

# Getting Doctors to Say Yes to Drugs: The Cost and Quality Impact of Drug Company Marketing to Physicians



**BlueCross BlueShield  
Association**

An Association of Independent  
Blue Cross and Blue Shield Plans

## INTRODUCTION

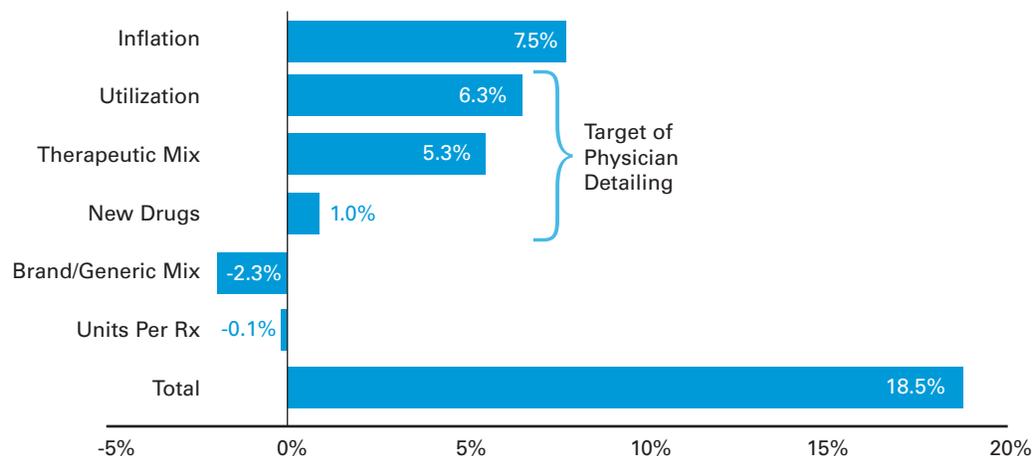
Much public attention has been focused on the price of prescription pharmaceuticals. However, while price inflation is significant, the shift to newer medications and the increased use of existing medications have traditionally accounted for close to three-quarters of the total cost rise.<sup>1</sup>

Both the choice of which medication(s) to use and the duration of that use depend upon physicians' prescribing decisions. Pharmaceutical companies, in turn, spend billions of dollars to influence those decisions. This paper examines the impact of that marketing effort on overall health care costs.

The Pharmaceutical Research and Manufacturers Association (PhRMA) suggests that any assessment of the cost of pharmaceuticals must include the value of what the money is buying. Prescription drugs not only save lives, they also can save money by replacing other, more expensive forms of care, such as hospitalization; increase productivity, by keeping individuals on the job; and improve quality of life.<sup>2</sup>

While that perspective is a useful one, a balanced assessment of the "value of medicines" cannot consist of an equation with only one side to it. A celebration of the obvious – that companies regularly discover and sell drugs that can be extraordinarily beneficial – is not a substitute for exploring the economic effects of industry marketing. The industry spent more than \$9 billion in 2001 to send sales representatives to physician offices and to hospitals and to put on various events designed to extract doctors from those offices and hospitals and bring them to restaurants, resorts and other places where the time spent with sales representatives would be exponentially increased. During the course of these activities, sales reps gave away drug samples with a retail value of \$11 billion.<sup>3</sup>

### Components of Cost Trend Per Member Per Year, 2001-2002



Source: Express-Scripts, 2003

The industry’s stated purpose has been to encourage “the right drug for the right person at the right time,” a goal that recognizes that no pill is universally beneficial. This paper examines the extent to which industry promotional efforts directed toward physicians contribute to both appropriate and inappropriate use of medications – the latter constituting the “wrong drug for the wrong person at the wrong time,” as it were. Examples would include marketing that leads physicians to prescribe drugs where no drug therapy is indicated; to prescribe high-cost drugs when lower-cost drugs would be equally effective; or to prescribe a wrong category of drug. In each instance, excess costs are added to the health-care system.

Moreover, just as the industry’s calculations of the assets of proper pharmaceutical use include increased worker productivity, higher “quality of life” and lowered spending on other forms of health care, an objective “value” balance sheet must include the liability side of the equation. These would include decreased worker productivity resulting from preventable adverse drug reactions from inappropriate prescriptions, “quality of life” problems and any extra medical costs incurred as a result.

## A TIMELY EXAMINATION

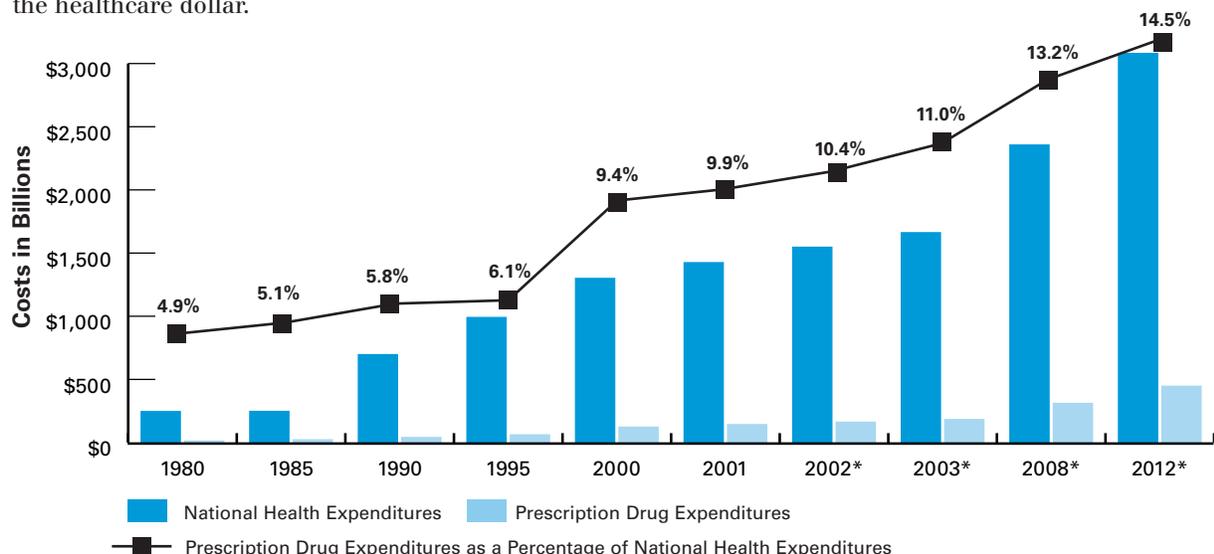
A close look at the industry’s marketing to physicians is particularly timely for three important reasons.

