sons. Students constantly hear their mentors, as well as the media, discuss the monetary aspect of medicine; it permeates the training environment. Although money has always been part of medicine, it has never been so prominent, and it has not been the primary motivator of most doctors' practices. Today's medical students are being inducted into a culture in which their profession is seen increasingly in financial terms. Add in such pressures as the need to pay off enormous debts, and it is not surprising that students' choices are dictated by the desire to maximize income and minimize work time.

Some established primary care physicians are also making career choices in response to this new culture and fleeing to concierge practices, often citing their desire to escape the constant pricing of every aspect of their day. Since concierge practices collect yearly premiums from patients, such doctors may ironically be less "primed" by money at each encounter and may avoid feeling "nickeled and dimed" by insurers. This arrangement creates an environment that can foster social interaction more than it does market exchange. But concierge medicine is unaffordable for most Americans, and it drives much-needed primary care providers away from the larger population.

How can we restore the balance between communal and market exchange in medicine in the current economic environment, given the imperative to cut costs? One answer may lie in an experimental new paradigm in primary care termed the "patient-centered medical home." The term itself suggests an emphasis on the social exchange that exists in a family rather than the market exchange of a business. The medical home is envisioned as a "compassionate partnership"[5] of primary care providers and patients, with coordinated care for patients' ongoing problems and increased attention to preventive measures. The insurer would pay a set fee for each patient cared for in the medical home to cover what is now nonreimbursed time. Substantial cost savings are expected to result from coordination of care. As policymakers refine this model and extend it to include medical specialists, they should take into account the lessons of behavioral economics. Caregivers should be appropriately reimbursed but should not be constantly primed by money. Success in such a model will require collegiality, cooperation, and teamwork — precisely the behaviors that are predictably eroded by a marketplace environment.

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The Neurontin Legacy — Marketing through Misinformation and Manipulation

C. Seth Landefeld, M.D., and Michael A. Steinman, M.D.

Old drugs usually fade away. Sometimes, however, they leave surprising legacies. In 1997, for example, a study comparing the effects of brand-name and generic formulations of levothyroxine led to an uproar over the discovery that the manufacturer of the brand-name product suppressed publication of the result that the two formulations were equivalent. Recently, lawsuits alleging damages from illegal marketing of another old drug, gabapentin (Neurontin), have yielded remarkable discoveries about the structure and function of pharmaceutical marketing.

Patented in 1977 and approved by the Food and Drug Administration (FDA) in 1993 in doses of up to 1800 mg per day as adjunctive therapy for partial complex seizures, Neurontin became a surprise blockbuster for Parke–Davis, a division of Warner–Lambert, which was purchased by Pfizer in

2000. U.S. sales rose from $98 million in 1995 to nearly $3 billion in 2004 before Neurontin faced generic competition and lost most U.S. sales.

The rise of Neurontin would have been unheralded except for a quirk of fate: a young biologist, David Franklin, went to work for Parke–Davis on April 1, 1996. Fresh out of postdoctoral training at Harvard, Franklin soon grew concerned that he was participating in illegal marketing. At a training seminar for "medical liaisons" on April 16, 1996, Franklin and his peers were told that FDA regulations required a fair and balanced presentation and prohibited promotion of a drug for off-label uses, selling by medical liaisons, and soliciting of inquiries from physicians. Six days later, a Parke–Davis executive reportedly told Franklin,

> I want you out there every day selling Neurontin. . . . We all know Neurontin's not growing for adjunctive therapy, besides that's not where the money is. Pain management, now that's money. Monotherapy [for epilepsy], that's money. . . . We can't wait for [physicians] to ask, we need [to] get out there and tell them up front. Dinner programs, CME programs, consultantships all work great but don't forget the one-on-one. That's where we need to be, holding their hand and whispering in their ear, Neurontin for pain, Neurontin for monotherapy, Neurontin for bipolar, Neurontin for everything. I don't want to see a single patient coming off Neurontin before they've been up to at least 4800 mg/day. I don't want to hear that safety crap either, have you tried Neurontin, every one of you should take one just to see there is nothing, it's a great drug.[1]

Three months later, Franklin left Parke–Davis and filed a suit (ultimately, *United States of America ex rel. David Franklin vs. Pfizer, Inc., and Parke-Davis Division of Warner-Lambert Company*) alleging that off-label marketing of Neurontin constituted "false claims" designed to elicit payments from the federal government. On May 13, 2004, Warner–Lambert agreed to plead guilty and to pay more than $430 million to resolve criminal charges and civil liabilities. A class-action suit was filed the next day in federal court on behalf of private parties who had paid for illegally marketed Neurontin; this case (now known as *In Re: Neurontin Marketing, Sales Practices, and Products Liability Litigation*) remains active.

The Franklin case placed more than 8000 pages of corporate documents in the public domain; these documents are now available in a searchable digital library at the University of California, San Francisco (www.dida.library.ucsf.edu). The class-action suit also generated detailed testimony and reports that are available through the Federal Judiciary's Public Access to Court Electronic Records Service Center (e.g., https://ecf.mad.uscourts.gov/doc1/09502786849).

The Neurontin cases have revealed the mechanisms of action of a comprehensive marketing campaign — its goals and strategies, tactics and programs, and the participation of particular physicians and institutions.[2] The campaign involved the systematic use of deception and misinformation to create a biased evidence base and manipulate physicians' beliefs and prescribing behaviors. These marketing methods were not found to be illegal in themselves; they were illegal insofar as they promoted off-label prescription. Thus, the importance of the cases lies largely in the light they shed on marketing methods that may be widespread but remain unseen because companies are rarely prosecuted for illegal marketing.

The Neurontin marketing plan consisted of both general strategies — such as the promotion of Neurontin use among high-prescribing physicians and cultivation of thought leaders — and tactical programs.[2] Local physicians were recruited, trained, and paid to serve as speakers in "peer-to-peer selling" programs, which the company saw as "one of the most effective ways to communicate our message." Academic leaders were solicited with educational grants, research grants, and speaking opportunities; some received up to $158,250 over a 4-year period. Advisory boards and "consultants" were convened so that the firm could cultivate relationships with them and deliver "a hard-hitting message about Neurontin."

Marketing "tactics" included education, publications, and research whose promotional intent was disguised, in addition to more transparent activities, such as advertising and sales visits.[2] "Educational programs" reflected the belief that "medical education drives this market!" Teleconferences involving practicing physicians were moderated by physicians who were paid as much as $176,100 over 4 years. Parke–Davis formed speakers bureaus and

sought "strong Neurontin advocates and users to speak locally for Neurontin." "Unrestricted educational grants" were made to for-profit medical-education companies that produced programs to discuss unapproved uses of Neurontin and to grant credit approved by the Accreditation Council for Continuing Medical Education.

A "publication strategy" was designed to increase the use of Neurontin for neuropathic pain and bipolar disorder, off-label indications with great revenue potential. Parke–Davis contracted with medical-education companies to produce articles on prespecified topics, target journals, titles, potential authors to be "chosen at the discretion of Parke–Davis," and "a consistent message" in keeping with promotional goals; some articles were ghost-written.

"Research" was designed and commissioned specifically to promote Neurontin use. A large seeding trial was conducted to "teach physicians to titrate Neurontin to clinical effect" and "to give neurologists the opportunity to titrate to higher doses [up to twice the FDA-approved limit] when needed." In a recently unsealed 318-page analysis of research sponsored by Parke–Davis, epidemiologist Kay Dickersin concluded that available documents demonstrate "a remarkable assemblage of evidence of reporting biases that amount to outright deception of the biomedical community, and suppression of scientific truth concerning the effectiveness of Neurontin for migraine, bipolar disorders, and pain."[3] For example, publication was delayed for a report on a multicenter, placebo-controlled study that found no effect of Neurontin on the primary outcome measure for neuropathic pain because "we [Parke–Davis employees] should take care not to publish anything that damages neurontin's marketing success." Ultimately, ghost-written manuscripts downplayed the lack of effect on the primary outcome and emphasized other outcomes and subgroup analyses that favored Neurontin. Although guest authorship and commercial bias in research are a well-recognized threat to scientific integrity, the documentation of comprehensive manipulation of research and publication related to Neurontin is remarkable.

What is Neurontin's legacy? First, we have learned that pharmaceutical marketing can be comprehensive, strategic, well financed, disguised as "education" and "research," influential, and very effective. Promotion of Neurontin was neither discrete, compartmentalized, nor readily apparent; instead, it was intercalated in nearly every aspect of physicians' professional lives, from the accoutrements of practice to lectures, professional meetings, and publications. Although some pharmaceutical marketing may be less opaque, deceptive, and manipulative, evidence indicates that drug promotion can corrupt the science, teaching, and practice of medicine.[4]

Second, such comprehensive marketing involved many people and institutions that apparently failed to recognize the serious ethical and legal problems with their actions. Employees of Parke–Davis, the medical-education companies it hired, and many physicians (consultants, advisors, educators, and researchers) all participated knowingly. Universities, hospitals, professional organizations, and foundations also participated, and oversight agencies such as the FDA and the Department of Justice did not intervene quickly. Apparently, there was a shared acceptance that Parke–Davis's marketing was simply business as usual.

