involved factors that pertain to the physician prescribing decision regardless of setting. A few non-US studies were used based upon their perceived insights into the social and psychological factors that prompt physicians to prescribe pharmaceuticals.

- Preference was given to peer-reviewed academic and empirical studies. A lack of this type of evidence prompted the inclusion of other sources, including foundation, government, and industry data sources. Every attempt was made to limit these alternative sources of information.
- Time sensitivity was manifest in areas where legal, social, economic, regulatory, and other considerations would render older studies less capable of contributing significantly to this review. However, studies that make a timeless contribution to the very nature of prescribing decisions were included.
- Duplicative or replication studies were included as either further or contradictory evidence where applicable. Every attempt was made to be as inclusive as possible.

It is distinctly possible, despite the best efforts to make this review as comprehensive and contemporary as possible, that omissions exist. This may be true for meaningful studies and articles in the topics covered and for topics not covered at all. Articles were selected based upon their representative nature in the established categories. Despite its possible shortcomings, this article is intended to facilitate a discussion of the importance of understanding factors that influence physician prescribing and to identify potential avenues for further research.

Initial Assumption

It would seem logical, a priori, that increasing selected marketing resources, by any one of the interested parties, would provide a positive return on investment. That is, whether the efforts were intended to increase brand share, as might be the case of pharmaceutical companies, or to increase appropriate utilization, as might be the case of managed care organizations and various government-sponsored health initiatives, efforts made to communicate these intentions to physicians would provide a positive return on investment. Sorescu et al. (2003) found, using the pharmaceutical industry as a setting, that “[dominant] firms that provide higher per-product levels of marketing [including sales] and technology support obtain much greater financial rewards from their radical innovations than do other firms” (16). This provides support for the initial assumption, across most marketing expenditures by the pharmaceutical industry, that there is, in fact, a correlation between marketing effort and financial return. How the different promotional

components each factor into influence upon prescribing will be explored in this review.

Factor Selection

AC Nielsen/HCI's study on important sources of medical information rated 24 different factors that influence prescribers. Released in June 2003, the study report included responses from 2,200 office-based high prescribers (17). The top 3 factors, conferences/symposia, continuing medical education (CME) courses, and medical journals, each had responses in excess of 70%. The next 3, all around 50%, were colleagues, dinner meetings, and pharmaceutical representatives. The extent to which these and other important sources of information translate into changed prescribing behavior will be discussed hereafter.

In October of 2001, the California HealthCare Foundation (CHCF) released a position paper, *Innovations in Physician Prescribing*, that assessed influences on physician prescribing (18). The report, based on primary and secondary research, identified five general classes of influences upon prescribing behavior: physician training and experience, colleagues and opinion leaders, pharmaceutical companies, health plans and other payers, and patients. The report identified technology as a key tool in delivering information that will enable physicians to make improved prescribing decisions.

Many factors that influence physician drug prescribing, organized into general categories suggested by these two sources, will be evaluated next. The broad categories are: marketing and pharmaceutical industry efforts, economic influences, the effects of nonmarketing sources of information, and other considerations. The last section of this article will suggest some future research directions and propose a theoretical model based upon this literature review.

Marketing and Pharmaceutical Industry Efforts

Pharmaceutical Detailing

From 1994 to 2002, the number of pharmaceutical sales representatives increased from about 30,000 to over 80,000 (19). Representatives have increased as a percentage of office-based physicians as well, from under 10% in 1994 to over 20% in 2002. Even the pharmaceutical companies themselves debate whether adding salespeople can give them a competitive advantage, yet the arms race continues. The prevailing

view, encouraged by firms that sell data to and consult with the major pharmaceutical firms, is that pharmaceutical representatives have a significant influence upon physicians' prescribing patterns. More and more, firms are beginning to realize that a new sales model must be developed (20). But just how much *can* pharmaceutical representatives influence physicians?

A comprehensive overview of physician perspectives on prescription drugs, developed by the Henry J. Kaiser Family Foundation, was published in March 2002. Part II of this National Survey of Physicians focused on interactions with representatives, drug advertising, and physician interactions with patients (21). A total of 2,608 actively practicing doctors responded to a mail survey. The sample was racially and ethnically weighted to be representative of the total physician population. The survey revealed that almost three quarters of physicians rate information from pharmaceutical representatives as either "very" or "somewhat" useful. An even higher number, 80%, believe that the information they receive from representatives is "very" or "somewhat" accurate. In this survey, 60% of physicians are aware that pharmaceutical companies possess data on individual prescribing, but less than a third believe this practice is unacceptable.

For the most part, physicians believe that commercial sources of information are less influential than scientific literature. An older but still valuable study assessed physician prescribing of two specific drugs "for which the information about efficacy conveyed by scientific sources differs markedly from that conveyed by commercial sources" in an attempt to control for social desirability bias (22). Results reveal that physicians prescribe medications for indications for which there is little scientific basis due to marketing sources of influence (advertising, detailing). The authors contend that this may be a result of physicians' "unwillingness to admit to reliance upon commercial sources or their lack of awareness of such influence."

Primary care physicians regard pharmaceutical representatives as being more influential upon their prescribing decisions than even their own peers, a 2003 Accenture study shows (23). Peer-reviewed clinical journals (80%) and industry association meetings (34%) were rated higher than sales representatives (30%), with colleagues (27%) and the Internet (16%) lagging behind. Although the study was limited in size ($n = 100$), the respondents did indicate that "approximately one-third of sales visits are helpful." Physicians want more current, comparative, and clinical information, based upon objective sources of information. Constraints upon their time and availability were limitations on how

much time physicians can give to pharmaceutical representatives. Physicians wished to see the representative because of the value of samples and because of their interest in new products and drug-specific information.

Health Strategies Group, Inc. released its Pharmaceutical Sales Force Effectiveness (SFE) study, version 3.2, in the spring of 2003 (24). The report's data were from the years 2001 and 2002, and it detailed sales force effectiveness by physician specialty, by drug therapeutic class, and by promotional activity. The report found that 85% of all pharmaceutical representatives who entered a medical office with the intent to sell actually engaged someone in the office. The other 15% left without such engagement, most likely because of too many patients or too many other representatives. Of the 85% who attempted to sell, 5% were turned away by a receptionist, 15% left samples at the front desk, 61% actually got to the sample closet and obtained a signature from a prescriber at that venue, and 20% got to sit down with a physician to deliver a sales call.

In this SFE study, physicians responded strongest to three components of an effective sales call: well-utilized resources, solid message content, and clear message delivery. The most appreciated resources were sales aids and reprints of significant articles. The components of the sales message that were essential to physicians were dosing, side effects, efficacy, and competitive data. Clear message delivery was helped by dialogue with interesting questions. Health Strategies Group tracked physicians who received sales calls that contained one, two, or all of these key components. Only 5% of all calls contained all 4 key tactics, and these calls were the only ones that led to a change in physician prescribing behavior.

A study that explored the connection between pharmaceutical representative interaction and formulary requests showed that the two are positively correlated (25). A group of physicians who had requested formulary additions was compared to a group who had not and assessed according to physicians' self-reported associations with drug company representatives. The first group was more likely to have spoken for or performed research for drug companies. "Moreover, physicians were more likely to have requested formulary additions made by the companies whose pharmaceutical representatives they had met. . . ."

Dolovich et al. (1999) investigated the impact that pharmaceutical representatives may have on physician prescribing in Ontario, Canada (26). The study tracked antibiotic prescriptions written by 641 physicians in the active group against 574 in the control group. The intent of

the study was to determine if industry salespeople could effect a change in physician prescribing habits by delivering evidence-based detailing. The results indicate that “the intervention did not result in major antibiotic market share changes for most of the targeted antibiotics.” Interestingly, there were differences in outcomes based upon prescribers’ gender as well as the number of years since graduation. Female physicians showed a slightly greater propensity to adhere to the intervention objectives than male physicians, and the more recent graduates were more likely to prescribe newer agents. The study, limited in size, demonstrates the lack of impact of academic detailing by pharmaceutical industry representatives upon physician prescribing behavior. The potentially significant differences between Canadian and US-based physician behavior and responsiveness and marketplaces should be investigated before attempting to apply the learnings from this study to American health care providers.