First, the amount of money spent on prescription pharmaceuticals has surged, in part due to the introduction of newer and more expensive drugs and in part due to the increasing prevalence of prescription drug usage to treat chronic conditions. Among the key statistics:

- U.S. sales of the major branded drug companies grew from \$12 billion in 1980 to \$58 billion in 1990 to \$116 billion in 2000, according to a recent PhRMA survey. Americans spent a total of \$141 billion on prescription drugs in 2001, or 10 percent of total health care spending, according to Center for Medicare & Medicaid Services data.
- The annual growth in prescription drug spending increased from 9.7 percent per year in 1995 to a peak 19 percent in 1999, according to IMS Health, a prescription tracking service. In 2002, the annual growth rate was 11.8 percent. For the first quarter of 2003, it was 11.5 percent, according to Express Scripts, a pharmaceutical benefit management company that covers 50 million lives.

### Pharmacy Costs and Growth Rate

Pharmacy costs have risen rapidly in recent years and are expected to account for an increasing share of the healthcare dollar.

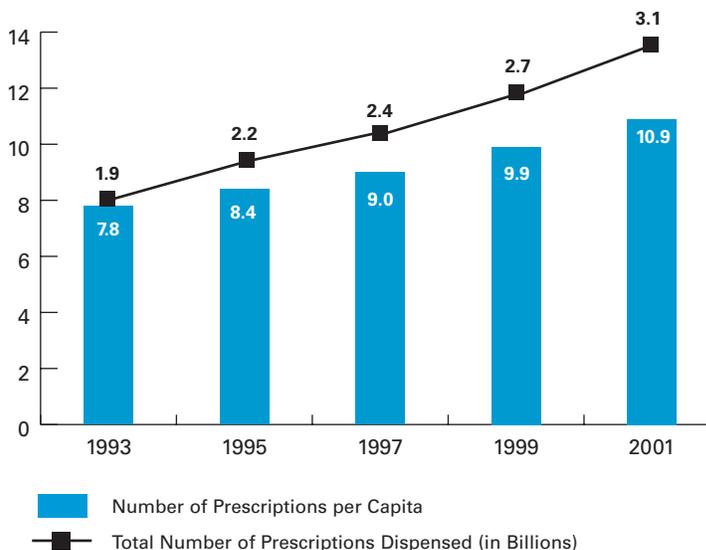


\*Projected Source: Centers for Medicare and Medicaid Services, 2003a

- Half of all U.S. adults age 18 or older now take at least one prescription medication and seven percent take at least five such medications. Among the Medicare population as a whole, 94 percent of individuals take at least one prescription drug and 23 percent (more than one in five) take at least five drugs. Among women 65 or older, 12 percent took 10 or more prescription medications.<sup>4</sup> Two-thirds of all patients who walk into a doctor’s office walk out with a prescription.<sup>5</sup>

### Prescriptions per Capita and Total Prescriptions Dispensed

People continue to use more drugs each year:



#### Drivers of drug utilization include:

- Promotional spending
- New medical guidelines
  - May call for more aggressive treatment of disease
- Outpatient setting
  - Drugs covered under pharmacy plan instead of medical plan
- Increased compliance
  - More convenient dosage, increased consumer awareness and fewer side effects
- Off-label use

Source: Adapted from National Institute for Health Care Management, 2002; U.S. Census Bureau, 2002

Second, there is renewed attention to alleged industry marketing abuses. Among the signs of concern:

- Drug company marketing practices have been the subject of increased scrutiny in the major general news media, including the *New York Times*, *Wall Street Journal* and *USA Today*, as well as in specialized publications serving the health-care field.
- Federal guidelines intended to discourage industry practices that might “interfere with, or skew, clinical decision-making” were issued on May 5, 2003 by the Office of the Inspector General of the Department of Health and Human Services. These types of industry practices, said the OIG, could lead to increased costs, inappropriate utilization and possible quality or safety problems.<sup>6</sup> PhRMA previously issued a new set of voluntary guidelines for its members that was effective July 1, 2002.
- Schering-Plough disclosed in late May that it could soon be indicted in a federal investigation into its overall prescription drug marketing practices, including whether it illegally gave financial grants and other items of value to doctors and other customers and whether it marketed drugs for unapproved uses.
- In mid-June, AstraZeneca agreed to pay \$555 million to settle federal fraud charges and also pleaded guilty to a criminal charge that it had induced doctors to falsely bill Medicare and Medicaid every month for what were free samples of its prostate-cancer drug – almost a direct repeat of the TAP Pharmaceuticals case. Separately, AstraZeneca earlier disclosed that it is under government investigation for its marketing inducements to doctors in relation to Prilosec and Nexium, drugs for ulcers and severe and persistent heartburn.

Thirdly, with legislation to add a \$400 billion Medicare drug benefit now on the front burner in Congress, and with private employers and health plans giving new scrutiny to the structure and cost of their pharmaceutical benefit offerings, the impact of industry marketing to physicians is of keen interest to policymakers, the business community and the general public.

## THE DOLLARS AND CENTS OF PHYSICIAN MARKETING

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The most expensive device in medicine, goes an oft-cited aphorism, is the doctor's pen. An estimated 70 to 80 percent of health care costs originate with a doctor's orders. For prescription drugs, of course, the figure is 100 percent.

To a pharmaceutical marketer, the doctor is the "first link in the chain of getting medication from manufacturer to consumer." In some respects the physician's pen is even mightier than the combined power of the U.S. Food and Drug Administration (FDA) and the medical literature. The FDA can approve a drug for a particular use based on the drug company's clinical trials, and it can require a drug company to promote it only for those uses. The medical literature can provide evidence on the most appropriate indications. However, any physician can legally prescribe any medication for any use.

It was in 1850 that the first "detail man," as pharmaceutical sales representatives are informally called, knocked on a door of an American doctor.<sup>7</sup> In the century and a half since, pharma representatives have become the "stealth bombers" of medicine, as one medical journal dryly put it.

They swoop in, change physicians' prescribing habits (better than any journal article or formal educator) and disappear again.<sup>8</sup>