Finally, these cases substantiate the emerging conviction that "drastic action is essential" to preserve the integrity of medical science and practice and to justify public trust.[4] We believe that such action should include the routine placement of legally discovered documents in the public domain, the study of such documents to inform strategies for minimizing abuses, the establishment of penalties that eliminate the profit to be gained through illegal marketing, and the independent public funding of peer-reviewed pharmaceutical research through a National Institute for Pharmaceutical Research that might be funded by a tax on all drug sales.[5]

Will our profession soon feel compelled to advocate for such actions to preserve our integrity, our social contract, and ultimately our privileges? Neurontin's most important legacy may be promoting our discussion of these issues and perhaps pushing us beyond the tipping point to action.

Drs. Landefeld and Steinman report serving as unpaid consultants to the plaintiff's attorney in *United States of America ex rel. David Franklin vs. Pfizer, Inc., and Parke-Davis Division of Warner-Lambert Company* and participating in the creation of the Drug Industry Document Archive by the University of California, San Francisco, Kalmanovitz Library, an effort that was funded in part by Thomas Greene, whose law firm represented David Franklin in the case. Dr. Steinman also reports receiving support from an educational grant funded by the Attorney General Settlement Fund that arose from the Franklin case. No other potential conflict of interest relevant to this article was reported.

The views expresssed in this article are those of the authors and do not necessarily

reflect the official views of the Department of Veterans Affairs.

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GLOBAL HEALTH

Toward the Elimination of Schistosomiasis

Charles H. King, M.D.

Related article, p. 121

Schistosomiasis remains one of the world's most prevalent diseases. Despite more than a century of control efforts and the introduction of highly effective antischistosomal drug therapy in the 1980s, the disease just will not go away. More than 207 million of the world's poorest people are currently infected with schistosomiasis, which is often a decades-long, chronic inflammatory disorder that is associated with disabling anemia and undernutrition as well as poor performance in school and at work.[1]

An interactive graphic on schistosomiasis is available at NEJM.org

Schistosomiasis, also known as bilharziasis, results from long-lived infection by multicellular intravascular parasites of one of five trematode species — *Schistosoma japonicum, S. mansoni, S. haematobium, S. intercalatum,* or *S. mekongi.* Parasite transmission and the consequent risk of human infection are strongly linked to specific geographic locations, because the parasite goes through several developmental stages that must occur in fresh water, including a period of growth within particular species of intermediate host snails (see diagram and interactive graphic).

Even after infection ends, disease persists. In some patients, especially those with intestinal schistosomiasis (see photo), the late fibrotic complications of schistosomiasis-associated inflammation lead to portal hypertension, which conveys a substantial risk of death due to variceal gastrointestinal bleeding. In patients with urinary schistosomiasis, late complications include irreversible urinary tract obstruction with an associated risk of renal failure and inflammation-induced bladder cancer. Arguably, the Asian form of intestinal schistosomiasis caused by the species *S. japonicum*, reported on by Wang et al. in this issue of the *Journal* (pages 121–128), carries the highest risks of infection-related inflammation and other complications.

In the 1980s, after the introduction of the highly effective antischistosomal drug praziquantel, it was believed that large-scale drug delivery through school-based or community-based programs could solve the problem of schistosomiasis transmission and, in so doing, eliminate the risk of parasite-associated disease. Although such mass-treatment campaigns substantially reduced the infectious burden and the parasite-associated morbidity, they often failed to curb parasite transmission in high-risk communities. Since these efforts failed to prevent immediate reinfection itself, they also did not do a very good job of reducing the substantial rates of illness associated with reinfection.

Why didn't mass treatment stop transmission? As it turns out, the very complexity of the parasite's life cycle helps to ensure that its transmission continues within local ecosystems. Whereas public health planners had assumed that a treatment-related reduction in the excretion of parasite eggs by humans would stem the transmission of the parasite, the process of infection is, in fact, more complicated, being abetted by "superspreaders" (especially untreated children who do not attend school) and by social and hydrologic linkages

REVIEW

Physicians and the Pharmaceutical Industry

Is a Gift Ever Just a Gift?

Ashley Wazana, MD

Context Controversy exists over the fact that physicians have regular contact with the pharmaceutical industry and its sales representatives, who spend a large sum of money each year promoting to them by way of gifts, free meals, travel subsidies, sponsored teachings, and symposia.

Objective To identify the extent of and attitudes toward the relationship between physicians and the pharmaceutical industry and its representatives and its impact on the knowledge, attitudes, and behavior of physicians.

Data Sources A MEDLINE search was conducted for English-language articles published from 1994 to present, with review of reference lists from retrieved articles; in addition, an Internet database was searched and 5 key informants were interviewed.

Study Selection A total of 538 studies that provided data on any of the study questions were targeted for retrieval, 29 of which were included in the analysis.

Data Extraction Data were extracted by 1 author. Articles using an analytic design were considered to be of higher methodological quality.

Data Synthesis Physician interactions with pharmaceutical representatives were generally endorsed, began in medical school, and continued at a rate of about 4 times per month. Meetings with pharmaceutical representatives were associated with requests by physicians for adding the drugs to the hospital formulary and changes in prescribing practice. Drug company–sponsored continuing medical education (CME) preferentially highlighted the sponsor's drug(s) compared with other CME programs. Attending sponsored CME events and accepting funding for travel or lodging for educational symposia were associated with increased prescription rates of the sponsor's medication. Attending presentations given by pharmaceutical representative speakers was also associated with nonrational prescribing.

Conclusion The present extent of physician-industry interactions appears to affect prescribing and professional behavior and should be further addressed at the level of policy and education.

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THERE ARE FEW ISSUES IN MEDICINE that bring clinicians into heated discussion as rapidly as the interaction between the pharmaceutical industry and the medical profession.[1-4] More than $11 billion is spent each year by pharmaceutical companies in promotion and marketing, $5 billion of which goes to sales representatives.[5,6] It has been estimated that $8000 to $13 000 is spent per year on each physician.[7,8] The attitudes about this expensive interaction are divided and contradictory. One study[9] found that 85% of medical students believe it is improper for politicians to accept a gift, whereas only 46% found it improper for themselves to accept a gift of similar value from a pharmaceutical company. Most medical associations have published guidelines to address this controversy. Perhaps the intensity of the discussion is related to the potential consequences were it confirmed that gifts influence prescription of medication that results in increasing cost or negative health outcomes.

This article addresses the question by way of a critical examination of the evidence. Two review articles[10,11] have addressed the factors affecting drug prescribing, but only 1 has focused on the impact of the physician-industry interaction on the behavior of physicians.[12] This article critically examines the literature and highlights articles with rigorous study methods.

METHODS

Studies were identified by searching MEDLINE for articles from 1994 to the present, using the expanded Medical Subject Headings *conflict of interest* and *drug industry*, limiting the search to articles in English while excluding review articles, letters, and editorials; each identified study was cross-referenced; a database of 400 articles gathered by the Medical Lobby for Appropriate Marketing[13] was searched; and 5 key informants were sought for their bibliographies on the topic.

A total of 538 studies that provided data on any of the main study questions were targeted for retrieval. Of the 29 studies that were published in peer-reviewed journals and identified as potentially relevant (containing quantitative data on 1 of 3 facets of physician-industry interactions), 10 were from MEDLINE and 19 from other sources. The data extractor (A.W.) was not blinded to the authors of the studies.

Those with an analytical design (having a comparison group) were considered to be of higher methodological quality.

See also p 391.

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Table 1. Interaction, Attitudes, and Impact of the Interaction Between the Medical Profession and the Pharmaceutical Industry*