A retrospective literature review authored by Wazana in *JAMA* (2000) attempted to identify the meaning of physician-pharmaceutical representative interactions (27). In this article, a total of 29 studies met inclusion criteria and mostly focused on family medicine, internal medicine, and resident physicians. The results were reported with regard to the effects of interactions with pharmaceutical representatives, gifts, samples, industry-paid meals, funding for travel to attend educational symposia, pharmaceutical representative speakers, continuing medical education sponsorship, and physician honoraria. The author states that “interactions with pharmaceutical representatives were . . . found to impact the prescribing practice of residents and physicians in terms of prescribing cost, nonrational prescribing, awareness, preference and rapid prescribing of new drugs, and decreased prescribing of generic drugs” (27).

This last point may clarify the results reported by Dolovich et al., in that the Wazana meta-analysis was more comprehensive—it included larger numbers of respondents from multiple articles and covered a longer period of time. The Wazana article included studies published from 1982-1998 with a total sample population across 29 studies of 8,122 physicians and residents. The author suggests that interactions guidelines, practical training, academic detailing, and “industry-independent drug information mailings” may mitigate the influences that representatives have on physician prescribing. A finding from the Wazana article that elicits interest is that most physicians and residents denied that gifts were an influence upon their behavior. There were mixed reactions over interactions with the pharmaceutical industry and the extent of the influ-

ence upon prescribing behavior. The three factors identified in this review that applied the greatest influence on physician behavior were samples, CME, and conference travel funding.

One of the most recent and perhaps most comprehensive assessments of pharmaceutical representative influence on physician prescribing was released as a working paper by the Marketing Science Institute in 2004 (28). Mizik and Jacobson use econometric analyses to quantify the persistence in physician prescribing, accounting for "own-growth" and "competitive stealing" effects. The study also assesses the diminishing effects over time and controls for spurious correlations (practice size, others) of physician-related factors. The authors contend that the data treatment overcomes limitations of previous studies and includes approximately 74,000 physicians over 2 years, for a total of over 2 million observations.

Mizik and Jacobson assessed both the level of sales representative detailing and the level of drug samples on the prescribing behavior of primary care physicians for three drugs. "For each of the three drugs in the study," the authors report, "we observe statistically significant, albeit rather small, effects of detailing on prescriptions," labeling physicians as "tough sells" as opposed to "easy marks." As a result, the authors question the value of large sales forces, allowing for the possibility that profits may be increased and/or prices reduced "through a reduction in [pharmaceutical sales representative] numbers."

An even more recent study published in October of 2004 in the *Journal of Marketing* by Narayanan et al. explored the effects that DTCA and detailing have on brand share and category effects (29). The authors use analysis of the second-generation antihistamines, confirmed by analysis of antivirals, to conclude that detailing does not have a strong effect on category sales, but bolsters brand share and revenues with long-term effects.

If pharmaceutical sales representatives influence physician prescribing, what is the mechanism by which they exert this influence? One study shows that pharmaceutical representatives' influence upon physician prescribing is directly correlated with the level of credibility they have with a physician. Almost 500 primary care physicians in Kentucky participated in a study that assessed the costs of prescribing and the credibility of pharmaceutical representatives (30). A positive correlation was found between representative activity and credibility and the costs of prescribing, especially for those physicians practicing in nonacademic settings. In a separate survey by J. Scott International, Inc., physicians stated they value representatives who have extensive

knowledge of their drug and the correlating disease state and of physician needs and time constraints (31). The 2003 survey asked almost 2,000 physicians about information that would convince them to prescribe more of a certain product. The results showed that “objective information about the product is the most convincing item a sales representative can offer.”

How does the public feel about the access and influence pharmaceutical representatives may have with physicians? Overall, patients believe that physicians exhibit sound judgment and that pharmaceutical representatives are not manipulating prescriptions. In *The Wall Street Journal Online* and Harris Interactive poll of over 4,000 adults reported in 2003, a majority of patients agreed that the pharmaceutical industry marketed its drugs “a little” or “much too aggressively” (32). Two-thirds of respondents, however, trusted their physician to make sound decisions on drugs. Only 8% preferred that their physician not meet with pharmaceutical representatives. The study points to the relative comfort that the public has with the ways drugs are promoted. Patients don’t necessarily feel that pharmaceutical representatives are the ones writing their prescriptions.

How can a variety of comprehensive and well-executed studies produce contrary results? Measuring exact effects can be difficult, given the numbers of confounding factors that exist in a physician’s professional life. In the aggregate, it seems that physicians do respond to attempts from pharmaceutical representatives to increase share of their branded products, however debatable the effect size may be. At the physician level, careful consideration has been given to the amount of influence afforded to this channel.

Industry-Sponsored Educational Programs/Continuing Medical Education

Nonaccredited educational programs, including a presentation from a licensed health care provider, are effective in reaching small groups of physicians. Scott-Levin Associates, Inc., a pharmaceutical industry researcher, surveyed 18,400 physicians who attended a pharmaceutical industry sponsored meeting about prescribing changes (33). More than 60% indicated that they would start or increase their subsequent prescribing of the promoted product as a result of their attendance.

Another study assessed physician-prescribing changes resulting from attendance at pharmaceutical-paid symposia on a specific product (34). Use patterns were tracked for almost two years prior to and about a year

and a half after the conference. Although the interviewed physicians did not think the symposia would affect their prescribing, significant increases in the use of the promoted products occurred after the meetings. The increased use varied significantly from overall national use patterns. These specific types of promotion are now discouraged by PhRMA, HHS, and AMA guidelines. It is interesting to note, however, that general industry-sponsored education programs can exert strong influences on physician prescribing.

In 2002, at least \$1.6 billion was spent on continuing medical education (35). Spending on CME has been rising, ostensibly due to restrictions on other promotional activities (36). CME and other educational conferences and materials should be, by definition, free from specific promotional efforts (37).

In the Wazana article, 10 out of the 29 assessed studies discussed CME as an interaction. In the assessment, CME was found to exert more influence upon physician behavior than promotional material (27). One study cited reported that “changes in prescribing practice (self-reported) in favor of the sponsor’s drug were also found.” Despite changes in CME presentation and monitoring since the publication of the study (1998), it may be reasonable to assume that CME may still be used as a promotional tool by the pharmaceutical industry.

A commentary published in *JAMA* in 2001 asserts that “CME is now so closely linked with the marketing of pharmaceuticals that its integrity and credibility are being questioned” (38). Relman, the author, claims that pharmaceutical companies link financial support to content, speaker lists, actual materials, and specific attendees. As evidence, he states that there is a new, growing, for-profit industry that facilitates CME for physicians, and he blames physicians more than the pharmaceutical companies for this trend. “[T]he professional educators in CME programs who deal with pharmaceutical products,” Relman says, “are failing to do what the medical profession and society at large expect of them.”

In a counterpoint to Relman, Holmer (of PhRMA) applauds the “leading role” his industry has played in CME (39). He acknowledges that specific products may benefit from CME support, and through this partnership pharmaceutical companies may even “generate increased sales.” PhRMA has included CME in its Code on Interactions with Healthcare Professionals, choosing to delineate what types of funding are acceptable. Any subsidy that may be viewed as inappropriate, including direct payments to a health care professional, should instead be given to the conference’s educational sponsor (40).

CME has become big business. More and more, education is going online. Internet CME courses allow the physician to complete courses with less effort and at less cost. One source has observed that “the emergence of online CME also presents an opportunity to pharmaceutical companies” (41). The pharmaceutical companies themselves have funded Pri-Med, a provider of CME, “to develop ‘industry-supported presentations’” (42). In a crowded market, and with restrictions on promotional activities, CME is emerging as an arena where investment by pharmaceutical companies is paying off.