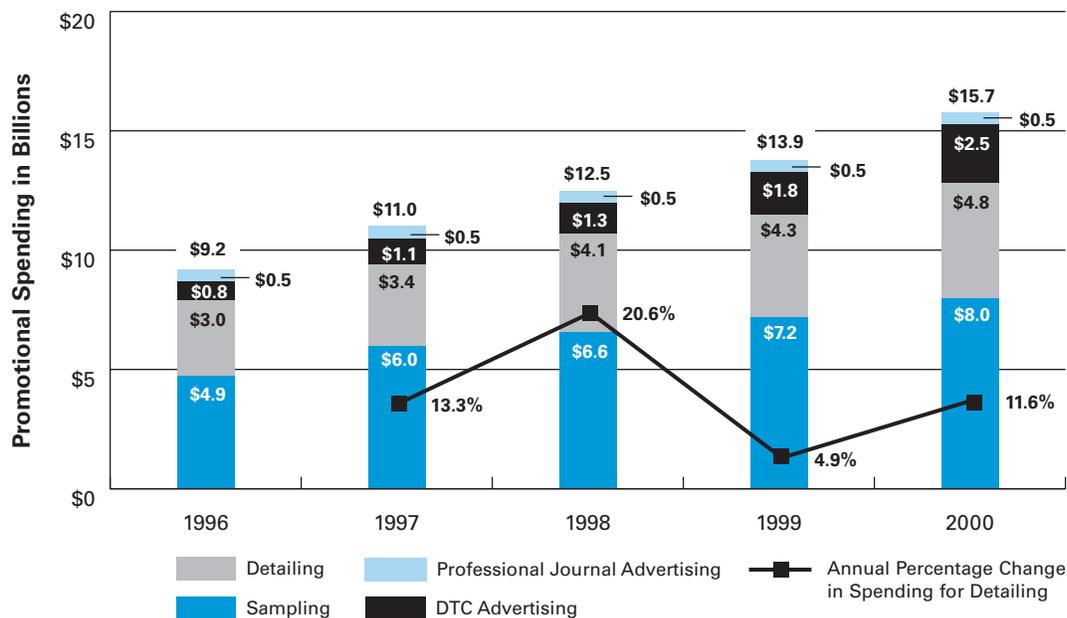
When the advocacy group Families USA examined the annual financial reports of the nine drug companies that account for the top 50 drugs prescribed to seniors, it found that \$45.4 billion was allocated for marketing, advertising and administration in 2001 versus just \$19 billion for research and development.<sup>9</sup> As more drugs and more expensive drugs jostle for attention, pharmaceutical companies have paid particular attention to promotional activities designed to sway the decisions of doctors. Some of the key indicators include:

- From 1996 to 2001 the size of the detail force for the top pharma companies more than doubled, going from about 42,000 to 90,000.
- The average "detail" call is generally believed to cost a pharmaceutical company about \$100-\$150 (not counting the cost of samples). Yet the average sales rep gets the chance to actually sit down with the physician and spend a few minutes in conversation just one out of five times (20 percent), and then for just a few minutes. It's more likely the rep will have to be content with a hurried chat with the doctor at the sample closet (37 percent of the time) or will simply be asked to leave samples at the front desk (28 percent). A discouraging one in seven times (15 percent) the sales rep will depart without having had the opportunity to either see the doctor or leave samples behind.<sup>10</sup>
- Nonetheless, the sales forces at individual drug companies have ballooned to the size of small armies. The top companies average 4,000 reps to sell to primary-care physicians and 850 reps for specialists, all backed by an average field force budget of \$875 million. The top-spending firms currently pour more than \$1 billion each into their sales forces every year.<sup>11</sup> By comparison, President Bush proposed spending \$940 million for grants to state and local health departments throughout the United States to rebuild their infrastructure to meet threats ranging from SARS to bioterrorism. The Agency for Healthcare Research and Quality, which oversees activities related to increasing the safety and effectiveness of medical practice, had a fiscal 2003 budget of just \$303 million.

As the president of one drug manufacturer explained to securities analysts after a successful new product launch: "This market does respond to promotion."<sup>12</sup> The evidence supports that assertion.

## Promotional Spending by Pharmaceutical Companies

Spending on detailing has grown significantly since the mid-1990s.



Note: Numbers may not add to totals due to rounding.

Source: IMS Health Inc. and Competitive Media Reporting, as reported by Kaiser Family Foundation, 2001

## INFORMATION THAT INFLUENCES

Pharmaceutical reps have become an integral part of the medical decision-making process. In part this is because of the nature of the educational process for physicians once they begin full-time practice. On the one hand, doctors are responsible for taking a certain amount of continuing medical education (CME) courses and participating in other activities designed to keep their knowledge current. On the other hand, there has been little investment in information systems designed to help busy doctors with the information they need when they need it. Pharma companies (and, in the device world, medical device makers) have stepped into this gap. The relationship is based on much more than cursory clusterings at the sample closet, and its impact is far more pervasive than many inside or outside health care realize.

Drug companies are a major source of funding for CME organized by physicians and hospitals and also organize an enormous number of CME activities on their own. At least until the voluntary industry rules of mid-2002, many doctors were able to digest the latest tidbits of information on pharmaceutical advances with a meal at a nice restaurant or sleep on the information at a luxury hotel. In 1996, there were 151,434 industry-sponsored events; by 2001, the frequency had more than tripled, to 370,348. That's an average of more than 1,000 industry-hosted events each and every day of the week, Sundays and holidays included.<sup>13</sup> Pharmacia and Pfizer alone hosted a combined 9,000 events in just 2001 for Celebrex, a drug co-marketed by the two companies to treat the pain of arthritis, while Merck sponsored 7,607 events that year for a competing drug, Vioxx.<sup>14</sup>

Most physicians say they have received perks from a drug company representative, with the majority (61 percent) reporting that they have received meals, tickets to events, or free travel.<sup>15</sup> Sometimes, both doctors and drug companies are tempted to cross the line between gifts and outright graft. In October, 2001, TAP

Pharmaceuticals paid the government an \$875 million fine after it admitted to boosting the income of urologists by conspiring to sell them the company’s prostate drug, Lupron, at a discount, while the Medicare and Medicaid programs were charged full price. One former TAP executive tells of doctors bragging, “Oh, there’s my Lupron boat, my Lupron summer house.”<sup>16</sup>

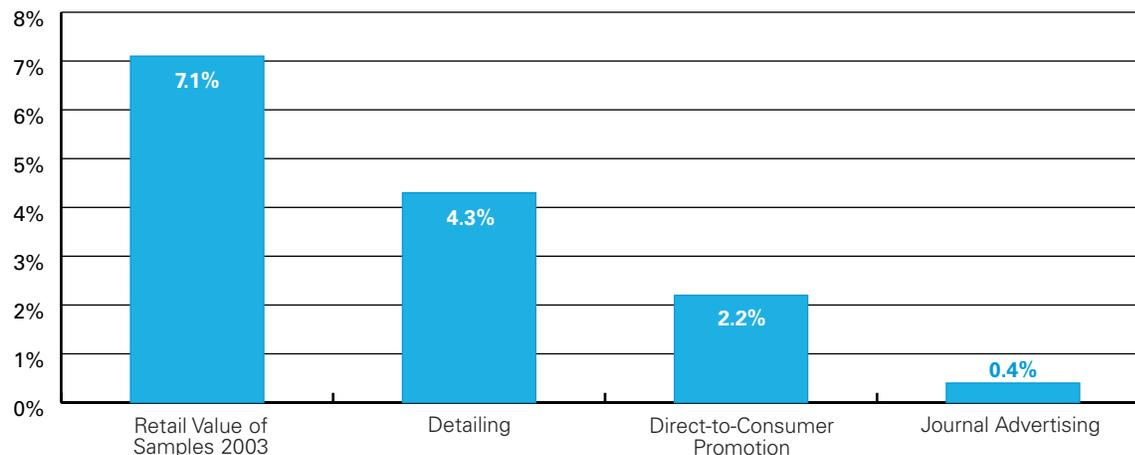
Despite the massive publicity about TAP’s legal troubles stories of “avarice and excess,” as the *British Medical Journal* put it, are still common. In the U.S., demands by doctors range from the minor stiff-arming of a rep to buy lunch for the physician’s whole office staff in exchange for a few minutes of the doctor’s time to more shrill requests for “education” trips that include picking up the tab for the doctor’s spouse. On the pharma side, meanwhile, one rep participating in an industry “chat room” related the story of a friend who found a way to manipulate various “educational” grants in order to buy “shotguns for his top ten docs [writing lipid-lowering drug prescriptions] as [Christmas] presents.” The physician who wrote the most “scripts” for the drug “got a used four-wheel drive on top of the shotgun for his hunting camp.”