Study, y	Site	Population (n)	Interactions	Measure
		Prepost Study		
Bowman and Pearle,[14] 1988	Washington, DC	Physicians attending CME (150)	CME	Impact on prescribing
		Cohort Studies		
Spingarn et al,[15] 1996	Philadelphia, Pa	Internal medicine residents (22 case, 53 control)	Teachings	Impact on prescribing
Orlowski and Wateska,[16] 1992	Cleveland, Ohio	Hospital physicians	Travel, CME	Impact on prescribing
		Case-Control Studies		
Chren and Landefeld,[17] 1994	Cleveland, Ohio	Faculty physicians (36 case, 69 control)	PR, meals, travel, honoraria, research	Frequency and impact on formulary addition requests
Bowman,[18] 1986	Washington, DC	2 CME with different sponsors (5, 6)	Honoraria	Impact on content
		Cross-sectional Studies		
Gibbons et al,[19] 1998	Washington, DC	Physicians and residents (268)	Gifts, samples, meals, travel, teachings	Attitudes
Sandberg et al,[20] 1997	Chicago, Ill	Fourth-year medical students (205)	Gifts	Frequency and impact on attitudes
Mahood et al,[21] 1997	Canada	Family medicine program directors (16)	Samples, teachings, CME, research	Frequency
Hopper et al,[22] 1997	Detroit, Mich	Primary care residents (28) and faculty (14)	PR, gifts	Attitudes
Sergeant et al,[23] 1996	Ontario	Family medicine residents (262)	PR, gifts, meals, CME	Frequency and attitudes
Caudill et al,[24] 1996	Kentucky	Primary care physicians (1603)	PR, promotional material	Frequency, attitudes, and impact on attitudes and prescribing
Strang et al,[25] 1996	Canada	Physicians (550)	PR, gifts, samples, meals, travel	Frequency and attitudes
Hodges,[26] 1995	Toronto, Ontario	Psychiatry clerks and residents (105)	PR, gifts, samples, teachings, CME	Frequency, attitudes, and impact on attitudes
Ziegler et al,[27] 1995	California	Internal medicine residents (27)	PR, teachings	Frequency, attitudes, and impact on knowledge
Andaleeb and Taliman,[28] 1995	Pennsylvania	Faculty physicians and osteopathic practitioners (95)	PR	Impact on attitudes
Poirier et al,[29] 1994	Pennsylvania	Physicians chair of P&T committee (26)	PR, gifts, samples, meals, promotional material	Attitudes
Thomson et al,[30] 1994	New Zealand	Family physicians (67)	PR, gifts, samples, CME, promotional material, travel	Frequency, attitudes, and impact on attitudes
Brotzman and Mark,[31] 1993	United States	Family medicine residents (122 case, 143 control)	PR, meals, CME	Impact on attitudes
Reeder et al,[32] 1993	United States	Emergency medicine chief residents (87)	PR, gifts, samples, meals, travel, teachings	Frequency and attitudes
Keim et al,[33] 1993	United States	Emergency residents (1385) and directors (80)	PR, gifts, meals, travel, teachings	Frequency and attitudes
Banks and Mainous,[34] 1992	Kentucky	Faculty physicians (169)	PR, gifts, samples, meals, travel, CME	Attitudes
Brotzman and Mark,[35] 1992	United States	Family medicine program directors (328)	PR, samples, teachings, gifts, promotional material	Frequency
Bucci and Frey,[36] 1992	United States	Family practice program directors (325)	PR, gifts, samples, meals, CME, teachings	Frequency and attitudes
Lichstein et al,[37] 1992	United States	Internal medicine program directors (444)	PR, meals, samples, travel, CME	Frequency and attitudes
McKinney et al,[38] 1990	Minnesota	Internal medicine residents and faculty (425)	PR, gifts	Frequency and attitudes
Lurie et al,[39] 1990	United States	Internal medicine residents and faculty (484)	PR, meals, travel, honoraria, research	Frequency, attitudes, and impact on formulary requests
Peay and Peay,[40] 1988	Adelaide, Australia	Physicians (59 case, 29 control)	PR	Impact on prescribing
Bower and Burkett,[41] 1987	United States	Family medicine physicians (317)	PR	Impact on prescribing
Haayer,[42] 1982	Twente, Holland	Family medicine physicians (118)	PR	Impact on prescribing

*PR indicates pharmaceutical representative; CME, continuing medical education; and P&T, pharmacy and therapeutics.

RESULTS

A total of 29 studies[14-42] were identified (TABLE 1). Of these, 16 addressed the extent of the physician-industry interaction, 16 identified the attitudes of physicians toward the interaction, and 16 evaluated the effect of the interaction on the practitioner.

Interaction Between Medical Professionals and the Pharmaceutical Industry

All 16 studies* identified (TABLE 2) used self-reporting cross-sectional survey designs, and all but 1[17] used a mailed survey. The response rate ranged from 30%[24] to 100%.[21] Most authors claimed that the response rate was consistent with that obtained in similar studies and that a self-report design would tend to underreport the actual frequency of interaction because of underestimates in recall or a social desirability bias.

Interactions with the industry were found to start as early as medical school[26] and to continue well into practice. Most physicians met with pharmaceutical representatives about 4 times a month,[25,27,30-32] and the frequency tended to stabilize during residency. Residents do not differ significantly from faculty[38,39] in the frequency with which they experience this interaction. Thomson et al[30] found decreased availability of peer physicians ($r = 0.36$, $P<.05$) and a positive attitude toward the pharmaceutical representative ($r = 0.39$, $P<.05$) to be the only predictors of the number of contacts.

The frequency with which physicians benefit from industry-sponsored meals [39] and samples [39] decreases as they enter practice, while frequency of receiving honoraria, [39] conference travel,[25] and research funding[25] increases. Both populations frequently use promotional material.[23] One study found that residents receive 6 gifts a year,[26] with no comparable data for physicians. All interactions were generally permitted except for lunch rounds,[21] pharmaceutical representative speakers,[21,37] and promotional material,[21,36] which were more controversial. As many as 85% of programs had policies on interactions.[21,23,33,35-37]

*References 17,20,21,23-27,30,32,33,35-39.

Attitudes Toward the Interaction

All 16 studies† reported here (TABLE 3) used a self-report design with similar rates of response and limitations.

Residents and physicians have similar attitudes about pharmaceutical representatives. They believe that representatives provide accurate information about their drugs[25] and are equivocal in their beliefs that representatives could provide accurate information on established or alternative drugs.[24-26,38] Most believe that representatives prioritize product promotion above patients' welfare[25] and are likely to use unethical practices.[22,33] Residents are less likely than physicians are to endorse the influence of the interaction on their behavior.‡

Most deny that gifts could influence their behavior[19,24,26,32,34,38] and are equivocal about the ethics of such a practice,[22,33] with residents more likely to admit that without gifts, their interactions with pharmaceutical representatives would be reduced.[24,26,38] Similarly, respondents agree that conference[37] and lunch rounds[27] attendance would decrease without industry-paid meals. Samples, continuing medical education (CME), and conference travel funding are felt to exert more influence (40% to 55%) than promotional material does (22%).[19,29,34] Each interaction elicited ethical concerns; travel funding generated the most concern (48%[29] to 75%[19]). Most physicians also agree that pharmaceutical representative speakers should be banned.[24,38] Residents' opinions are divided.[24,26] Programs with concerns about these interactions were more likely to be military, nontraditional, or to have another source of funding.[37]

Effect of Interaction

Sixteen studies§ were identified (TABLE 4) that assessed the impact of the physician-industry interaction on the knowledge, attitudes, and prescribing practices of physicians. Studies used cross-sectional, case-control, or preinteraction and postinteraction methods to assess the impact of particular interactions.

†References 19, 22-27, 29, 30, 32-34, 36-39.
‡References 22, 24, 25-27, 29, 33, 34, 38, 39.
§References 14-18, 20, 24, 26-28, 30, 31, 39-42.

Interactions With Pharmaceutical Representatives

There was an independent association between meetings with pharmaceutical representatives and formulary addition requests for the drug of the representative's company, both with respect to control physicians who did not meet representatives and with respect to requests for other companies' drugs.[17,39] Most of the requested drugs presented little or no therapeutic advantage over existing formulary drugs, but the merit of the requests was not related to interactions with the pharmaceutical industry. This, as well as the strength, consistency, specificity, and independence of the results, make it unlikely that the interaction occurred because the physician was already convinced of that drug's influence.[17]

Interactions with pharmaceutical representatives were also found to impact the prescribing practice of residents and physicians[39] in terms of prescribing cost,[24] nonrational prescribing,[42] awareness, preference and rapid prescribing of new drugs,[40] and decreased prescribing of generic drugs.[41] These findings were independent of other variables in all but 1 study,[41] in which such an analysis was not done.

Attitudinal outcomes were examined in matched residency programs with and without restrictions on interactions. Exposure to pharmaceutical representatives was highly associated with a perception of the benefits of such an interaction and the appropriateness of other interactions. Whether exposure to pharmaceutical representatives or to critical faculty role models influences residents' attitudes remains unknown.[31] There were other correlates of positive attitudes,[24,28,30] but the directionality of these latter associations is not as clear as with the above quasi-experimental study.[31]

Gifts

Receiving a gift[20] and the number of gifts received[26] correlated with the belief that pharmaceutical representatives have no

Table 2. Interaction Between the Medical Profession and the Pharmaceutical Industry*

Measure	Residents	Physicians
	Overall	
Policy, % of programs	Limited,[21,23,33,35-37] 25[21] to 86[23]	
	Interaction with PR	
Interaction	51% of residents[23] (83% of programs [1-3/wk])[32]	85%[30] to 87%[17]
Frequency	0.25/mo[26] to 3.1/mo[38] (higher than in fourth year)[26] Brief: 1.5/mo[39] to 8.7/mo[27] Extended: 0.3/mo[39] to 3.5/mo[27]	3 to 4/mo (NS)[30,38] Brief: 1.6/mo[39] Extended: 0.6/mo (NS)[39]
Policy, % of programs		
Permitted ad lib	84[30,37]	
Limited	64[33] to 79[35]	
Prohibited	34[33]	
	Gifts	
Interaction	80% of medical students received a book[20] (90% of programs[32])	
Frequency	6/y (average value $60)[26]	
Policy, % of programs		
Permitted	86 to 89[35,36]	
	Samples	
Interaction	66% of residents (66% of programs[32])	86%[25]
Frequency	2/y[26] to 2.4/y[39] (interns, 4.8/y; $P<.02$)[26]	1.3/y (fewer than residents; $P<.001$)[39]
Policy, % of programs		
Permitted	71 to 94[35-37]	
	Promotional Material	
Interaction	91% of residents patient education items[23] 52% of residents seeking drug information from PR[27] (82% of programs)[35]	
Frequency		5.4% Daily 31% Weekly 48% Monthly 14% Yearly[19]
Policy, % of programs		
Permitted	43[36], 62[21]	
	Industry-Paid Meals	
Interaction	80% of residents [26] (80% of programs[32])	41%[20]
Frequency	14/y[26] to 15/y[39] (interns, 31/y; $P<.05$)	2.3/y (fewer than residents; $P<.001$)[39]
Policy, % of programs		
Permitted	88[36]	
	Conference Travel	
Interaction	3% of residents [26]	42%[25]
	Lunch Rounds and PR Speakers	
Interaction	54% of programs[32]	
Frequency	Attended lunch rounds (20/y)[27]	
Policy, % of programs		
Permitted	38 lunch rounds[21] 38 to 86 PR speakers[21,35,37]	
	CME Funding	
Policy, % of programs		
Permitted	88[36,37]	
	Honoraria	
Frequency		1.2/y[39]
	Research Funding	
Frequency, %		54%[25]
Policy, % of programs		
Permitted	69[36]	

*PR indicates pharmaceutical representative; CME, continuing medical education; and NS, not significantly different from residents. Blank spaces indicate data do not apply or were not collected.

impact on prescribing behavior; receiving gifts of high relevance to practice was also associated with a positive attitude.[30] The former association was independent of the student's ability to recall the donor.