Medical Journal Advertising

Advertising pharmaceutical products directly to health care professionals in medical journals totaled \$278.9 million in 1999, a slight decrease from the amount spent in 1992 (43). The number of pages of ads has decreased, partially offset by rising space rates. By 2002, however, the industry’s total journal ad spending had increased to over \$752 million (44).

In general, journal ads perform a dual role: they both inform and influence (45). By informing they help to speed the adoption of novel therapies (thereby benefiting consumers), and they influence through increased brand recognition (thereby reducing physicians’ decision costs). Therefore, advertising has been shown to be pro-competitive, reducing product price following entry of a new product.

PERQ/HCI Research, a pharmaceutical promotion research firm, has studied the effectiveness of journal advertising and has concluded that the right message and execution determine product acceptance more than advertising spending (43). The firm reports that journal ads provide positive return on investment, especially in conjunction with pharmaceutical detailing (46). Rizzo (1999) tracked 46 drugs with annual data between 1988 and 1993 and found that “advertising decreases the price elasticity of demand in the pharmaceutical industry.” He concludes that “given the inverse relationship between elasticity of demand and price, it is likely that consumers pay higher prices as a result of the advertising that occurs in this industry” (47). A significant part of the effect was accounted for by detailing efforts, however, and his study may have neglected to account for physician-specific effects.

A study published in 1992 in the *Annals of Internal Medicine* assessed the accuracy of journal ads (48). Wilkes et al. had specialist physicians and pharmacists compare actual ads to FDA standards to assess accuracy. More than half of the ads “were judged by two or more re-

viewers to have little or no educational value.” Because some of the value of journal advertising as a motivator of prescribing is linked to the message and execution, most ads then have likely not delivered the expected returns.

Direct-to-Consumer Advertising

Expenditures for direct-to-consumer (DTC) advertising have increased in recent years. DTCA spending, as a percentage of total pharmaceutical firm promotion, has increased most markedly since the revised FDA guidelines in 1995 (49). As a result, Americans’ awareness of DTC ads is high (50). How has this affected physician prescribing?

One study in *Health Affairs* contends that “evidence is accumulating to suggest that clinical quality of care is harmed by DTC advertising” (51). Critics of DTC advertising contend that the relationship between physician and patient is being altered due to industry-informed consumers. The negative effects this may have on prescribing behavior may be correlated to inaccuracies in advertising information; pressures from patients to receive newer, less-studied therapies; and communications regarding brand names instead of discussions on managing and maintaining health (13, 51).

Ipsos PharmTrends, an industry research group, tracked changes in patient requests for specific brand products from 2001 to 2002 (52). Ipsos found that consumers are increasingly requesting DTCA brands and are more likely, as a result, to receive samples and then to fill prescriptions. Overall, the survey found that patient trial through sample use created by DTC advertising increased market share for leading DTCA drug classes, indicating pressure on the prescriber and/or improved diagnosis and treatment.

The effects of DTCA upon the physician/patient relationship may not be known for many years. There are some early indications that DTCA may not be as harmful as some critics assert. A 2003 FDA survey obtained physicians’ thoughts on DTC ads and the effects they had on patient care (53). More than half of those surveyed “believed that the patient’s exposure to the ad had benefited the physician-patient relationship in some way.” These benefits included the patients’ ability to ask better questions, increased responsibility for health care, and improved knowledge of therapies and treatments. The majority of physicians did believe, however, that DTC ads could be im-

proved by reducing confusion surrounding efficacy, adverse events, and risks.

The Kaiser Foundation survey revealed that patients were motivated to discuss health care issues with their physician as a result of having seen drug advertisements (21). A high proportion of physicians (60%) also feel that the Internet influences their patients at least “somewhat often.” However, the news media (80%) and friends and family (80%) continue to be more powerful motivators of patient-physician communication. This demonstrates that DTCA is only one factor in raising awareness and driving communication between physicians and patients.

Rosenthal et al. asserts in the *New England Journal of Medicine* that a study found almost three-fourths of family practice physicians surveyed believe that DTC ads pressure them “into prescribing drugs that they would not ordinarily prescribe” [as quoted in Sherer (13)]. But data collected on actual drug dispensing showed that less than 6% of patients received a prescription for the drug they initially asked about as a result of DTCA exposure.

Which conditions predispose consumer patients to regard DTCA as a valuable source of information? What are the characteristics of physicians who value DTCA most? Gönül, Carter, and Wind (2000) explored both physicians’ and patients’ receptiveness to DTC advertising (54). In general, physicians find DTCA less compelling than do patients, although physicians highly value DTC advertising when it is brought to their attention by patients. Younger and less educated patients and those with a chronic condition are most likely to value DTC. The recently sick, older patients, and more educated patients place more trust in their physician and are less likely to introduce DTCA awareness. From the provider perspective, “more experienced physicians . . . and physicians who receive a lot of patients per week . . . value pharmaceutical advertising more than other physicians do.” Overall, the results of this study substantiate prior research and confirm the conditional value of DTC advertising. It would appear that DTC ads, under specific conditions, actually enhance the physician/patient relationship.

Narayanan et al. (2004) quantified the effects of DTCA on pharmaceutical firm financial performance measures, finding that DTCA provides category sales effects, yet does augment brand share as with detailing (29). In the study, DTCA had long-term effects on revenue. Moreover, the interaction effects among detailing, DTCA, and price had statistically significant effects on brand shares. This study confirms the overall impression that has existed regarding DTCA: it enhances

synergistically the other marketing promotion elements that companies use and can bolster categories as it enhances individual brands.

The debate over DTC advertising continues. Proponents argue that patients are motivated to discuss health concerns. Critics assert that DTCA increases prices and influences poor choices. Recent information indicates that DTCA may be reaching a critical level of spending and maturation and that its effects may be just starting to show. A DTC advertising review of 41 brands by IMS Consulting in 2004 “showed that a positive ROI was achieved on a consistent basis, with a median ROI of almost \$2 for each \$1 invested, [with] 20 percent of brands having an ROI over \$3 for each \$1 invested” (55). Thus, assessing the long-term impact of DTC advertising on prescribing patterns may be helpful as marketing managers become more savvy in allocating DTCA dollars to appropriate brands and in developing more effective DTCA campaigns.

Most recently, the *Wall Street Journal* reported that erectile dysfunction drugs have not met sales expectations as a class (56). The article suggests that DTC advertising has not entirely met expectations for sales generation. It also states that DTCA can be crucial to sales in this therapeutic area, as Glaxo has had a tough time meeting growth expectations for Levitra[®] due to a ban on prescription drug advertising in most markets outside of the US. Pfizer has pulled its DTC ads for Viagra[®] since the FDA objected to missing information on side effects late in 2004. Based upon this and recent developments with Celebrex[®], Pfizer is now considering DTCA in a whole new light. A recent *Fortune* article summarizes the situation nicely (57):

Pfizer CEO Hank McKinnell is now rethinking his company’s approach . . . [he] believes ads—especially those on television—still aren’t communicating the notion that consumers should engage in their own cost-benefit analysis with a doctor before taking a drug. “I’m beginning to think direct-to-consumer ads are part of the problem . . . By having them on television without a very strong message that the doctor needs to determine safety, we’ve left this impression that all drugs are safe. In fact, no drug is safe. We’ve not done a good enough job communicating that . . . I see a role for direct-to-consumer advertising, but there are unintended consequences that we’re all going to have to deal with.

Drug Samples

A comprehensive review of literature on drug samples can be found in Groves et al. (2003), sorted by study design since 1986 (post-PDMA) (58).

Samples can provide pharmaceutical representatives with access to physician offices. Physicians may use these samples to offset, partially or totally, the cost to the patient of filling a prescription. And samples can be a strong influence on physician prescribing. In 1999, pharmaceutical companies distributed a total of \$7.2 billion in free samples (59). In the Kaiser Foundation survey, 92% of physicians reported having received free drug samples (21).

In one study, published in the *Journal of General Internal Medicine*, physicians were tracked to measure the effects of samples on their prescribing decisions (60). A total of 154 physicians self-reported their decision criteria for a single diagnosis. The study reported that physicians often dispensed and prescribed “drugs that differ from their preferred drug choice.” Physicians indicated that they used samples to help reduce the cost of filling a prescription. Perhaps not surprisingly, the study found that “younger [physician] age was independently associated with drug sample use.”