Whether the role of the rep is providing freebies or fostering the free flow of information -- or a combination of both functions – the result is a continuing influence on prescribing decisions. For example:

- The more contact internal medicine residents have with pharmaceutical company representatives, for example, the more likely they are to believe that these representatives provide useful information.<sup>17</sup>
- Virtually every practicing physician uses information about drugs that is provided by pharmaceutical reps.<sup>18</sup>
- Nearly three-fourths of physicians in a national poll said the information they received from pharma reps was “very” useful (15 percent) or “somewhat” useful (59 percent), while more than eight in ten said the information was “very” (9 percent) or “somewhat” (72 percent) accurate.<sup>19</sup>
- More than half (55 percent) of a group of “high-prescribing” doctors surveyed by the industry data tracking group ImpactRx said that drug reps serve as their primary source of information about newly approved drugs. Only about one quarter of the doctors (26 percent) mentioned medical journals as their first information source.

### Pharmaceutical Companies’ Spending on Promotion as a Percentage of Sales, 2002

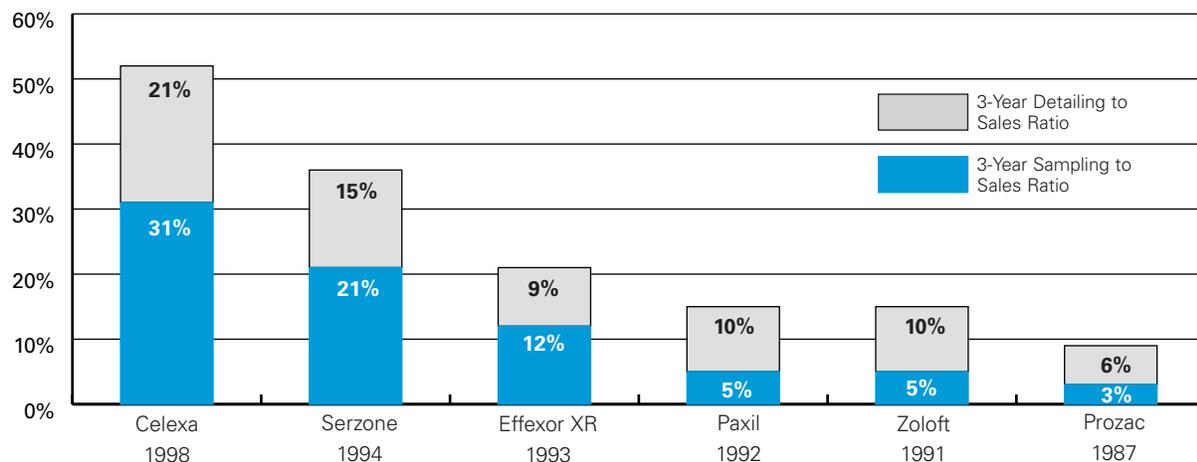
Pharmaceutical companies spend 14 percent of their sales revenue on promoting their products. Detailing accounts for 4.3 percent of sales revenues.



Source: Adapted from Kaiser Family Foundation, 2003

### Promotion Costs as a Percentage of Sales in 1997-1999: The Example of Antidepressants\*

Detailing efforts are often focused on a small number of drugs. The amount companies invest on promoting drugs can vary substantially, even within the same class.



\*Numbers in parentheses after drug names are the year the FDA approved the drug.

Sources: Detailing data from Scott-Levin Personal Selling Audit, 2001; Sales data from Scott-Levin, Source Prescription Audit, 2001; Sampling data from IMS Health, 2001; DTCA data from Competitive Media Reporting, Strategy Report, 2001; Manufacturer and FDA Approval Date obtained from the Food and Drug Administration's *Orange Book*.

Research “shows a strong correlation between receiving industry benefits and favoring their products.”<sup>20</sup> For instance, physicians who requested that a new drug be added to their hospital’s formulary were more likely to have accepted money from drug companies to attend or speak at symposia or were more likely to have requested additions of drugs made by companies with whose reps they had met.<sup>21</sup> In an outpatient environment, the availability of drug samples “led physicians to dispense and subsequently prescribe drugs that differ from their preferred drug choice.”<sup>22</sup>

While doctors overestimate their immunity to behavior-change strategies, they simultaneously underestimate the sophistication the industry brings to devising those strategies. Drug companies have used data from pharmacies to focus their marketing efforts on specific doctors since the mid-1990s. Yet just 60 percent of physicians were aware in one recent survey that sales reps receive information about precisely how often they prescribe certain drugs.<sup>23</sup>

Indeed, the sales generated by prompting physicians to say, “yes” to a particular company’s drug have been calculated down to the penny. Scott Neslin, the Albert Wesley Fry Professor of Marketing at Dartmouth College’s Amos Tuck School of Business, analyzed the marketing of 391 drugs with revenues of at least \$25 million each during the time period 1995 to 1999. The purpose was to measure the average return-on-investment (ROI) of increasing the budget allocated to four major pharma marketing strategies: detailing; direct-to-consumer advertising; medical journal advertising; and physician meetings and events. Detailing yielded an overall ROI of \$1.72 for each extra \$1 invested, suggesting that “detailing pays off even at very high levels of expenditure,” Neslin concluded.

For new drugs with more than \$200 million in annual revenues and launched during 1997-1999, there was a \$10.29 average ROI for each extra dollar invested in detailing. In comparison, the ROI on putting extra money medical journal advertisements for the same drugs during the same period was \$5.42 and the ROI on direct-to-consumer advertising just \$1.37.<sup>24</sup>

That the influence of pharma reps leads to more prescribing by the physicians with whom they interact is clear. So too is the dubious nature of some of the strategies used to influence that prescribing. The key question, however, is the extent to which the industry's promotional tactics lead to an increase in appropriate use versus inappropriate use of drugs by patients.

## "BETTER CARE" OR "MORE PRESCRIPTIONS"?

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Like sales reps everywhere, pharma sales reps are paid to sell.