Samples

Accepting samples was associated with awareness, preference and rapid prescription of a new drug,[40] and a positive attitude toward the pharmaceutical representative.[30]

Industry-Paid Meals

There was an independent association between benefiting from sponsored meals and formulary addition requests for any drug[39] that was clearly dose-related.[17]

Funding for Travel or Lodging to Attend Educational Symposia

Accepting funding to attend a symposium was independently associated with increased formulary addition requests for the sponsor's drug.[17] This interaction was also found to impact hospital prescribing practices 2 years after 2 groups of physicians accepted all-expenses-paid trips to a drug-sponsored symposium. This occurred despite the continued prescribing of the 2 drugs that the new ones were to replace and the lack of concern about the interaction among all but 1 beneficiary.[16] The physicians were not randomly selected, thus raising the unlikely possibility that physicians more partial to the sponsor's drug chose to participate. It is nonetheless striking to note that the changes occurred at an institutional level.

Pharmaceutical Representative Speakers

Resident exposure to pharmaceutical representative speakers at lunch rounds was associated with dissemination and learning of inaccurate information about the sponsor's and competitor's drug.[27] Attendance at rounds given by a physician pharmaceutical representative was associated with appropriate and inappropriate treatment decisions by attending residents, independent of

variables including the resident's memory of the presenter's affiliation.[15] Although not a randomized trial, the factors leading to attendance seemed unrelated to the outcome.[15]

CME Sponsorship

Drug company CME, sponsorship affected presentation content in that the sponsor's drug was always preferentially highlighted, although the same drugs were discussed in each event.[18] Changes in prescribing practice (self-reported) in favor of the sponsor's drug were also found.[14] The participants were not randomized, but it is unlikely that their self-selection reflected a bias for the sponsor's drug. The consistent findings across all events also minimize the lack of control groups. These were findings in settings where industry guidelines were applied.

Honoraria, Research Funding, Employment

Accepting a drug company honorarium to present data on a new therapy and receiving research support were independently associated with a formulary addition request for the sponsor's drug as well as any drug.[17,39] One study examined the impact of employment but did not find it significant.[13]

COMMENT

Limitations

MEDLINE was not personally searched before 1994 and other databases were not searched. However, 1 of the studies examined[12] searched MEDLINE and HEALTH from 1978 to 1993, and the methods ensured a thorough exploration of the published literature.

Industry-Physician Interaction

Residents and physicians interact with the pharmaceutical industry frequently and in multiple settings and fashions, beginning as early as medical school. Residents benefit more from drug-sponsored meals, whereas physicians receive more honoraria, conference travel, and research funding. Both meet equally often with pharmaceutical representatives.

Table 3. Attitudes Toward the Physician–Pharmaceutical Industry Interactions*

Measure	Residents	Physicians
Interaction With PR		
Knowledge and technique		
Adequate/accurate knowledge overall		20%[29] to 35%[25]
of their drug		65%[25]
of new drugs	32%[26]; LS, 2.8[38]	LS, 2.8[38] to 3.6[24]
of established drugs	25%[26]; LS, 2.9[38]	LS, 2.7[38] to 3.5[24]
of alternatives		19%[25]
Fairly portray their product		20%[25]
Provide misleading information	44%[27]	
May use unethical practice	74%[33]; LS, 3.2[22]	LS, 3.7 ($P = .04$)[22]
Goal is product promotion		92%[25]
Value		
PR support CME	77%[26]; LS, 4.0[38]	LS, 3.9[24] to 4.2[38]
Positive	29% to 85%[26,27,32]; LS, 2.4[38] to 3.7[22]	LS, 2.1 to 3.7[22,30,38]
Influence behavior	25% to 49%[23,26,27,33,39]; LS, 1.8[22] to 2.5[38]	58%[34] to 70%[25]; LS, 1.75 to 3.2[22,24,38]
Concerned about influence		52% to 68%[29]
Too much contact	LS, 2.8[22]	LS, 3.4 ($P = .003$)[22]
Plan to interact with PR in the future	76.1%[23]	
Policy		
Should be allowed to interact with PR	82.3%[23]	
Gifts		
Influence behavior	8% to 27%[19,26,32]; LS, 1.7[38]	8 to 13%[19,26]; LS, 1.6 to 1.8[24,38]
Inappropriate/unethical	4% to 49%[19,33]	4% to 88%[19,29]
Ethical for gifts with/without patient benefit	LS, 3.9/LS, 2.8[22]	LS, 4.0/LS, 2.5[22]
Leads to higher costs of drugs	35.9%[23]	
Would maintain same contact without gifts	45%[26]; LS, 2.8[39]	LS, 2[24] to 4.0[39] ($P<.05$)
Samples		
Inappropriate	12%[33] to 33%[19]	33%[19] to 60%[29]
Influential	55%[19]	42%[34] to 55%[19]
Should be offered		86%[25]
Promotional Material		
Useful	58.4%[25]	
Influential	22%[19]	22%[19]
Inappropriate		12%[19] to 60%[29]
Industry-Paid Meals		
Influential	24%[19]	24%[34,19]
Unethical	33%[19]	12%[27] to 33%[19]
CME attendance would decline without		
Should be allowed		21%[25]
Conference Travel		
Inappropriate	39%[33] to 75%[19]	48% to 75%[29,19,30]
Influential	42%[19]	42%[19]
Partial/full funding should be allowed		47%/15%[25]
Lunch Rounds and PR Speakers		
Appropriate	10%[19] to 11%[27]	10%[19]
Influential	12%[19]	12%[19]
Attendance would be same without lunch	0%[27]	
Should be banned	10%[26]; LS, 3.7[39]	LS, 3.5[39] to 4.2[24]
CME Funding		
Influential		40%[34]
Content should be chosen by physicians	92.5%[23]	

*Results for residents and physicians do not significantly differ unless identified by P values. LS indicates Likert scale: "strongly agree"-5, "agree"-4, "neutral"-3, "disagree"-2, "strongly disagree"-1. PR indicates pharmaceutical representative; CME, continuing medical education. Blank spaces indicate data do not apply or were not collected.

Physicians and residents were similarly skeptical of the motives and comprehensive knowledge of pharmaceutical representatives but expressed a similar lack of concern about the influence of gifts, promotional material, meals, and lunch rounds. They had similar concerns about pharmaceutical representative speakers, CME funding, and conference funding; physicians were more concerned than were residents about the influence of representatives. All admitted that contact with representatives and attendance at educational events would decline were it not for gifts and meals.

Outcome of Interaction

Although some positive outcomes were identified (improved ability to identify the treatment for complicated illnesses), most studies found negative outcomes associated with the interaction. These included an impact on knowledge (inability to identify wrong claims about medication), attitude (positive attitude toward pharmaceutical representatives; awareness, preference, and rapid prescription of a new drug), and behavior (making formulary requests for medications that rarely held important advantages over existing ones; nonrational prescribing behavior; increasing prescription rate; prescribing fewer generic but more expensive, newer medications at no demonstrated advantage.)