In another study that looked specifically at family practice residents’ and faculty’s prescribing habits in the antihypertensive market, samples were found to have a substantial effect (61). The authors reviewed first-line (generic) versus second-line (branded) prescribing during two time periods—one when samples were provided and one when samples were prohibited. The study found that “following prohibition of sample distribution, there was an increase in first-line antihypertensive use from 38% to 61%.” Tenured faculty were less likely overall, however, to use first-line drugs compared to the residents. Further studies should be conducted to replicate these findings and to determine whether this is a specialty-focused or therapeutic-area-focused finding.

Accel Healthcare Communications conducted an online survey of 150 high-volume primary care physicians that clarified the reasons why doctors see sales representatives (62). Ninety-two percent of physicians stated that they wanted drug samples, the top-rated response. Samples proved so valuable to physicians in this study that 63% of respondents said they would stop meeting representatives if samples were discontinued. Physicians are looking for objective and meaningful data in addition to samples. Accel recommends that sales representatives use

samples to access physicians and then deliver new information regarding treatment with their specific product.

Groves et al. reported the impact of drug samples on the quality use of medicines in the *Journal of Clinical Pharmacy and Therapeutics* in 2003 (58). The Canadian paper summarizes the findings of 16 original research studies on the influence of samples; many of the studies were done in the US. Samples are distributed mostly for branded products, making more available to the physician and patient at mostly higher product costs. This has a decided impact on the overall costs of drugs. Pharmaceutical companies use samples for many different reasons: to launch a new product, to compete with another drug, to change the image of a product, or to enhance demand and familiarity. Despite calling for more research on the quantitative impact of samples, the authors conclude that “sampling is a critical driver in the promotion and adoption of new products.”

Mizik and Jacobson (2004) also assessed the effects of drug samples on prescribing behavior (28). Once again, the extensive analysis of their large database revealed a small but statistically significant effect size of drug samples on prescriptions. The maximum effect was tied to the “rising star” drug, a possible indication that physicians were more responsive to information about a drug of interest. It might be interesting to tie these findings to the amount and intensity of DTC advertising for these products and to the influence of published outcomes studies to determine whether physician/patient interactions and reputable journal articles were factors in these varying response rates.

Gifts and Promotional Items

The extant literature contains a significant amount of data on gifts and their influence upon prescribing patterns. Much of the focus on gifts is presented within the context of medical ethics. Peppin’s systematic review of the arguments against representative-physician interaction and gift giving sets out compelling reasons for the “moral impermissibility” of this relationship (63).¹ In the end, however, the effects of these arguments are equivocal, in that they present logically compelling reasons to shun such relationships, but are lacking any empirical evidence to support them.

Recent changes in gift-giving policies, however, have altered the amount that may be spent on gifts. As a result, new research should be done to estimate the impact of new types of gift giving or the shifts toward other resources and their resultant effects. But is the amount spent

on a gift directly correlated with its effects? That question is explored after the changes in gift-giving policy are outlined.

In 1992, the American Medical Association (AMA) developed guidance on gifts for its physician members. It stated: “Gifts to physicians from pharmaceutical and medical device companies primarily should entail a benefit to patients and should not be of substantial value” (64, 65). In April of 2002, the Executive Committee of the Pharmaceutical Research and Manufacturers of America (PhRMA) adopted its own, similar view on the subject. The voluntary code states that modest amounts may be spent by pharmaceutical representatives on physicians (but not on spouses or guests), only if “the interactions of company sales representatives with healthcare professionals are to benefit patients and enhance the practice of medicine” (66). Following that, the Office of the Inspector General (OIG) for the Department of Health and Human Services (HHS) released guidelines for the promotion of pharmaceuticals, published in the *Federal Register*. Although voluntary, the guidelines called for developing a compliance committee, conducting training and education, monitoring activities, and responding to problems (67). Most pertinent, gifts and gratuities were listed as questionable activities. The OIG guidance gives credence to the PhRMA code. As a health care source observes, the industry code “provides useful and practical advice . . . and . . . adherence to the code will . . . help demonstrate a good-faith effort to comply with the applicable federal health program requirements” (68). As a result, under all guidelines, substantial gifts should no longer be a significant promotional activity for pharmaceutical companies and are expected to be greatly reduced.

The issue of gift giving has become so sensitive to some lawmakers that in 2002, Vermont became the first state to mandate the reporting by physicians of the receipt of gifts that are valued at \$25 or more (69). The definition of gifts includes meals, trips, or consulting fees, but it excludes drug samples. It has been reported that other states are considering similar measures.

Promotional items, or gifts of relatively insignificant monetary value, have been distributed by pharmaceutical representatives under the auspices that these items might be of some benefit in the delivery of health care. The real intent of leaving gifts of nominal value is to attempt to capture “mindshare” of the prescriber by having some presence of a product beyond the sales call or in exchange for the physician’s time spent with the pharmaceutical representative. What amount of money defines the boundary between “significant” and “insignificant” with regard to gift giving? Aside from the arbitrary limits set by some lawmak-

ers, this issue can be explored by examining social science research on the nature of influence.

It has been reported that physicians overwhelmingly believe that the acceptance of gifts has little or no impact on their prescribing decisions. In a 2002 *Medical Economics* article, Murray reported the results of a survey: "71% of physicians do not think that accepting gifts, trips, and hospitality from pharmaceutical companies diminishes their objectivity" (70). This finding was confirmed among a sample of radiation oncologists: "74% felt that they should be free to accept gifts of small value" (71). This second study included an interesting (and statistically significant) finding. Physicians overwhelmingly believe that gifts influence their peers' prescribing more than they influence their own prescribing. Perhaps this methodology controls for social desirability bias to reveal the true impact of gifts upon a physician's own prescribing.

Another study set out to compare the attitudes of physicians and patients toward gifts (mostly of nominal value) from the pharmaceutical industry (72). Patients felt that gifts might influence prescribing and were inappropriate. Physicians believed that "knowledge of guidelines" best predicted prescribing. The study illustrates the differences that can exist between patient and physician on the importance and appropriateness of gifts to the medical profession. Perhaps some level of physician awareness of patients' feelings on this subject creates a social desirability bias among studies on gifts. These studies are in some respects in direct contrast to theory, begging for research that controls for social desirability bias.

Katz, Caplan, and Merz (2003) present the issues regarding size of gifts and potential impact in their review in the *American Journal of Bioethics* (73). Their argument is that gifts, regardless of value, create a sense of obligation in the recipient, even if there is no awareness of this feeling of indebtedness. This exchange dynamic is not related to the size of the gift; in fact, it is true even if the gift is unwanted or refused. "Regardless of the size of the gift," the article states, "it is widely considered distasteful or bad form to take but make no effort to give in return" [quoting Cialdini (74)]. Finally, physicians are limited in the way that they may express their reciprocity, most often in the form of product support. If physicians contend that pharmaceutical representatives are a valuable source of information and that gifts are "the cost of doing business," then gifts are an unnecessary expense, given that the information exchange would take place anyway. The authors conclude that based upon the influence of gifts, regardless of monetary value, "there is no

level . . . below which it is guaranteed that marketing wares have no effect on the recipient.”

An interesting area of research might explore the extent to which drug samples may be perceived as or have the effect of a gift. If a physician requests samples, certainly the sense of indebtedness may be acute. If a physician routinely accepts samples but does not have a sense of obligation at the time of receipt, is there a “gift effect” at the time the samples are distributed? It seems reasonable, based upon the aforementioned research, that this might be the case. Perhaps the receipt and use of samples is having a more profound effect upon prescribing than mere convenience; the reciprocity factor may enhance the value of samples as gifts.

Comprehensive Analyses of Pharmaceutical Industry Marketing Efforts

Two studies, both funded by the Association of Medical Publications (AMP), used vast databases to assess the effects of four pharmaceutical marketing elements on financial returns: detailing, DTC advertising, medical journal advertising, and physician meetings and events. These four tools comprise most of the review conducted already in this article, are mechanisms by which pharmaceutical companies attempt to influence physician prescribing, and are combined neatly in these two studies in a comprehensive manner.