Selling pharmaceuticals is not dissimilar to selling Pepsi-Cola, a Pepsi-exec-turned-pharma-exec told *Business Week*. Putting that lesson into practice, the executive successfully doubled the sales and marketing dollars for his company's five best-selling drugs while laying out "demanding performance goals" directly related to revenues.<sup>25</sup>

Like a sales rep selling soda pop, pharma rep compensation is tied closely to meeting revenue targets. Incentive bonuses, sometimes paid quarterly, can add up over the course of the year to as much as three times total salary.<sup>26</sup> Meanwhile, periodic sales competitions among reps can result in calls to physicians with such distinctly non-clinical information as the plea: "Three more patients [getting prescribed a particular drug], and I get a Jaguar?"

In other industries, financial incentives such as those long common in the pharmaceutical industry have corrupted the information-providing process. Sales commissions by brokerage houses, for example, have been shown to influence brokers' investment recommendations. In the pharma world, an evaluation of information provided by sales reps at 13 "noontime conferences" with doctors found that more than 10 percent of statements that reps made were inaccurate and that all such inaccuracies were favorable to the promoted drug.<sup>27</sup>

However, sales reps are typically just conveying information they have been given by their employer, which may or may not meet a rigorous test of objectivity. For example, an analysis of a guide to medical therapy research put out by European pharmaceutical firms found that the medical literature quoted reflected a highly selective use of studies of varying scientific validity; studies showing overuse of drugs were completely excluded.<sup>28</sup> After examining U.S. drug industry promotional practices, the American College of Physicians' Ethics and Human Rights Committee concluded:

Physicians and industry have a shared interest in advancing medical knowledge. Nonetheless, the primary ethic of the physician is to promote the patient's best interests, while the primary ethic of industry is to promote profitability. Although partnerships between physicians and industry can result in impressive medical advances, they also create opportunities for bias.... Physicians must keep in mind that industry-supplied medical information, although neutrally packaged, is in fact promotional.<sup>29</sup>

An editorial in the *New England Journal of Medicine* put it more bluntly: "[T]o rely upon the drug companies for unbiased evaluations of their products makes about as much sense as relying on beer companies to teach us about alcoholism."<sup>30</sup>

Writing in the journal *Health Affairs*, Bert Spilker, MD, a senior vice president of PhRMA, presented the role pharma reps in a classic educational context. "Sales representatives," he wrote, "perform valuable functions that promote better patient care."<sup>31</sup> One way of testing that thesis is to use the framework for quality of care developed by the National Academy of Sciences' Institute of Medicine. The IOM concluded that underuse, overuse and misuse of medical services and technology accounts for as much as 30 percent of all health care costs. To what extent do pharma marketing efforts to physicians contribute to increasing or decreasing waste?

## OVERUSE, UNDERUSE AND MISUSE OF DRUGS

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In some areas of medicine, it is likely that industry promotional practices have by themselves had little impact on the prescribing decision. For instance, while the initial high price of the drug AZT to treat AIDS was controversial, AZT came along at a time when physicians were desperate for any sort of effective therapy for an incurably fatal disease. The educational programs sponsored by the drug's makers likely provided a speedy guide to the minimal information on dosage, management and possible adverse effects that physicians needed in order to feel comfortable writing a prescription for a drug they were already prepared to use. Similarly, drug-company promotional practices related to vaccines are only a small part of the influences reminding doctors that children should be inoculated. Health plans, for example, are graded publicly on successful vaccination, while the parents of children often find they cannot enroll their child in school without evidence of vaccination.

In other areas of medicine, the industry's promotional efforts have helped reduce "quality waste" by addressing underuse of effective medications for serious health problems, thereby saving money and lives. A paper by researchers with no industry support cited treatment of hypertension in the 1970s; thrombolysis for acute myocardial infarction in the 1980s; and secondary prevention of coronary artery disease by reducing cholesterol and anticoagulation for atrial fibrillation in the 1990s as situations where pharmaceutical company marketing has played "an important role in improving outcomes for patients."<sup>32</sup> Another example is the use of anti-bacterial therapy to eradicate ulcers.<sup>33</sup> The industry also cites the proliferation of company-sponsored programs in disease management, which help ensure greater use by physicians of therapies that can improve the quality-of-life of individuals with asthma, diabetes, congestive heart failure and other chronic diseases. The IOM has noted that some therapies can take as much as 15-20 years from the publication of research showing their efficacy until the time they work their way into everyday practice.<sup>34</sup> Given this lag, there are undoubtedly targeted areas where industry promotional practices can play a positive role in helping to improve the efficiency and effectiveness of care.

Finally, there are places where industry promotional practices to clinicians have contributed to overuse and misuse of prescription drugs and to excess costs. The culture of medical training and practice, sociologist Eliot Freidson has written, is one in which physicians are "morally committed to intervention on behalf of each patient."<sup>35</sup> That commitment, in turn, makes physicians receptive to promises that a new drug or device will be "better" than a previous therapy. At the same time, the medical culture also encourages each individual doctor to rely upon his or her personal experience and intuition rather than any sort of systematic review of evidence. The result is a bias towards action, and a supreme confidence that this bias is actually the exercise of keen, independent judgment.

In one study of medical residents that illustrates this point, 61 percent of the respondents said that they themselves were unaffected by industry promotion. However, when asked their opinion about *other* doctors, just 16 percent of the residents believed that their colleagues exhibited the same steely resistance.<sup>36</sup> As it turns out, the skeptical view is the correct one.

## "NEW" DOES NOT ALWAYS MEAN "IMPROVED"

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In a classic 1982 study of Boston-area doctors, more than two-thirds of respondents said their own training and experience were "very important" in prescribing decisions. Sixty-two percent said the same thing about the role of scientific papers. A majority said drug industry ads and salesman were "minimally important."

Yet when researchers studied these same doctors' assessments of the painkiller Darvon and of a set of medicines that dilate blood vessels to treat senility, many doctors confused their own (influenced) judgment with the (objective) research literature. Seventy-one percent said that decreased blood flow in the brain --

which the dilating medicines supposedly could alleviate -- was a major cause of senility. The medical evidence contradicted that belief; rather, the concept was one championed by drug makers. Similarly, half the doctors believed Darvon was more potent than aspirin, another conclusion advocated by drug reps by unsupported by science.

“Although the vast majority of practitioners perceived themselves as paying little attention to drug advertisements and [salespeople], as compared with papers in the scientific literature,” wrote Jerry Avorn and colleagues, “their belief about the drugs revealed quite the opposite pattern of influence...”<sup>37</sup>

Avorn and colleagues’ findings about physicians’ false sense of immunity to biased information remain relevant. For example, General Motors Corp. found itself spending \$52 million in 2001 for prescriptions that physicians wrote for Prilosec, a widely promoted and expensive drug for severe and persistent heartburn -- even though a subsequent analysis found that 91 percent of the patients receiving prescriptions had no prior prescription related to heartburn and no prior diagnosis of the problem.<sup>38</sup> The maker of Prilosec, AstraZeneca, recently disclosed that it is under government investigation in regard to its marketing inducements to doctors in promoting Prilosec and Nexium, used for similar indications. Prilosec sales in 2001 were \$4.6 billion.