No study used patient outcome measures. Studies demonstrating an effect on research findings[43-47] were excluded because they were not limited to physicians or to clinical activity. Some detected an influence of some interactions using self-report measures but were limited by the aforementioned biases and were less informative than the analytic studies reporting specific outcomes. However, most of these studies examined only 1 interaction or the effect of 1 intervention at a time, even if the effect of these interactions was posited as being cumulative. One study gave a high estimate for the effect of 2 interactions but had not entered this finding into the regression analysis.[17]

Most studies found a significant association that was consistent and strong for all interactions examined and which was biologically plausible and coherent with

Table 4. Effect of Physician–Pharmaceutical Industry Interactions on the Practitioner*

Interaction	Outcome	Findings
Interaction with PR	Attitude	Exposure to PR associated with positive perception of PR (β = .638; P = .02) (R),[31] perception of appropriateness of other interactions (r = 0.706; P = .02) (R)[31] Perceived support by PRs (r = 0.384; P<.01),[28] the availability (r = 0.30; P<.001) and applicability (r = 0.30; P<.001) of PR information and of the PRs themselves (r = 0.54; P<.001),[24] and receiving practical prescribing information[30] associated with positive perception of PR (P)
	Formulary request	"Request made at suggestion of PR in the last year" (R, 4%; P, 20%)[39]
		Contact with PR associated with increased likelihood of request for PR's drug vs those who did not meet PR (OR, 3.4; 95% CI, 1.8-6.6), and vs request for other company's drug (OR, 4.9; 95% CI, 3.2-7.4) (P)[17]
	Prescribing	Frequency of contact associated with change of practice (R, r = 0.049, P = .003; P, r = 0.016, P = .003),[39] higher prescribing cost (r = 0.155; P<.01) (P),[24] and rapid prescription of a new drug (r = 0.35; P<.002) (P)[40] Relying on PR associated with decreased likelihood of prescribing generic by 66% (P)[41] and less rational prescribing (r = 0.195; P<.03) (P)[42]
Gifts	Attitudes	Receiving a gift[20] and number of gifts received (r = 0.24; P<.04)[28] are associated with belief that PRs have no impact on behavior (R) Receiving high-relevance gifts is associated with positive attitude toward gifts (P)[30]
Samples	Attitudes	Positive attitude toward the PR (P)[30]
	Prescribing	Awareness, preference, and rapid prescription of a new drug (r = 0.35; P<.002) (P)[40]
Industry-paid meals	Formulary request	Increased likelihood of request for any drug (r = 0.089; P = .03)[39]; 8% of requesting physicians vs 3% of controls "occasionally" shared meals; 14% vs 1% "often" shared meals (P<.01) (P)[17]
Conference travel	Formulary request	Increased likelihood of request for sponsor's drug (OR, 7.9; 95% CI, 1.1-55.6) vs controls who did not benefit (P)[17]
	Prescribing	4.5- to 10-fold increase in preconference prescribing rate of sponsor drug (compared with 2.5- to 3.5-fold national rate increase) (P)[16]
PR speakers	Knowledge	Learning of inaccurate information (only 26% able to identify inaccurate claims) (R)[27]
	Prescribing	Appropriate treatment for complications of discussed illness (OR, 8.4; 95% CI, 2.1-38.9) (R)[15] Inappropriate treatment (higher cost, more invasive) for milder forms of the discussed illness (100% vs 79% of those not in attendance; P = .03) (R)[15]
CME funding	Content	More frequent mention (2.5 to 3 times) of positive effects of sponsor's medication and negative or equivocal effects of competitor's (P<.05) (P)[18]
	Prescribing	Highest increase (5.5% to 18.7%) in the rate of prescription of the drugs made by the CME sponsor, while decrease or smaller increase in rate of competitor's drug (P<.05) (P)[14]
Honoraria	Formulary request	Increased likelihood of request for any drug (r = 0.178; P = .003),[39] from those who benefit "occasionally" (OR, 4.0; 95% CI, 1.0-16.8) and "often" (OR, 29.1; 95% CI, 3.4-246.6) (P)[17] Increased likelihood of request for sponsor's drug vs controls who did not benefit (OR, 3.9; 95% CI, 1.2-12.7), and vs request for other company's drugs (OR, 2.2; 95% CI, 1.1-4.2) (P)[17]
Research funding	Formulary request	Increased likelihood of request for any drug (r = 0.102; P<.05)[39]; 61% of requesting physicians vs 29% of controls benefited (P = .002) (P)[17] Increased likelihood of request for sponsor's drug (OR, 9.5; 95% CI, 2.6-35.7) vs controls who did not benefit (P)[17]

*CME indicates continuing medical education; PR, pharmaceutical representative; P, physicians; R, residents; S, students; OR, odds ratio; and CI, confidence interval.

other theories[48] (TABLE 5). Dose response was demonstrated in all interactions in which it was examined. Some studies were even able to establish specificity by identifying a stronger endorsement of a company's product, although nonspecific outcomes (eg, decreased prescription of nongeneric products, more expensive and less rational treatment) are just as meaningful. The independence of the association was established with a matched analysis or multivariate analysis in all but CME and gifts, although, the bias in the case of CME funding seems small. Nonetheless, the temporal direction of the association was established for only 4 interactions: an increase in the physician prescribing rate of the CME sponsor's drug[14]; an increase in hospital prescribing rate of the conference travel sponsor's drug[16]; increased nonrational prescribing choice of the sponsor's drug after related resident teaching given by physician pharmaceutical representatives[15]; and an association between interactions with pharmaceutical representatives and positive attitudes toward them.[31] This latter association is limited by the possibility of a confounder responsible for the differences in attitudes among the 2 groups of residents. The causal directions of all other studies are not as clear, suggesting that interactions could have followed the outcomes. Chren and Landefeld[17] argue that their findings demonstrate the impact of interactions with pharmaceutical representatives, honoraria, and sponsored research. There are no ideal data to date, but the literature points to important concerns for 3 interactions with physicians: pharmaceutical representative speakers, CME sponsorship, and conference travel. Many less rigorous studies also detected the impact of the interactions with pharmaceutical representatives. These outcomes occurred despite physicians' forgetting the sponsors' names[15,20] or physicians' beliefs that they could not be influenced.[16]

Policy Implications

Several professional societies,[53-57] have developed guidelines to modulate the interaction between physicians and the pharmaceutical industry. Despite the guidelines' recommendation that students and residents should be informed about them, there was a lack of awareness. Among residents, only 23%[23] to 50%[32] knew about them, whereas 62% of physicians knew of at least 1 guideline.[19] Also, enrollment in a program with guidelines affected whether they would accept gifts, but having read the national guidelines and awareness of the program's policy did not.[23] Enrollment in a program with guidelines also affected the frequency of and attitude toward these interactions.[31] Whether it was the guidelines themselves or the presence of critical faculty who served as role models that influenced the interactions cannot be elucidated from these studies. Only a few training programs have proposed their own guidelines (35% of US internal medicine programs,[37] 58% of US family medicine[35] programs, 61% of US emergency medicine programs,[33] and 25% of Canadian family medicine programs[21]) and fewer distribute these guidelines[21] or give formal instruction on them.[23]

Finally, most such guidelines allow for physician–pharmaceutical representative interaction whereas subsidies for travel and other amenities at a symposium can only be given to residents. This article questions the adequacy of the guidelines for many of the above interactions, specifically, the lack of guidelines regarding resident–pharmaceutical representative interaction, the efficacy of the guidelines for industry-sponsored CME events, and the allowance of industry-sponsored conference travel for residents despite the fact that these have been disallowed for physicians. This is of great concern in terms of travel scholarships, for which residents have conference subschedules designed by a group of mentors hired by the same industry sponsor and are immersed in this group for the duration of the conference. Concerns about CME could be addressed by prioritizing the Association of American Medical Colleges guidelines and concerns by other authors.[58] Also, the American College of Physicians' suggestion that physicians should be guided in making decisions about their activities by whether they would be willing to have their interactions known does not address the fact that physicians do not always comprehend how interactions affect them.

Another attempt to address growing concern about physician-industry interaction has been the introduction of practical training. Twenty-five percent[37] to

Table 5. Hill Criteria for Causality and Industry-Physician Interactions[48]*

	Consistency†	Strength	Specificity‡	Dose-Response	Biological Plausibility§	Coherence	Temporal Relationship	Experiment[31]
Interaction with PR	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Gifts	Yes	Yes	...	Yes	Yes	Yes	...	Yes
Samples	Yes	Yes	...	Yes	Yes	Yes	...	...
Industry-paid meals	Yes	Yes	...	Yes	Yes	Yes	...	...
PR speakers	Yes	Yes	...	...	Yes	Yes	Yes	...
CME funding	Yes	Yes	...	...	Yes	Yes	Yes	...
Conference travel	Yes	Yes	Yes	Yes	Yes	Yes	Yes	...
Honoraria	Yes	Yes	Yes	Yes	Yes	Yes	...	...
Research funding	Yes	Yes	Yes	Yes	Yes	Yes	...	...

*Ellipses indicate data were not collected. CME indicates continuing medical education.
†More than 1 study found an effect for each interaction.
‡Only 1 study examined specificity and defined it as increased likelihood of choosing product of sponsor over competition in association with interaction.[25]
§Mechanism: for gifts, meals, honoraria, and travel subsidy[49]; interaction with pharmaceutical represtative (PR)[50-52]; research funding[43-47]; the mechanisms for all other interactions are reviewed in the text.

75%[21] of programs taught about industry marketing techniques and critical appraisal of industry product claims. Yet these attempts left many residents wanting: family medicine, psychiatry, emergency medicine, and internal medicine residents wanted more teaching[26,33,38] both in medical school (45%) and residency (60.6%).[21] Reports of some programs that have been implemented are optimistic,[9,22,33,59-62] However, 2 of the studies are older[9,60] and another program[62] was conducted infrequently. Also, only short-term effects on attitude and knowledge were examined, leaving the impact on long-term behavior unknown. Clearly, there is a need for systematic interventions. Positive changes in prescription patterns and physician knowledge[40,63,64] associated with such alternatives as academic detailing and industry-independent drug information mailings suggest other avenues for action.