Neslin conducted the first study, ROI Analysis of Pharmaceutical Promotion (RAPP), in 2001 (75). Data from 391 brands, inclusive of all with greater than \$25 million in revenues in 1999, were analyzed using ordinary least squares regression to determine how each of the 4 factors affected ROI and to determine how the ROIs varied according to 3 categories of brand size. Three time periods were used, with brands assigned according to date of launch: pre-1993, 1994-1996, and 1997-1999.

For the median brand, ROIs (with 95% CIs) were highest for journal advertisements ($\$5.00 \pm \0.88) and for meetings and events ($\$3.56 \pm \1.92). Pharmaceutical representative detailing yielded positive returns as well ($\$1.72 \pm \0.19). DTC advertisements, however, showed a low ROI ($\$0.19 \pm \0.52), with a 95% confidence interval that spanned zero, making inferences questionable. This provides support to the Narayanan et al. study mentioned previously in that DTCA affects class effects more than brand share effects. Perhaps DTCA is still too new

(only since 1995) for research to provide conclusive evidence on its effects of patient demand upon physician prescribing.

The RAPP results also demonstrate that larger and newer brands benefit most from all four types of promotion. ROI for journal spending decreased directionally across all three time periods for all three brand sizes. These results seem to correlate with the overall findings from the review of journal advertising in that this promotional tool can produce desired effects only if the message is clear and credible, and during the years studied in RAPP, journal advertising total spending had stagnated. The results also corroborate the findings in Mizik and Jacobson, where newer and larger brands commanded the most attention from physicians and the best returns on effort.

The second study, *Analysis of ROI for Pharmaceutical Promotion: A Second Independent Study (ARPP)*, was released a year later, in 2002 (76). Wittink used the same data as the RAPP study, augmented with 1 additional brand, for a total of 392, and with 1 more year of data (includes 2000).² Results match RAPP results in many ways, including the confirmation “that all four promotional tactics work.” Moreover, DTC spending has not provided ROIs as robust as other tools. The maturation of DTC, however, may be revealing its power. The addition of one year of data shows that ROI (for the largest brands only) finally breaks the threshold for underutilization (\$1.00). Nonetheless, the author generally concludes that “there is overspending on DTC advertising.”

In the ARPP analysis, detailing continues to show strong ROI, especially for the largest brands launched most recently. If large brands can be equated to dominant firms, then this analysis correlates with the findings from Sorescu et al., mentioned in the introduction of this article, which showed that superior resources beget superior results. This resource advantage is most acute for dominant firms in the Sorescu study and most acute for the largest brands in the ARPP study (16).

One caveat with both the RAPP study and the ARPP study is with the conclusions on pharmaceutical detailing. For the largest brands launched most recently, marginal ROI was reported to be \$10.29 in the RAPP study and \$11.60 in the ARPP study. These returns are far greater than any of those reported for most of the other marketing resources and greater than those reported for any other size brand or for any other time period. Based upon these results, both authors recommend that firms consider diverting resources away from lower ROI tools toward pharmaceutical detailing. This reveals the potential weakness of the methodology: it is predictive only of a linear relationship when, in fact, a

curvilinear relationship might instead exist. There may be a point at which it is no longer advisable to invest in detailing, as the ROI plateaus and then begins to decline.

An inverted U-shaped effect was shown in two studies: one an analysis of insurance coverage, detailing, sample activity, and price upon physician prescribing, the other a study of individual physician-level responsiveness to detailing and samples (77, 78). The first's findings on detailing included "too little or too much cumulative personal selling is suboptimal and that any repetitive detailing or free sample activity must be done with caution." The second echoed the same conclusion: "There are diminishing effects of detailing on prescription behavior." The mechanism to explain this might be the saturation of physician patience and time and the resulting response of behavior contrary to stimulus. It is not true that a "more is better" relationship exists across all ranges of spending.

Economic Influences

Managed Care Influences

Managed care organizations (MCOs) provide some level of health insurance coverage for their customers in exchange for an annual fixed premium. Prescription drug coverage may vary, but one similarity exists among almost all plans: the insurance companies attempt to control costs by having some type of preferred drug list (PDL), or formulary. This formulary may serve as the basis for control over the types, brands, and lengths of therapy that prescribers may write for patients.

In 2001, *Managed Care Digest* reported that health maintenance organizations (HMOs), one type of MCO, increased their control of physician prescribing during the 1990s: "The percentage of HMOs that placed no controls on physician prescribing practices fell dramatically during the 1990s, to 7.7% in 1999 from 22.8% in 1990" (79). Types of prescribing controls exerted by HMOs included financial incentives, drug utilization reviews (DURs), quality assurance, practice guidelines, and prior authorization requirements. HMOs used DURs to monitor prescribing patterns to assess physician adherence to the PDL. Most recently, the trend is away from the HMO structure for most commercial providers, although some models still show great promise as a form of health care delivery.

Fillit et al., in the *American Journal of Managed Care* (1999), reported an example of how a DUR may affect physician prescribing (80).

In this study, a Medicare population at risk for multiple medications (polypharmacy) was reviewed to ensure safety and adherence to clinical guidelines. The patients in the review discussed their prescription and nonprescription medications, and physicians were supplied with clinical guidelines to assess pharmaceutical needs. "Overall," the study concludes, "forty-five percent of physicians reported making at least one change in their prescribing to a member at risk for polypharmacy." More than a third of physicians reported that they discontinued unneeded medications. The study demonstrates the significant impact a managed care organization can have on physician prescribing through utilization controls.

Often, the most restrictive formulary in a market, whether established by a commercial plan or the government (such as a state-run Medicaid program), can exert significant influence on the prescribing patterns of physicians beyond even the covered lives (spillover effects). In Maine, one of the states most active in establishing a restrictive formulary, a change to the state's Medicaid coverage of proton pump inhibitors affected the entire market (81). Linear regressions confirmed that Maine prescribers used the preferred drug over alternatives, even in the cash-paying and third-party-paying populations. The effects in Maine were significant relative to neighboring states (Vermont and New Hampshire), indicating that restrictive drug formularies can have profound effects on physician prescribing, even beyond the intended covered lives. Recently, however, Maine has put a moratorium on the restrictions on the antipsychotic class (Risperdal®, Zyprexa®, etc.) due to higher hospitalization costs. This move indicates the realization by some entities that control of costs through preferred drug lists can be a double-edged sword, putting off some short-term costs for potentially higher long-term expenditures.

What happens if a managed care organization does not like the choice of prescription drug that a physician writes? Can the pharmacist be told to comply with an MCO request to change the prescription? As of 1996, according to an article by Storms, approximately 25% of HMO formularies allowed therapeutic substitution (82). In the case of therapeutic substitution, a decision made by the physician may be "undone" by the administration. Storms addresses the potential near-sightedness of MCOs. "Most managed care organizations," he states, "have not looked at the total impact of these formulary restrictions . . . [r]ather, they have only looked at the cost of the drugs dispensed." His recommendations include rejecting the influences of the HMO upon prescribing decisions for the sake of their immediate financial outcomes. Instead, Storms con-

tends, physicians should consider the best possible long-term health outcomes for their patients.

Looking at the component on insurance coverage and physician choice from Gönül et al., we see that the restrictive nature of HMO and Medicare formularies can create limits on the effects that pharmaceutical detailing may have (77). Compared to the effects seen on physician prescribing for patients with private insurance, HMOs and Medicare formularies dampen “the main positive effect of detailing and samples on the drug prescription probability.” This leads the authors to conclude that “personally selling to physicians with mostly HMO patients is wasteful.” These results speak to power that can be wielded by restrictive formularies that encourage generic use.