Indeed, researchers studying British general practitioners recently reported that frequent contact with a drug company representative as a source of educational material “was significantly associated with a greater willingness to prescribe new drugs and to agree to patients’ requests to prescribe a drug that is not clinically indicated, dissatisfaction with consultations [with patients] ending in advice only and receptiveness to drug advertisements and promotional literature.”<sup>39</sup>

In addition to influencing physicians to prescribe unnecessary medications, industry promotional activities can lead to the prescription of an expensive new medication when a less-expensive one is equally effective. Not surprisingly, industry-sponsored research has focused on instances where an expensive medication appears to provide a substantial clinical advantage. So, for instance, PhRMA frequently cites the work of economist Frank Lichtenberg of Columbia University, who concluded that treating conditions with newer medicines instead of older ones increases drug costs but significantly lowers non-drug medical spending. Each additional dollar spent on using a newer prescription medicine (instead of an older one) saves roughly \$7.20 in other health care costs, he found.<sup>40</sup>

In a similar vein, Robert Dubois, MD of medical software company Zynx Health dismissed in one sentence the possibility that industry educational activities cause clinically and economically harmful overuse. Said Dubois, in a recent health policy journal article partly funded by the industry: “Although there have been reports that pharmaceutical representatives occasionally make inaccurate statements to prescribing physicians, there are no objective data showing that drug promotion...results in the inappropriate use of drugs.”

He added: “[While] excessive promotion could lead to excessive product use, [and]...this should be the subject of further research...[the current evidence] supports the contention that promotion is not accompanied by excessive use, at least in some circumstances.” “Some circumstances,” in this instance, was a conclusion based on one case study by Dubois of one class of drugs in the 1990s.<sup>41</sup>

In contrast to the limited scope of Dubois’ work, a meta-analysis of the research literature in a medical journal concluded that “interactions with pharmaceutical representatives” are linked to “non-rational prescribing... rapid prescribing of new drugs and decreased prescribing of generic drugs.”<sup>42</sup>

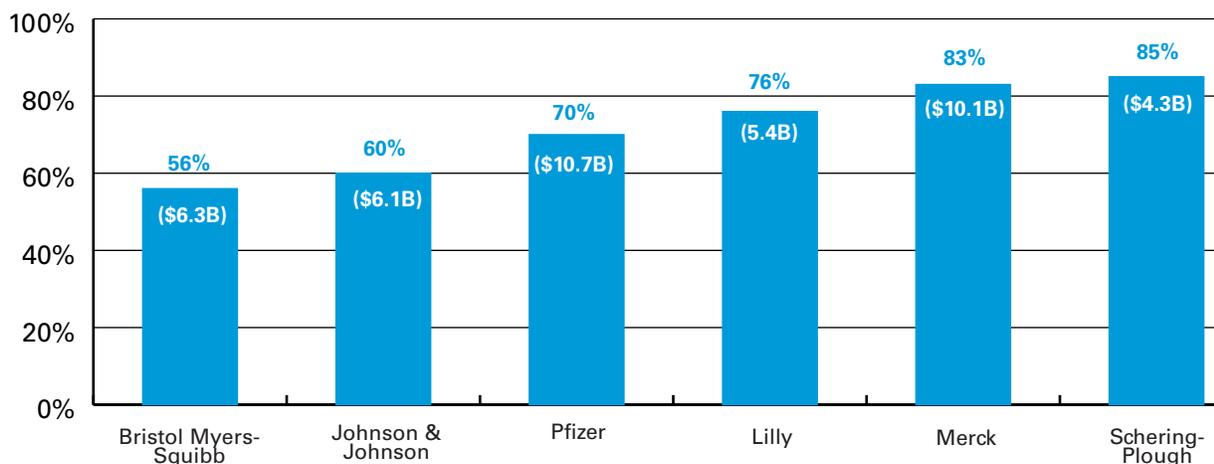
In one example of excess costs that result from promotional activities, diuretics and beta-blockers are recommended as first-line therapy for patient with hypertension. Yet while the study concluded that “the most effective drug was also the least expensive” physicians write more prescriptions for the costly brand-name calcium channel blockers and ACE inhibitors. “Heavy promotion” of alternative drugs was cited as an important contributing factor.<sup>43</sup>

Costly brand-name drugs are the beneficiaries of costly promotional campaigns. In the year 2000, just 34 drugs out of 9,482 on the market accounted for half of the overall increase in national drug spending. Just

two drugs – the heavily promoted Vioxx and Celebrex – accounted for 9.2 percent of the entire increase in prescription drug sales in the year 2000 and a total of \$3.5 billion in sales. It is unlikely that the health-care system received full value for this money, given the evidence that these drugs are no more effective than over-the-counter ibuprofen (i.e., Advil) at reducing pain and inflammation and are only slightly less likely to cause ulcers.<sup>44</sup>

### Percentage of 2001 U.S. Sales for Top Five Drugs at Pharmaceutical Companies\*

The dependence of many companies' fortunes on a small number of drugs creates a strong incentive for them to promote these drugs heavily to increase or at least maintain sales.



\*Numbers may not add to totals due to rounding.

Source: Company reports as cited by the Centers for Medicare and Medicaid Services, 2003e

Indeed, while pharma industry research highlights instances where drugs have substituted for more expensive hospitalization, a recent *Annals of Internal Medicine* analysis of COX-2 inhibitors such as Vioxx and Celebrex concluded that using the drugs in treating arthritis “may cost an additional \$275,809 per year” to gain one “QALY” (a standard quality-adjusted-life-year measure). This “is more than twice the cost per QALY associated with initiating dialysis and continuing aggressive care for hospitalized patients who are seriously ill.”

Those results would change “only if the cost per...tablet is decreased by nearly 90 percent,” the analysis continued. “Our study yielded those findings despite our construction of a model that was explicitly biased in favor of [the tablets].”<sup>45</sup>

Even before the *Annals* study appeared, managed care plans have increasingly taken the drugs off the “preferred” formulary list due to “questions about their relative efficiency and side effects, cardiovascular toxicity in particular.”<sup>46</sup>

The use of broad-spectrum antibiotics is another example where drug-industry promotional activities may impose serious costs. A recent analysis of National Ambulatory Medical Care Survey data found that since 1991 “physicians are increasingly turning to expensive, broad-spectrum agents, even when there is little clinical rationale for their use” compared to simpler, generic antibiotics. By 1998-99, more than one in five adult prescriptions for broad-spectrum antibiotics and one in seven prescriptions for children were for conditions that were primarily viral, such as the common cold or acute bronchitis.<sup>47</sup>