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Health Industry Practices That Create Conflicts of Interest

A Policy Proposal for Academic Medical Centers

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Conflicts of interest between physicians' commitment to patient care and the desire of pharmaceutical companies and their representatives to sell their products pose challenges to the principles of medical professionalism. These conflicts occur when physicians have motives or are in situations for which reasonable observers could conclude that the moral requirements of the physician's roles are or will be compromised. Although physician groups, the manufacturers, and the federal government have instituted self-regulation of marketing, research in the psychology and social science of gift receipt and giving indicates that current controls will not satisfactorily protect the interests of patients. More stringent regulation is necessary, including the elimination or modification of common practices related to small gifts, pharmaceutical samples, continuing medical education, funds for physician travel, speakers bureaus, ghostwriting, and consulting and research contracts. We propose a policy under which academic medical centers would take the lead in eliminating the conflicts of interest that still characterize the relationship between physicians and the health care industry.

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THE CURRENT INFLUENCE OF market incentives in the United States is posing extraordinary challenges to the principles of medical professionalism. Physicians' commitment to altruism, putting the interests of the patients first, scientific integrity, and an absence of bias in medical decision making now regularly come up against financial conflicts of interest. Arguably, the most challenging and extensive of these conflicts emanate from relationships between physicians and pharmaceutical companies and medical device manufacturers.[1]

As part of the health care industry, pharmaceutical and medical device manufacturers promote the welfare of patients through their commitment to research and product development. Their investments in discovering, developing, and distributing new pharmaceutical agents and medical devices have benefited countless patients. Most companies also support continuing medical education (CME). However, their ultimate fiduciary responsibility is to their shareholders who expect reasonable returns on their investments. Indeed, manufacturers are acutely aware of the conflict between patient vulnerability and profit incentives.

Recent congressional investigations, federal prosecutions, and class action lawsuits have brought to light documents demonstrating how company practices frequently cross the line between patient welfare and profit-seeking behavior.[2-4] Concerned physicians, journalists, and federal prosecutors are exposing still other aspects of an unhealthy relationship between manufacturers and the medical profession.[5-7]

These transgressions have prompted pharmaceutical firms to regulate themselves more stringently. That effort is

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commendable, but physicians' behavior is a large part of the problem and industry efforts to date have not resolved the crisis. The standing of the profession, as much as the integrity of the pharmaceutical and medical device industries, is jeopardized by allowing obvious conflicts to continue.

The serious threat that this state of affairs poses for professionalism, and for the trust that patients have in physicians, makes the need for effective guidelines on industry-physician relationships both apparent and urgent. Marketing and market values should not be allowed to undermine physicians' commitment to their patient's best interest or to scientific integrity.

To remedy the situation and prevent future compromises to professional integrity, academic medical centers (AMCs) must more strongly regulate, and in some cases prohibit, many common practices that constitute conflicts of interest with drug and medical device companies. The guidelines we suggest are designed to promote broader professional self-regulation.

Why AMCs?

Academic medical centers, which include medical schools and their affiliated hospitals, should provide leadership for medicine in the United States. Just as pharmaceutical manufacturers look to AMCs for influential advice and support, so does the medical profession. Academic medical centers also have a major responsibility for training medical students and house staff. Research reveals that the habits learned or acquired during training persist into practice.[8] Objectivity and scientific integrity should be central tenets of physician training.

Academic medical centers are also in a position to take immediate action. They are sufficiently well organized to gain commitments to a set of new principles in relatively short time. Moreover, independent research into the impact of medications and devices on population health is concentrated in AMCs; therefore, unwarranted influence by manufacturers must be avoided. For these reasons, academic medicine should take the leadership in reforms, and other physicians and medical institutions should adopt their standards.

Defining Conflicts of Interest With Industry

Conflicts of interest occur when physicians have motives or are in situations for which reasonable observers could conclude that the moral requirements of the physician's roles are or will be compromised. In terms of industry influences, financial conflicts of interest occur when physicians are tempted to deviate or do deviate from their professional obligations for economic or other personal gain.[9] The bias thus introduced violates both the best interests of patients and the standards of scientific integrity. Policing such conflicts clearly lies within the scope of professional responsibilities set forth in the *Physician Charter on Medical Professionalism*.[10,11]

Traditionally, marketing by pharmaceutical and device companies has centered on company representatives or "detail persons" who visit individual physicians and provide information on new products. This practice has increased in scale and many other marketing strategies are also used. Approximately 90% of the $21 billion marketing budget of the pharmaceutical industry continues to be directed at physicians, despite a dramatic increase in direct-to-consumer advertising.[12] In 2000, for example, the industry sponsored 314 000 events specifically for physicians.[13] Moreover, industry contracted with many hundreds of physicians to serve on advisory boards or speakers bureaus.[5] The purpose behind such industry contacts with physicians is unmistakable: drug companies are attempting to promote the use of their products.

The following list, while not exhaustive, indicates the interactions with industry that must be addressed[14]: gifts, even of relatively small items, including meals; payment for attendance at lectures and conferences, including online activities; CME for which physicians pay no fee; payment for time while attending meetings; payment for travel to meetings or scholarships to attend meetings; payment for participation in speakers bureaus; the provision of ghostwriting services; provision of pharmaceutical samples; grants for research projects; and payment for consulting relationships.

These interactions have been examined by a variety of physician and industry groups, including the American Medical Association, the American College of Physicians, the Accreditation Council for Continuing Medical Education (ACCME), and the Pharmaceutical Research and Manufacturers of America.[2] The Office of the Inspector General of the Department of Health and Human Services has also released guidelines endorsing the Pharmaceutical Research and Manufacturers of America code.

In our view, the guidelines produced by these various groups and organizations are not sufficiently stringent and do not adequately uphold a professional commitment to patient welfare and research integrity. None of these groups establishes monitoring mechanisms or pinpoints responsibility for compliance. The profession itself must exert much tighter control over the relationships between manufacturers and physicians.

Myths of the Small Gifts and Full Disclosures

Most of the recommendations from medical and industry groups share 2 key assumptions. The first is that small gifts do not significantly influence physician behavior. The second is that disclosure of financial conflicts is sufficient to satisfy the need to protect patients' interests. Although these 2 assumptions are widely accepted among physicians, compelling research findings using a variety of methods have called their validity into question.

Psychologists, sociologists, and economists have explored human be-

havior in a conflicted situation using innovative experimental techniques.[15] Their research has established that behavior is not entirely rational, individuals are not always conscious of their motives, and many popular beliefs about how individuals act in light of specific information are simply wrong.[16]

Social science research demonstrates that the impulse to reciprocate for even small gifts is a powerful influence on people's behavior. Individuals receiving gifts are often unable to remain objective; they reweigh information and choices in light of the gift.[17] So too, those people who give or accept gifts with no explicit "strings attached" still carry an expectation of some kind of reciprocity.[17] Indeed, researchers suggest that the expectation of reciprocity may be the primary motive for gift-giving.[15]

Researchers have specifically studied industry gifts to physicians. Receiving gifts is associated with positive physician attitudes toward pharmaceutical representatives.[18,19] Physicians who request additions to hospital drug formularies are far more likely to have accepted free meals or travel funds from drug manufacturers.[20] The rate of drug prescriptions by physicians increases substantially after they see sales representatives,[21] attend company-supported symposia,[22] or accept samples.[23,24] The systematic review of the medical literature on gifting by Wazana[25] found that an overwhelming majority of interactions had negative results on clinical care.

The assumption that disclosure to patients is sufficient to resolve problems created by physicians' conflicts of interest is also unfounded. First, physicians differ in what they consider to be a conflict, which makes the disclosure of conflicts incomplete. Because declarations of conflict are usually unverified, their accuracy is uncertain. Second, recipients of information who are not experts in a particular field often find it impossible to identify a biased opinion that they read or hear about that subject.[17] Third, disclosure may be used to "sanitize" a problematic situation, suggesting that no ill effects will follow from the disclosed relationship.[26] Rather than eliminate the conflict, it is easier to disclose it and then proceed as though it did not exist.[5]

More Stringent Regulation

Because gifts of even minimal value carry influence and because disclosure is an inadequate safeguard, the guidance presently provided by the medical profession, the pharmaceutical industry, and the federal government fails to protect the best interests of patients and the integrity of physician decision making. For these reasons, many current practices should be prohibited and others should be more strictly regulated to eliminate potential sources of unwarranted influence.

Gifting. All gifts (zero dollar limit), free meals, payment for time for travel to or time at meetings, and payment for participation in online CME from drug and medical device companies to physicians should be prohibited. A complete ban on these activities by eliminating potential gray areas greatly eases the burden of compliance. It also frees physicians from deciding whether a gift is appropriate and removes a principal mode by which detail persons gain access to physicians' offices and influence their decision making.

Pharmaceutical Samples. The direct provision of pharmaceutical samples to physicians should be prohibited and replaced by a system of vouchers for low-income patients or other arrangements that distance the company and its products from the physician. The availability of free samples is a powerful inducement for physicians and patients to rely on medications that are expensive but not more effective. Samples also provide company representatives with access to physicians. The increasing reliance on direct-to-consumer advertising by drug companies only heightens the tension between current marketing practices and good patient care.