Primary care physicians need to be involved in formulary decision making, not merely managed through formulary implementation, for true cost savings to occur and for patient care to be enhanced. Network and group model physicians involved with one plan in Washington, DC, illustrate this clearly (83). Almost all of the 243 physicians surveyed “believed that education and feedback were appropriate methods to control costs in an HMO”; however, “intrusive administrative interventions” were less likely to be accepted. Both network and group model physicians indicated that “patient expectations often dictate more costly prescribing than is necessary.”

This last point shows that the limits that managed care organizations have on controlling physician prescribing still exist in concert with the strong pull of the physician/patient relationship. A recent study used three different types of statistical analyses to assess physician prescribing in a managed care environment (84). It attempted to “quantify the role of interphysician variability relative to overall variability in managed care pharmacy expenses,” by comparing the results of two managed care plans that differed in their pharmacy expenditures. The study found that there were large variabilities in individual physician prescribing, despite similarities in systematic prescribing. The authors concluded that “other factors [than MCO intervention] were most likely driving these [increased] costs.”

While managed care restrictions are uniquely positioned to have direct controls upon physician prescribing, their effects can only partially explain changes to physician prescribing. The impacts of other types of influences, some discussed in this paper, are strong, yet sometimes insidious. There appears to be no single major factor, however, that administrators or policy makers may use to affect physician prescribing.

Price/Cost Information

A comprehensive look at pharmaceutical pricing and distribution channel costs can be found at the Web site for the US Department of Health and Human Services (85).

The actual cash price of a drug cannot be easily measured. Surveys of pharmacies can reveal a wide variety of prices for the cash-paying customer, creating a market where “there is no one price for a specific drug product” (14, 86). Managed care plans, with pharmacy benefits, can mask the price of a drug to the consumer because the insurance company is paying for the bulk of the cost. The cost of pharmaceuticals differs widely from health plan to health plan, due to variations in contracting and rebates.

As a result, the communication of drug price to a physician can be manipulated. The HHS paper established that insured consumers pay less for drugs than uninsured consumers due to the bargaining power of large groups of purchasers. As the percentage of cash customers has decreased (from 63% in 1990 to 25% in 1998), the trend toward masked costs has increased (86). Perhaps the most recent trend toward patient-directed (read: risk-shifted) plans will once again increase price transparency for consumer patients.

The California HealthCare Foundation report states that “physicians are generally unaware of drug costs and therefore do not factor relative costs into their drug selection decisions” (18). A study of family physicians published in the *Archives of Family Medicine* in 2000 confirmed this (87). Less than a quarter of surveyed physicians were able to correctly report medication price. Approximately 90% of physicians underestimated the costs of branded drugs and overestimated the costs of generic drugs. The study concluded that the increased availability of price information might be an independent factor in helping physicians prescribe more cost-effectively.

Gönül et al. (2001) confirmed that physicians are, for the most part, unaware of price (77). Price sensitivity, however, can be increased through detailing and sampling activities. This implies that detailing may have counterproductive effects, from the perspective of the pharmaceutical companies, and that the public good may not be necessarily harmed by the marketing activities of pharmaceutical firms.

Overall, physicians are unaware of true medication costs. This may exclude price from the set of factors that motivate prescribing. It is more likely, though, that physicians are including their (skewed?) perceptions of pricing in their decision model for evaluating drug options.

More investigation should be done on the complex issue of physician awareness of drug pricing and its effects on prescribing patterns. Until or unless physicians obtain a more objective impression of price, studies should emphasize measuring price as price elasticity, perception, or sensitivity.

The Effects of Nonmarketing Sources of Medical Information

Not-for-Profit Activities

The Centers for Disease Control and Prevention (CDC) and other organizations have teamed up to increase physician attention to the issue of judicious use of antibiotics. The success of these activities was measured for the years 1996-2000 and reported in *Pediatrics* (88). Dispensed medication data were used to indicate the extent to which physicians embraced the initiative's efforts. Results show that antibiotic rates decreased for all assessed age groups and that first-line antibiotic use increased, especially for middle ear infections (otitis media). The report concluded that "attention by public health and professional organizations and the news media to antibiotic resistance may have contributed to changes in diagnostic thresholds, resulting in more judicious prescribing." Public education campaigns by not-for-profit groups can exert influence upon prescribing patterns.

Peer Influence

One-to-one peer influence is being used and evaluated more as a tool to influence physician prescribing. As part of a comprehensive program to reduce pharmaceutical expenditures, peer-to-peer academic detailing has proven to be an effective tool (89).

In one study, infectious disease physicians studied the effects of peer review on the inappropriate prescribing of antibiotics (90). The study found that simply lecturing physicians on recommended therapies and publishing guidelines is not enough to change behavior. Involving physicians with "interactive, hands-on workshops" and offering peer feedback increase adherence to prescribing guidelines. Academic detailing, or the selling of clinical recommendations by health care professionals to physicians, has been consistently effective. "When combined with these strategies," the authors conclude, "closed formularies become a powerful tool in changing prescribing behavior."

Another study by Steele et al. published in *Annals of Pharmacotherapy* examined the effect peer academic detailing can have on a physician when a PharmD delivers it (91). The study compared three groups: one received visits from clinical pharmacists, another received written assessments of how their prescribing compared to their peers, and the last group received neither intervention. Measured outcomes included prescribing costs and the number of prescriptions written. About a third (30.3%) of the recommendations written by the clinical pharmacists resulted in prescribing changes. None of the groups decreased the number of written prescriptions, but the face-to-face group was the only one to show a statistically significant drop in prescription costs, even when including the salaries of the clinical pharmacists. This might be attributed to the substitution of generic products for more expensive branded products. The study shows the power of peer influence, especially when it is delivered in a professional and evidence-based manner.

In Oregon, the Health Resources Commission has released results from two academic detailing pilot programs (92). Simply sending literature on drug classes changed prescribing patterns in the range of 5-10%, the pilots showed. "However, when they were visited by an academic detailer," an *Oregon Health Forum* newsletter reports, "that rate jumped to between 40 and 50 percent." The state will fund a complete program in 2004 to physicians who treat Oregon Health Plan patients, estimating that they can save between \$200,000 and \$400,000 with academic detailing. Health insurance companies, including Regence Blue-Cross BlueShield, have pursued similar programs in Oregon recently. Academic detailing has begun to show positive return on investment due to its strong ability to influence prescribing decisions.

As mentioned in the managed care review, formulary restrictions alone cannot function as an effective motivator. Physicians want to maintain some level of autonomy in the delivery of patient care. They look to other physicians and health care professionals to help them decide what is best. Academic detailing is expensive, and its use has been mostly tied to situations where documented financial returns exist.

Medical Literature

Peer-reviewed, breakthrough literature can play a part in motivating physicians to alter their prescribing habits. The overwhelming quantity of medical literature can be daunting (93). How literature becomes breakthrough is outside the scope of this review. It is sufficient to note, however, that the extent to which popular media outlets report a particu-

lar study's results, as well as the extent to which practitioners acknowledge a study's impact, helps to delineate the "breakthrough" nature of a study. Studies that have considerable impact through effects on large numbers of providers operate through much the same mechanisms by which individual prescribers are affected by lesser known studies and are thus equally important to this review. Additionally, medical literature is discussed in a "market of information" that is, to some extent, facilitated by pharmaceutical industry efforts.

As examples, results of clinical studies reported in areas such as hormone replacement therapy, antihypertensive therapy, and most recently, COX-2 inhibitors, demonstrate breakthrough literature. Two recently published articles, both widely discussed in the nonmedical mass media outlets, assessed the first two of these therapeutic areas, with seemingly conflicting results.

Hersh et al. assessed the national use of postmenopausal hormone therapy and published the results in January 2004 in *JAMA* (94). The authors compared the total number of estrogen/progestin combination prescriptions in the US from 1995 to July 2003, evaluating the impact of a trial published in July 2002 that showed increased cardiovascular and other events in women taking this combination. Total prescriptions were evaluated using two separate databases. Following the publication of the trial, overall prescriptions declined steadily. The two top products in this category declined 66% and 33% in one year. The authors conclude that "clinical practice responded rapidly to recent evidence of harms associated with hormone therapy."