An editorial in the *Annals of Internal Medicine* by a researcher with the Centers for Disease Control and Promotion specifically singled out the promotional activities of pharmaceutical companies on behalf of broad-spectrum antibiotics as a cause for concern. Overuse of these drugs, noted the editorial, “affects our ability to

treat infections of major international importance, such as HIV infection, tuberculosis and malaria, as well as common infections primary care physicians face daily, such as otitis media, sinusitis and pneumonia.”<sup>48</sup>

More troubling still is the reaction of the industry when the peer-reviewed literature endangers the scientific claims of an expensive medication class. Drug manufacturers have at times engaged in promotional activities designed to discredit the evidence. One recent example concerns treatment for hypertension, where simple “mono-therapy” was endorsed by the comprehensive in the ALLHAT study.<sup>49</sup>

A complete balance sheet on value of medicines should also take into account the cost of adverse drug reactions resulting from “marketing pressures to prescribe new and potentially more toxic drugs in preference to prescribing well-established safer drugs.”<sup>50</sup> Researchers have pointed to avoidable problems ranging from liver damage and deaths from the anti-inflammatory Duract (since withdrawn from the market)<sup>51</sup> to neurological damage from broad-spectrum anti-infectives<sup>52</sup> to possible side effects from long-term use of powerful pain medications promoted aggressively by their manufacturers.<sup>53</sup> There has been no rigorous economic analysis of the cost of these problems.

It should be noted that supporters of drug industry “detailing” say that pharma reps are an important source of reporting adverse drug reactions to the FDA and of conveying FDA warnings to physicians. Critics vigorously dispute that assessment. What may be more relevant is the lack of information for reps to use with doctors: a recent FDA report that said some 60 percent of 1,339 promised post-marketing studies of drugs – crucial for tracking side effects – have not even been begun. Among “fast-track” drugs to treat life-threatening diseases, 28 percent of the studies have not begun.<sup>54</sup>

Any calculation of the excess costs imposed on the health care system and to patients of “overuse” and “misuse” of drugs must also consider a distressing amount of allegedly unethical or illegal promotional activities by major drug companies selling widely used drugs.. Some recent examples include:

- The maker of a drug that treats bacterial vaginosis is accused of classifying as vaginal “infections” a set of symptoms that may well have no link to identifiable infectious pathogens.<sup>55</sup>
- Warner-Lambert, now a division of Pfizer, is accused of promoting its epilepsy drug, Neurontin, for dozens of unapproved uses ranging from migraines to manic depression. In recent litigation involving Warner-Lambert, confidential memos show that executives of the company paid dozens of doctors tens of thousands of dollars each to speak to other physicians about how Neurontin could be prescribed for treating more than a dozen other conditions for which it had not been approved. Dr. David P. Franklin, a former Warner-Lambert employee who filed a federal “whistle-blower” lawsuit against the company, said he decided to become a whistle-blower after being shown an article reporting that the drug had actually worsened the behavior of a child with attention deficit disorder.

Data collected by the company also demonstrated how doctors who attended dinner meetings paid for by the drug company wrote 70 percent more prescriptions than doctors who did not attend the dinners. Neurontin eventually went on to record \$2.8 billion in annual sales, of which more than 78 percent represented prescriptions for unapproved uses – certainly an excess cost to the health-care system.<sup>56</sup>

- Schering-Plough disclosed in late May that it could soon be indicted in a federal investigation into its overall prescription drug marketing practices, including whether it illegally gave financial grants and other items of value to doctors and other customers and whether it marketed drugs for unapproved uses. Two months earlier, AstraZeneca disclosed that it is under government investigation for its marketing inducements to doctors in promoting Prilosec and Nexium, drugs for ulcers and severe and persistent heartburn.

In mid-2002 a listing of large companies that had been targets of government or private litigation related to their business practices included Bristol-Myers Squibb, GlaxoSmithKline, Johnson & Johnson and Merck.<sup>57</sup>

## TURNING "YES" INTO "MAYBE" OR "NO"

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Organizations and institutions that buy prescription drugs are deploying a number of strategies to counter the promotional strategies of those who sell the drugs and to do a better job of providing clinicians with the kind of information that they need. Pharmacy benefit management companies (PBMs), hospitals, managed care organizations (MCOs) and employers have developed elaborate formularies of "preferred" drugs that are designed to provide the greatest clinical benefit for the least cost. Physicians and patients alike are encouraged to use these drugs, an encouragement that often comes with either bureaucratic or financial incentives.

Purchasers have also turned to "counter-detailing," attempting to provide information to counter information provided by the drug companies. In Oregon, the state Medicaid program used a committee of medical experts to examine different therapeutic classes of drugs and then publicize comparisons of effectiveness and price. Some PBMs and health plans have adopted a similar strategy to improve the cost-effectiveness of pharmaceuticals prescribed for their covered populations, with organizations such as Blue Cross and Blue Shield of Michigan, the Rochester, N.Y.-based Excellus Blues plan and the Oregon-based Regence Blues plan drawing national recognition for their counter-detailing work.

Similarly, some hospitals have also begun counter-detailing their own medical staffs with regard to the medications used in an inpatient setting. At Massachusetts General Hospital, a pioneering program in counter-detailing was recently boosted by physical restrictions in the access of device and drug reps. The hospital now requires them to make an appointment with staff members in advance, and they are barred from parking in the hospital's patient or visitor garages.<sup>58</sup>

The American Medical Association has said it supports counter-detailing as an educational effort as long as physicians are not "coerced" into using a drug that might be cheaper but less effective.<sup>59</sup> The group has also called on drug companies to curtail the practice of "shadow detailing," whereby a drug rep accompanies the physician into the exam room, without the explicit agreement of the patient being treated. The group's leaders also said they were concerned about doctors being paid by companies for allowing the reps to accompany them.<sup>60</sup>

In a variant of counter-detailing, physicians are being urged to act on their own to evaluate information from drug reps more systematically. One suggested framework uses the acronym STEP, for Safety, Tolerability, Effectiveness and Price. "Until your drug representative produces valid data that a drug is at least one STEP better, your current practice need not change," proponents of this approach counsel.<sup>61</sup>

In response, drug companies are coming up with new "counters" of their own. Decisions made by patients have been the target of direct-to-consumer advertising, a strategy that has engendered substantial attention and analysis since the FDA eased restrictions on TV and radio ads in 1997. Efforts by state governments to restrict the freedom to prescribe have drawn industry lawsuits. And PBMs, MCOs and employers have become the object of detailing forces of their own.

Pharma companies are also intensively investigating "e-detailing;" i.e., the use of on-line communication with physicians. In a brief summary of a forthcoming report, Forrester Research reported that 58 percent of physicians who participate in "e-details" say they prescribe more of that drug.<sup>62</sup>

Perhaps more troubling, as "evidence-based medicine" grows in importance, is that pharma companies have become a significant source of financial support for physicians writing clinical practice guidelines.<sup>63</sup>

While this prescription-by-prescription struggle shows no signs of disappearing, some more thoughtful approaches aimed at encouraging genuine "value prescribing" are also starting to emerge. In one example of this strategy, the Academy for Managed Care Pharmacy, with support from several large pharmaceutical companies, has developed a standardized format for formulary decisions that is intended to make them more science-based. The AMCP format asks companies applying for formulary inclusion to specifically address comparison products and a therapy intervention framework, as well as provide answers to written questions related to costs, safety and outcomes.