Drug companies believe that the interactions between sales representatives and physicians serve several purposes, which include introduction of physicians to new medications, encouragement to use the most effective medications, improvement of the likelihood that they will follow good practice guidelines, and access to medications for low-income patients. From the perspective of medical professionalism, however, far better methods for securing these goals exist, all of which would be free of the pitfalls of marketing strategies.

Drug Formularies. Hospital and medical group formulary committees and committees overseeing purchases of medical devices should exclude physicians (and all health care professionals) with financial relationships with drug manufacturers, including those who receive any gift, inducement, grant, or contract. These policies would help ensure that decision making for formulary drugs and medical devices is based solely on the best available scientific evidence.

Continuing Medical Education. The widespread influence of drug manufacturers on current CME activities makes more stringent regulation necessary.[27] Manufacturers should not be permitted to provide support directly or indirectly through a subsidiary agency to any ACCME-accredited program. Manufacturers wishing to support education for medical students, residents, and/or practicing physicians should contribute to a central repository (eg, a designated office at an AMC), which, in turn, would disburse funds to ACCME-approved programs. This arrangement would permit the central repository and the ultimate recipients of funds to remain free from influence by any one donor company. To ensure accountability and to acknowledge generosity, the amount of funds contributed and the eventual use of the funds should be posted on a publicly available Web site.

This policy would likely reduce the contributions made by drug and device companies to CME programs. Companies acknowledge that they carefully evaluate the market impact of expenditures and support only

those demonstrating an increased use of their products.[28] Other ways of funding CME programs will have to be identified.

Funds for Physician Travel. Pharmaceutical and device manufacturers interested in having faculty or fellows attend meetings should provide grants to a central office at the AMC. That office could then disburse funds to faculty and training program directors. Trainees would no longer be directly dependent on industry largesse for educational opportunities.

Speakers Bureaus and Ghostwriting. Faculty at AMCs should not serve as members of speakers bureaus for pharmaceutical or device manufacturers. Speakers bureaus are an extension of manufacturers' marketing apparatus. Because AMC faculty have a central role in the training of new physicians and represent their own institution, they should not function as paid marketers or spokespersons for medicine-related industries. By adhering to this recommendation, academic leaders will be upholding the principle that faculty opinion should be data driven and not for hire. For these same reasons, faculty should be prohibited from publishing articles and editorials that are ghostwritten by industry employees.

Consulting and Research Contracts. Because the process of discovery and development of new drugs and devices often depends on input from academic medicine, consulting with or accepting research support from industry should not be prohibited. However, to ensure scientific integrity, far greater transparency and more open communication are necessary. Accordingly, consulting or honoraria for speaking should always take place with an explicit contract with specific deliverables, and the deliverables should be restricted to scientific issues, not marketing efforts. So-called "no strings attached" grants or gifts to individual researchers should be prohibited. A contract with no identified deliverables is tantamount to a gift and should be regarded as such.[29]

To promote scientific progress, AMCs should be able to accept grants for general support of research (no specific deliverable products) from pharmaceutical and device companies, provided that the grants are not designated for use by specific individuals. As long as the institution stands between the individual investigator and the company making the grant, the likelihood of undue influence is minimized but certainly not eliminated.

To better ensure independence, scientific integrity, and full transparency, consulting agreements and unconditional grants should be posted on a publicly available Internet site, ideally at the academic institution. This is important because company-funded research is more likely to produce positive results and on occasion companies have restricted the dissemination of research results unfavorable to their products.[30]

One might argue that such an approach simply transfers the pressure surrounding financial conflicts to the institution and, as in the case of Oliveri at the University of Toronto, institutions have given in to pressure from pharmaceutical firms.[31] But the requirements of public access and peer pressure will more effectively operate at the institutional level and such a policy is preferable to banning all contact between manufacturers and academic centers.

Going Forward

The benefits of such policies may convince the leadership of AMCs and medical schools to adopt them. We realize that some AMCs will be concerned that voluntarily adopting more stringent regulations may put them at a competitive disadvantage compared with those that do not.[32] However, we hope their leadership will recognize that we call for changes in current AMC practices that are, in many respects, modest. For example, existing guidelines prohibit all gifts from industry except those that are small; going one step further and eliminating token gifts should not cause great disruption and may bring greater clarity. Grants and consulting are not prohibited but must be transparent and subject to peer review. Although such steps may cause significant challenges for medical schools and affiliated institutions, students, physicians, and the public deserve unbiased medical education, research, and clinical care.

Industry has good reason to accommodate itself to these policies and will continue to seek assistance from academic consultants and researchers. Commercial entities working with AMCs cannot be pleased about the diminished respect and growing public mistrust of their activities in the current environment.

Medical schools must be prepared to monitor compliance and enforce the rules we have outlined. There will be costs associated with oversight and perhaps a decline of collegiality among faculty. But these negative aspects will depend to some extent on the prevalence of violations. If AMC leaders educate colleagues and build a consensus around these principles, compliance will follow.

What then might the world of medicine look like if these proposals are widely adopted? First, decisions by physicians on which prescription to write and which device to use might become more evidence-based; medical societies' practice guidelines might become less subject to bias. A greater reliance on objective sources for accurate and up-to-date information would also promote better patient outcomes. Second, total expenditures on prescription drugs might decline. An increased use of generic products, increased use of comparable but less expensive patent-protected products, and, in some cases, a decreased reliance on pharmaceutical agents might be observed. Third, although AMCs and professional societies would have to find alternative sources for funding programs, the absence of industry representatives at AMC meetings and lunches and in corridors would increase the sensitivity among medical students and house staff to the values of medical professionalism and scientific integrity.

Rules would be standardized, not, as now, with some departments prohibiting drug company lunches, others allowing them; some hospitals permitting the sales representatives to see their physicians, others not. Medical society meetings would also assume a more professional tone and the substance of the programs would become more scientific.

Ultimately, the implementation of these proposals will substantially reduce the need for external regulation to safeguard against market-driven conflicts of interest, and the medical profession will reaffirm very publicly its commitment to put the interests of patients first.

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Policy Forum

Following the Script: How Drug Reps Make Friends and Influence Doctors

Adriane Fugh-Berman*, Shahram Ahari

It's my job to figure out what a physician's price is. For some it's dinner at the finest restaurants, for others it's enough convincing data to let them prescribe confidently and for others it's my attention and friendship...but at the most basic level, everything is for sale and everything is an exchange.

—Shahram Ahari

You are absolutely buying love.

—James Reidy [1]

In 2000, pharmaceutical companies spent more than 15.7 billion dollars on promoting prescription drugs in the United States [2]. More than 4.8 billion dollars was spent on detailing, the one-on-one promotion of drugs to doctors by pharmaceutical sales representatives, commonly called drug reps. The average sales force expenditure for pharmaceutical companies is $875 million annually [3].

Unlike the door-to-door vendors of cosmetics and vacuum cleaners, drug reps do not sell their product directly to buyers. Consumers pay for prescription drugs, but physicians control access. Drug reps increase drug sales by influencing physicians, and they do so with finely titrated doses of friendship. This article, which grew out of conversations between a former drug rep (SA) and a physician who researches pharmaceutical marketing (AFB), reveals the strategies used by reps to manipulate physician prescribing.

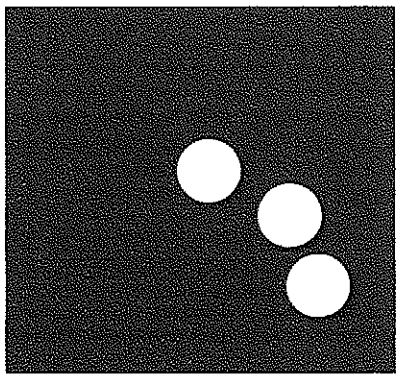
Better Than You Know Yourself

During training, I was told, when you're out to dinner with a doctor, "The physician is eating with a friend. You are eating with a client."

—Shahram Ahari

Reps may be genuinely friendly, but they are not genuine friends. Drug reps are selected for their presentability and outgoing natures, and are trained to be observant, personable, and helpful. They are also trained to assess physicians' personalities, practice styles, and preferences, and to relay this information back to the company. Personal information may be more important than prescribing preferences. Reps ask for and remember details about a physician's family life, professional interests, and recreational pursuits. A photo on a desk presents an opportunity to inquire about family members and memorize whatever tidbits are offered (including names, birthdays, and interests); these are usually typed into a database after the encounter. Reps scour a doctor's office for objects—a tennis racquet, Russian novels, seventies rock music, fashion magazines, travel mementos, or cultural or religious symbols—that can be used to establish a personal connection with the doctor.

Good details are dynamic; the best reps tailor their messages constantly according to their client's reaction. A friendly physician makes the rep's job easy, because the rep can use the "friendship" to request favors, in the form of prescriptions. Physicians who view the relationship as a straightforward goods-for-prescriptions exchange are dealt with in a businesslike manner. Skeptical doctors who favor evidence over charm are approached respectfully, supplied with reprints from the medical literature, and wooed as teachers. Physicians who refuse to see reps are detailed by proxy; their staff is dined and flattered in hopes that they will act as emissaries for a rep's messages. (See Table 1 for specific tactics used to manipulate physicians.)