In a separate trial published in the same issue of the same journal, Stafford et al. evaluated the impact of clinical trials on α -blocker use during roughly the same time period (1996-2002) (95). Throughout the 1990s, α -blockers were used extensively as antihypertensives. In April 2000, the "unfavorable Antihypertensive and Lipid-lowering Treatment to Prevent Heart Attack Trial (ALLHAT) [included] early termination involving the study's doxazosin mesylate [α -blocker] arm." The authors assessed "changes in prescribing . . . in the context of other potential concurrent influences on medication use between 1996 and 2002, including changes in α -blocker drug prices, generic conversion, drug promotion, and competition." US pharmacies dispensed fewer prescriptions following the trial publication, but the changes were "modest," despite being statistically significant. For the three-year period following the publication of ALLHAT, α -blocker new prescriptions declined 26%. What may have blunted the decline of α -blocker

use is the indication to treat benign prostatic hyperplasia (BPH), obtained in the mid-1990s. Despite the ALLHAT data, physicians may have chosen to maintain their patients with both hypertension and BPH on an α -blocker and add a different antihypertensive to treat high blood pressure.

Both trials demonstrate the impact that important outcomes studies can have on physician prescribing. How these data are disseminated, and by whom, deserves a further look to determine ways to heighten and bring immediacy to their impact. More and more, significant medical breakthroughs are being reported to the general public as well. Exploring this impact in the face of increasing direct-to-consumer advertising by altering consumer pressure on prescribers is also worth further consideration.

Other Considerations

Physician Experience

Physician experience can play a major role in prescribing behavior. Physician experience can be divided into two types: (1) initial training and education, including medical school, residency, and possible fellowship, and (2) ongoing, including outcomes and adverse effects, patient feedback, and personal use. This distinction is important to note because some studies mentioned in this article have evaluated the effects of influences within a residency setting. The literature on ongoing physician experience is limited.

Any interaction with a patient should include a discussion of the desired outcomes, the possible adverse effects of pharmaceutical treatment, and the possible treatment alternatives. An article on the physician-patient relationship characterized this interaction as “an ‘agency relationship’ where informed agents make decisions for uninformed clients” (96). The variables involved in whether a prescription is written, or regarding the type of prescription that is written, include the ‘need’ for a prescription by the patient, the acute or chronic nature of the disease, and the level of communication between the physician and the patient.

An interesting article by Stolley et al. entitled “The Relationship Between Physician Characteristics and Prescribing Appropriateness” measured the dependent variable by a panel of experts (97). The overall perception of “detailers” by the “better prescribers” was negative.

Among the factors that were correlated with “prescribing appropriateness” were reliance upon journal articles for information on new drugs, additional training, frequency of peer consultation and referral, and *fewer* years of experience. This more “modern” and “cosmopolitan” physician was found to be more concerned with quality and less influenced by sales representatives.

The total of this understanding is that the experience of the physician can be paramount even to the acquired knowledge or initial desires of the patient. The impact of prescribing habits obtained during the initial training phases, including medical school, residency, and possible fellowship, needs to be further investigated. One article demonstrates, for instance, that a successful training program can impart information processing skills to residents, which in turn increases their ability to make more informed decisions (98).

It is possible that habits are formed at those times when pressures induce physicians-in-training to limit, rather than to expand, their options. More research is needed to assess the level of experience needed for a physician to feel comfortable with a new medication, as well as to determine the number of failures or adverse events a physician may see before discontinuing prescribing of a known product.

The Use of Technology

Just as the Internet has opened up medical information for consumers, technological innovations have the power to change the way physicians may research and prescribe medications. The roles of new technologies in influencing the prescribing patterns of health care professionals can be profound. They may be used to advertise, as in the case of banner or pop-up ads on the Internet. The use of e-mail is becoming the preferred method for receipt of invitations to pharmaceutical events (99). New technologies may also be used to deliver key information at critical decision points in the delivery of health care.

Pharmaceutical firms are using the Internet to access physicians who are difficult to see or to reach physicians who are expensive to visit. E-detailing, or the delivery of a sales message using electronic media, has exploded in recent years. The top 20 companies will spend almost \$200 million in 2003 on e-detailing alone (100). E-detailing will most likely become a more commonplace complement to field-based sales representatives (10).

A study published in *Pediatrics* in 2001 demonstrates the power of interventional technology in the prescribing of antibiotics for ear infections (101). Onscreen messages about evidence-based recommendations delivered to physicians at the point of care affected the average duration of therapy written. Most importantly, the study showed that the technology decreased the number of inappropriate prescriptions. The study is significant because it is the first to show how technology can *reduce* prescribing output.

In Hawaii, one organization piloted the use in 2000 of an e-prescribing application with a handheld device to “generate cost savings” (102). Increased compliance with formulary and “appropriate use of generic medications” produced a reported 15% increase in generic utilization. As a result, the use of this technology was expanded. Other benefits claimed included increased patient safety and convenience. The California Health Care Foundation paper advocates the use of handheld technologies, PC-based clinical and administrative information systems, and electronic distribution of timely reports as key drivers for proper drug selection (18). The foundation advocates computerized prescribing as “the promise of the future” due to its ability to provide updated guideline and formulary information as well as patient-specific clinical information and to its ability to reduce errors and drug-drug interactions.

Keys et al. described an example of computerized tracking and control in the *American Journal of Health-System Pharmacy* in 1995 (103). Over 160,000 pharmacy claims totaling over \$4 million were reviewed for variances from drug use criteria. Plans were implemented to deliver academic detailing to physicians, and savings were documented. “Potential drug costs savings totaling nearly \$280,000 were [initially] identified,” the study states, and ongoing monthly savings of more than \$12,000 were found. The study demonstrates the type of financial impact technology can have on the delivery of drugs, as well as the immense impact it can have on physician prescribing.

Technology alone cannot treat patients; it can be used as a tool to motivate change in pharmaceutical prescribing. As information becomes just-in-time, physicians will be able to have important information at their fingertips at the point of care. Who prepares this information, how it is delivered, and the efficiencies it brings to the workplace will determine the extent of the benefits that technology can bring to the practice of medicine.

CONCLUSIONS

Future Considerations

The factors that influence physician prescribing are powerful and pervasive. As mentioned in the introduction of this paper, the amount of money spent by pharmaceutical companies on direct-to-consumer (DTC) advertising is increasing significantly. This is done, ostensibly, with the hope that consumers will ultimately ask their doctor for or about a particular drug. First, future assessments should focus on better understanding the influence of consumer pressure on the physician/patient relationship and subsequent prescribing decisions. An article that appeared in *U.S. News and World Report* in 2001 is indicative of the growing interest among the general public in better understanding how physicians choose drugs (104). It mentions DTC advertising as a factor that is abhorred by physicians but respected as a motivating influence. “Many doctors cringe when patients come to them asking for a specific medicine shown in an ad,” the article states. “But [the physicians] are reluctant to say no, often fearing that spurned patients simply will take their business to another physician.” Clearly, the influence of patients upon physicians can be significant, and an attempt to further quantify this influence should be made.

Second, future research might consider accounting for interphysician variability in the response rates to different stimuli. As most of the research covered in this article deals with aggregate results, explaining sensitivities to different influence factors would allow for more specialized contacts by involved parties. Examining the effects of the dynamics of physician interaction on prescribing decisions would reflect the empirical reality of the physician in an outpatient setting, in other words, the study of information effects *among* physicians in addition to “what happens *in* the individual physician” (15). This might also include assessing the influence of social desirability bias, perhaps by collecting physicians’ perceptions of influences upon their own prescribing compared to those factors they perceive as influencing their peers.

Third, more research is needed to explore the decision heuristic of when writing *no* prescription might be preferable to prescribing a pharmaceutical therapy. There are certainly instances when prescriptions may be overused, including acute illness that might otherwise be resolved on its own (viral respiratory infections, for example), or when compliance with behavioral modification might replace or enhance a

drug for chronic illness (as might be the case for obesity, alcoholism, reflux esophagitis, etc.). Much of the literature in this area is centered on the appropriate use of antibiotics and can serve as an example of how public campaigns might influence a physician to forgo the writing of a prescription.