Agreements between Florida and the drug companies Bristol-Myers Squibb and Pfizer follow a similar logic. In return for being included in the state's Medicaid formulary, the two companies have agreed to fund disease management programs with guaranteed dollar savings to the state. Detailed clinical outcomes of the programs are being evaluated by the University of Florida.<sup>64</sup>

Going one significant step further is a pilot collaboration and “outcomes guarantee” agreed upon in Britain by Parke-Davis Foundation (now Pfizer), Keele University and the North Staffordshire Health Authority. The university designed an audit and intervention program based on British clinical recommendations on prevention of coronary artery disease. Those guidelines will be used in a geographic area where the population is known to have high cholesterol levels. For their part, general practitioners agreed to closely adhere to those guidelines and use statins appropriately. Finally, Pfizer agreed to refund to the health authority any “wasted resources” if use of its brand-name statin does not achieve agreed-upon results in lowering the low-density lipoprotein (LDL) cholesterol of the targeted population.

The project began in 2000, but results have not yet been analyzed. However, in a recent paper describing the effort, the authors concluded: “An outcomes guarantee has the potential ensure predictable health gains for a given drug expenditure. This may be particularly relevant in the future as the high costs of new medicines and concern about their inappropriate use could result in resistance to uptake.”<sup>65</sup>

## DISCUSSION

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“The pharmaceutical industry is extraordinarily privileged. It benefits enormously from publicly funded research, government-granted patents, and large tax breaks, and it reaps lavish profits. For these reasons, and because it makes products of vital importance to the public health, it should be accountable not only to its shareholders, but also to society at large.” -- Marcia Angell, M.D., editor, *New England Journal of Medicine*, June 22, 2000.

Because every use of a prescription drug starts with a prescription, it is important to examine the costs and benefits of pharmaceutical industry efforts to influence doctors' prescribing decisions. Although there are a number of limits to the available data, what has been most prominent by its absence is any sustained effort to examine the negative side of the balance sheet. Most critics of the industry, for example, have focused on the price of drugs or on alleged unethical inducements to prescribe, as opposed to the overall impact on the cost and quality of care of the prescriptions.

This paper has presented evidence that there are both savings and substantial unnecessary economic and human costs imposed on the system as a result of promotional activities to clinicians. One of the few analyses in the health services research literature of the economic impact of the overuse and misuse of prescription drugs concludes:

Inefficient drug selection has the potential to drive the cost of therapy more rapidly than is indicated by changes in the prices of individual drug products themselves. If this form of disguised “inflation” could be controlled, ensuring access to medically necessary, cost-effective pharmacotherapy may be more affordable than standard analyses of prescription drug expenditures would make it appear.<sup>66</sup>

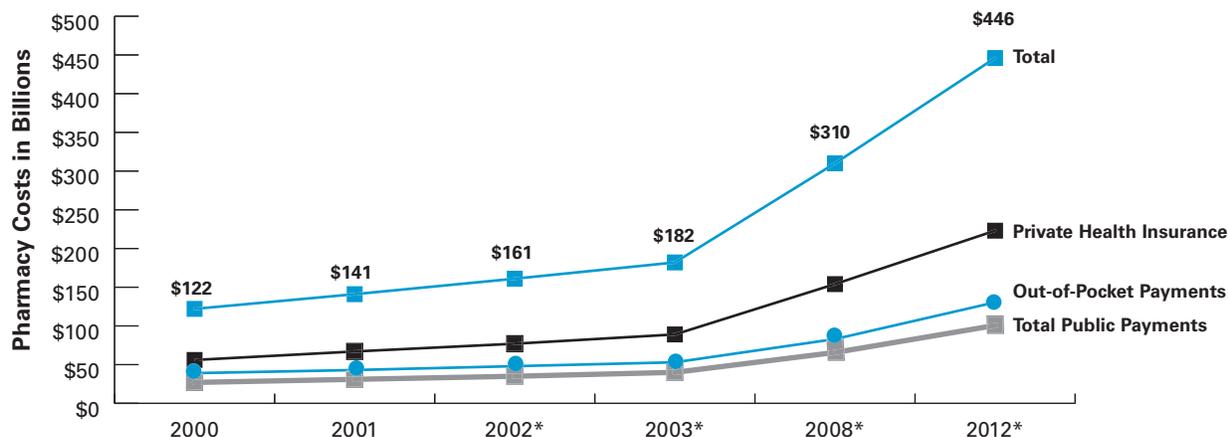
One need not go to extremes of argument – e.g., banning all contact between physicians and pharma representatives – to conclude that substantial changes in current marketing practices are needed to protect the public. Some of the activities that contribute to medical care that wastes money and fails to help patients are condoned even under current ethical guidelines. Moreover, the extent of the activities that violate either industry guidelines or perhaps even legal restrictions is disturbing. The companies who have allegedly participated are industry giants, and the amount of money involved runs into the billions of dollars. These practices have victims –some Americans will lose their health insurance entirely while others will see their benefits reduced because of rising costs that could have been avoided.

Some within the industry already agree that substantial change is needed. As one author on the Web site of *Pharmaceutical Representative* magazine noted, pharma reps need to switch their focus from “increasing script (prescription)-writing” to “making doctors successful at what they do or want to do.” Information provided in the process must be “factual, objective and from a credible third party.”<sup>67</sup> Similarly, industry sources quoted in a recent *Wall Street Journal* article acknowledged that the current system of using “detail” persons has led to an “arms race” yielding diminishing returns as doctors increasingly refuse to spend significant time with them.<sup>68</sup>

Access by patients to innovative pharmaceuticals – to the “right drug for the right person at the right time” is important and becoming more so as chronic disease increases in prevalence among the U.S. population. But achieving that access while minimizing the economic and social harm caused by overuse and misuse of prescription drugs is also important and becoming more so. That is particularly true at a time when rising health care costs threaten to outpace society’s ability to pay for them and when a government-sponsored prescription benefit for Medicare seems likely to increase the demand for drug therapy even more.

### Pharmacy Spending by Payer

The increase in pharmacy costs is hitting all market segments.



\*Projected

Source: Centers for Medicare and Medicaid Services, 2003c

The public and private organizations that pay much of the total cost of prescriptions drugs and the pharma companies that produce those drugs can ensure the efficient and effective use of medications. To do so, however, they must first objectively examine what promotional practices to physicians are appropriate as a means of maximizing the value of medicines that are vital to the health of patients everywhere.

### About the Author

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