Fourth, most of the extant literature that has attempted to quantify effects on prescribing patterns has used ordinary least squares regression with empirical share data or survey data. Supplementing and extending these analyses with more advanced techniques will better approximate the complex heuristics that physicians call upon when choosing medications for their patients. One example is the methodology (fixed-effects distributed-lag model) briefly explained previously in the Mizik and Jacobson (2004) study (28). Another technique that might be used more frequently is stated preference/revealed preference modeling. Mark and Swait (2003) demonstrate a solid example of this methodology in their assessment of prescribing decisions for the treatment of alcoholism. The authors conclude that “stated preference techniques offer the opportunity to understand how physicians will receive new medications that are not yet available but that may be marketed in the future” (105).

Fifth, examining the mix of factors that influence prescribing at various stages of product or innovation class adoption might be explored. Miller (1974) reviews literature in this very way and concludes, for instance, that “detail men are the most influential source of drug product information in the early stages of the adoption process” (15). He finds that in any subsequent stage, it appears that physician prescribing is more robust to the effects of commercial sources of influence. Applying quantitative methodological techniques to uncover the dynamics of the complex process of prescribing decisions in various adoption stages would be valuable.

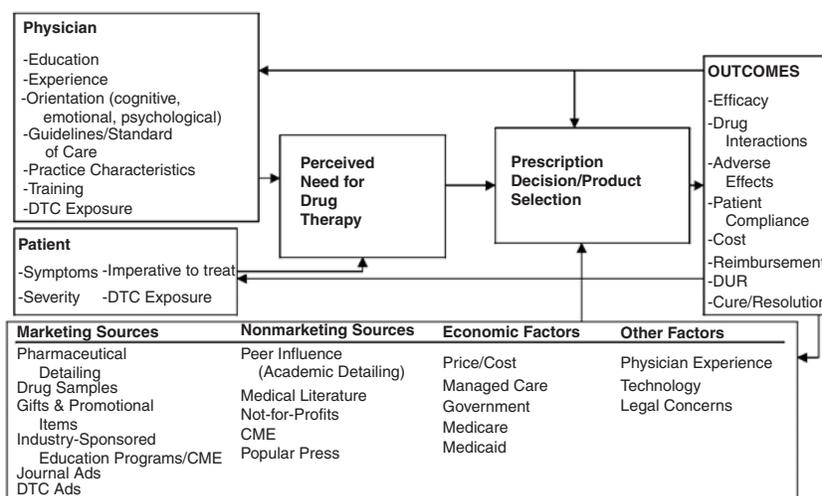
Finally, developing theoretical models of physicians’ prescribing behavior, even by therapeutic area, would bring immense rigor and comprehensiveness to this research stream. Few attempts have been made in this area, with most too old to be of much predictive value today (106-109). One fairly recent study by Freeman et al. (1993) attempted to model prescribing patterns for drugs used to treat panic disorder (110). Their model explained approximately 60% of the variance in physician prescribing in this therapeutic area. Efforts such as this would bring value to many entities, both in endeavoring to affect various influential factors and in attempting to modify the weights of these factors.

Proposed Theoretical Model

An attempt to develop a general theoretical model of physician prescribing in the outpatient setting, based upon the factors enumerated in the present article, can be seen in Figure 2. The model is based upon empirical examination and the review of extant literature and has three major components: (1) antecedents, (2) the process of translating a perceived need into a prescription decision/product selection, replete with factors discussed in this review that may affect this process, and (3) outcomes. There are feedback loops from outcomes to the antecedents of the next prescribing decision, to the patient, and through physician experience to the product selection for the reevaluation of the current decision.

The model includes education, experience, orientation (cognitive, emotional, and psychological), guidelines/standard of care, practice characteristics, training, and DTCA exposure as physician-based antecedents that enter a prescribing decision. Included in patient-centered antecedents are symptoms, imperative to treat, severity, and DTCA exposure. The factors discussed as marketing and pharmaceutical efforts,

FIGURE 2. Proposed Model of Prescription Decision Making for a Physician in an Outpatient Setting.



nonmarketing sources, economic factors, and other factors serve as influences upon physician prescribing.

The purpose of this attempt at a model is to spur further consideration of a comprehensive view of factors and their placement and significance upon physician prescribing. Each category, and each individual factor within each category, could be examined independently for effects of influence upon physician prescribing. Interactions among the various factors might also be examined.

Summary

The pharmaceutical industry can have a profound effect on a physician's prescribing. The extant literature suggests that as the industry has increased its promotional activity, including direct sales efforts, physician prescribing has been affected. It is worthwhile to note that the bulk of the literature takes a negative approach toward the pharmaceutical industry. This built-in bias is an important finding in itself. It is this author's contention that no comprehensive, meaningful solution to the increasingly acute issue of increasing health care costs can emanate from a position of disrespect for any of the involved parties. The unique aspects of service industries, and of health care specifically, allow for the opportunity for concessions and opportunities alike to abound for each constituency.

In summary, then, industry-sponsored education programs can exert strong influences upon physician prescribing, yet the debate over DTC advertising continues. Proponents of DTCA argue that patients are motivated to discuss health concerns. Critics assert that DTCA increases prices and influences poor choices. More information is needed to assess the long-term impact of DTC advertising on prescribing patterns.

CME is emerging as an arena where investment by pharmaceutical companies is paying off. Pharmaceutical samples have had a critical influence upon prescribing patterns and are also being used by health care administrators to increase use of generic and preferred brands of pharmaceuticals. Considering the amount and variety of promotional tools that the pharmaceutical industry has at its disposal, compared to the strength of the tools and resources available to nonmarketing sources, it seems reasonable that there are effects from their deployment. New technologies, deployed with the correct strategies, in addition to changes in public perceptions and/or policy, seem to hold the most potential for harmonizing with the rather loud voice of industry influence.

While managed care restrictions are uniquely positioned to have direct controls upon physician prescribing, their effects can only partially explain changes to physician prescribing. Other factors must be included for physicians to exhibit changed behavior. Public education campaigns by not-for-profit groups can exert influence upon prescribing patterns. Academic detailing has begun to show positive return on investment due to its strong ability to influence prescribing decisions, but it is limited in use by its relatively large expense. Technology alone cannot treat patients; it can be used merely as a tool to motivate change in pharmaceutical prescribing. Pricing as a factor needs to be studied further because physicians are, for the most part, unaware of true medication costs. This may exclude price from the set of factors that motivate prescribing. More likely, however, physicians are including their perceptions of pricing in a decision heuristic for evaluating drug options.

How any interventions are managed, and by whom, will play a big part in the future of pharmaceutical prescribing and in cost trends. Integrating nonindustry efforts with DTCA and pharmaceutical industry efforts may well pose the greatest chance of constructively influencing prescribing patterns. After all, whatever interest exists in exploring factors that influence prescribing patterns most likely is due to attempts to gain control over costs, and, as those responsible for the costs of health care become more broadly defined, the interest in factors that influence prescribing will most likely not diminish.

Overall, the body of evidence on the factors that influence physicians' prescribing of pharmaceuticals is relatively small. This paper serves as a literature review of some of the factors that may influence prescribing behavior and subsequently develops a theoretical framework based upon these factors. Certainly, more research is needed to further identify the correlation of factors and their interactions upon actual physician prescribing of pharmaceutical products.

RECEIVED: July 5, 2004

REVIEWED: October 27, 2004

REVISED: November 29, 2004; January 17, 2005

ACCEPTED: February 11, 2005

NOTES

1. The author's Note 4 states the following: "It is interesting to note that if any therapy was presented in the medical literature based on research designed as poorly as that suggesting PSRs influence on physicians, it would be mercilessly bantered out of existence. Research on medical therapy based on such problematic designs as surveys would probably never have reached the printing stage."

2. The classifications of brand size were also adjusted to better reflect the reality of the market. There is no indication that these changes altered the results of the study. The ARPP study also assesses the ROI for three separate therapeutic areas (arthritis, asthma, hypertension), which are beyond the scope of this present article.

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