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(Photo: "Bitter Pills?" by net_efekt, at http://www.flickr.com/photos/wheatfields/316337784/. Published under the Creative Commons Attribution License.)

Gifts create both expectation and obligation. "The importance of developing loyalty through gifting cannot be overstated," writes Michael Oldani, an anthropologist and former drug rep [26]. Pharmaceutical gifting, however, involves carefully calibrated generosity. Many prescribers receive pens, notepads, and coffee mugs, all

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Competing Interests: Shahram Ahari is a former pharmaceutical sales representative for Eli Lilly, and the primary findings of this paper summarize points he made in testimony as a paid expert witness on the defendant's side in litigation against a New Hampshire law prohibiting the sale of prescription data. Adriane Fugh-Berman has accepted payment as an expert witness on the plaintiff's side in litigation regarding menopausal hormone therapy.

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Abbreviations: AMA, American Medical Association

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Table 1. Tactics for Manipulating Physicians

Physician Category	Technique	How It Sells Drugs	Comments
Friendly and outgoing	I frame everything as a gesture of friendship. I give them free samples not because it's my job, but because I like them so much. I provide office lunches because visiting them is such a pleasant relief from all the other docs. My drugs rarely get mentioned by me during our dinners.	Just being friends with most of my docs seemed to have some natural basic effect on their prescribing habits. When the time is ripe, I lean on my "friendship" to leverage more patients to my drugs...say, because it'll help me meet quota or it will impress my manager, or it's crucial for my career.	Outgoing, friendly physicians are every rep's favorite because cultivating friendship is a mutual aim. While this may be genuine behavior on the doctor's side, it is usually calculated on the part of the rep.
Aloof and skeptical	I visit the office with journal articles that specifically counter the doctor's perceptions of the shortcoming of my drug. Armed with the articles and having hopefully scheduled a 20 minute appointment (so the doc can't escape), I play dumb and have the doc explain to me the significance of my article.	The only thing that remains is for me to be just aggressive enough to ask the doc to try my drug in situations that wouldn't have been considered before, based on the physician's own explanation.	Humility is a common approach to physicians who pride themselves on practicing evidence-based medicine. These docs are tough to persuade but not impossible. Typically, attempts at geniality are only marginally effective.
Mercenary	The best mercenary docs are typically found further down the prescribing power scale. There are plenty of 6's, 7's, and 8's [lower prescribing doctors] who are eagerly mercenary but simply don't have the attention they desire fawned on them. I pick a handful out and make them feel special enough with an eye towards the projected demand on my limited resources in mind. Basically, the common motif to docs whom you want to "buy out" is to closely associate your resource expenditure with an expectation—e.g., "So, doc, you'll choose Drug X for the next 5 patients who are depressed and with low energy? Oh, and don't forget dinner at Nobu next month. I'd love to meet your wife."	This is the closest drug-repping comes to a commercial exchange. Delivering such closely associated messages crudely would be deemed insulting for most docs so a rep really has to feel comfortable about their mercenary nature and have a natural tone when making such suggestions.	Drug reps usually feel more camaraderie with competing reps than they do with their clients. Thus, when a doctor fails to fulfill their end of the prescriptions-for-dinners bargain, news gets around and other reps are less likely to invest resources in them.
High-prescribers	I rely on making a strong personal connection to those docs, something to make me stand out from the crowd.	Friendship sells. The highest prescribers (9's and 10's) are every reps sugar mommies and daddies. It's the equivalent of spitting in the ocean to try to buy these docs out because, chances are, every other rep is falling head over heels to do so.	The highest prescribers receive better presents. Some reps said their 10's might receive unrestricted "educational" grants so loosely restricted that they were the equivalent of a cash gift, although I did not personally provide any grants.
Prefers a competing drug	The first thing I want to understand is why they're using another drug as opposed to mine. If it's a question of attention, then I commit myself to lavishing them with it until they're bought. If they are convinced that the competitor drug works better in some patient populations, I frame my drug to either capture another market niche or, if I feel my drug would fare well in a comparison, I hammer its superiority over the competing drug.	If, during the course of conversations, the doctors say something that may contradict their limited usage of our products, then the reps will badger them to justify that contradiction. This quickly transforms the rep from a welcomed reprieve to a nuisance, which can be useful in limited circumstances. We force the doctors to constantly explain their prescribing rationale, which is tiresome. Our intent is to engage in discourse but also to wear down the doc until he or she simply agrees to try the product for specific instances (we almost always argue for a specific patient profile for our drugs).	For reps this is a core function of our job. We're trained to do this in as benign a way as possible. No doc likes to be told their judgment is wrong so the latter method typically requires some discretion.
Acquiescent docs	Most docs think that if they simply agree with what the rep says, they'll outsmart the rep by avoiding any conflict or commitment, getting the samples and gifts they want, and finishing the encounter quickly. Nothing could be further from the truth. The old adage is true, especially in pharmaceutical sales: there is no such thing as a free lunch.	From the outset of my training, I've been taught to frame every conversation to ultimately derive commitments from my clients. With every acquiescent nod to statements of my drug's superiority I build the case for them to increase their usage of my product. They may offer me false promises but I'll know when they're lying: the prescribing data is sufficiently detailed in my computer to confirm their behavior. Doctors who fail to honor their commitments, no matter how casually made, convert the rep into a badgering nuisance. The docs are often corralled into a conversational corner where they have to justify their previous acquiescence.	Gifts are used to enhance guilt and social pressure. Reps know that gifts create a subconscious obligation to reciprocate. New reps who doubt this phenomenon need only see their doctors' prescribing data trending upwards to be convinced. Of course, most of these doctors think themselves immune to such influence. This is an illusion reps try to maintain.

Table 1. Continued

Physician Category	Technique	How It Sells Drugs	Comments
No-see/ No-time (hard-to-see docs)	Occasionally docs refuse to see reps. Some do it for ethical reasons, but most simply lack the time. Even when I don't manage to see the doctor, I can still make a successful call by detailing the staff. Although they're on the doc's side for the most part, it's amazing how much trouble one can rile up when the staff are lavished with food and gifts during a credible sounding presentation and then asked to discuss the usage of a drug on their patients.	It's a victory for me just to learn from the staff about which drugs are preferred, and why. That info provides powerful ammunition to debate the docs with on the rare occasions that I might see them. However, it's a greater success when the staff discusses my meds with the doc after I leave. Because while a message delivered by a rep gets discounted, a detail delivered by a co-worker slips undetected and unfiltered under the guise of a conversation. And the response is usually better then what I might accomplish.	One's marketing success in a particular office can be strongly correlated to one's success in providing good food for the staff. Goodwill from the staff provides me with critical information, access, and an advocate for me and my drug when I'm not there.
Thought leaders	As a rep, I was always in pursuit of friendly "thought leaders" to groom for the speaking circuit. Once selected, a physician would give lectures around the district. I would carefully watch for tell-tale signs of their allegiance. This includes how they handled questions that criticized our product, how their prescribing habits fluctuated, or simply how eager they were to give their next lecture.	The main target of these gatherings is the speaker, whose appreciation may be reflected in increased prescribing of a company's products. Local speaking gigs are also auditions. Speakers with charisma, credentials, and an aura of integrity were elevated to the national circuit and, occasionally, given satellite telecast programs that offered CMEs.	Subtle and tactful spokespersons were the ideal candidates. I politely dismissed doctors who would play cheerleader for any drug...at the right price, of course.

These descriptions are based on SA's experience working for Eli Lilly and testimony in IMS Heath Inc. v. Ayotte, US District Court, New Hampshire. Actual tactics may vary.
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items kept close at hand, ensuring that a targeted drug's name stays uppermost in a physician's subconscious mind. High prescribers receive higher-end presents, for example, silk ties or golf bags. As Oldani states, "The essence of pharmaceutical gifting...is 'bribes that aren't considered bribes'" [1].

Reps also recruit and audition "thought leaders" (physicians respected by their peers) to groom for the speaking circuit. Physicians invited and paid by a rep to speak to their peers may express their gratitude in increased prescriptions (see Table 1). Anything that improves the relationship between the rep and the client usually leads to improved market share.

Script Tracking

An official job description for a pharmaceutical sales rep would read: Provide health-care professionals with product information, answer their questions on the use of products, and deliver product samples. An unofficial, and more accurate, description would have been: Change the prescribing habits of physicians.

—James Reidy [4]

Pharmaceutical companies monitor the return on investment of detailing—and all promotional efforts—by prescription tracking. Information distribution companies, also called health information organizations (including IMS Health, Dendrite, Verispan, and Wolters Kluwer), purchase prescription records from pharmacies. The majority of pharmacies sell these records; IMS Health, the largest information distribution company, procures records on about 70% of prescriptions filled in community pharmacies. Patient names are not included, and physicians may be identified only by state license number, Drug Enforcement Administration number, or a pharmacy-specific identifier [5]. Data that identify physicians only by numbers are linked to physician names through licensing agreements with the American Medical Association (AMA), which maintains the Physician Masterfile, a database containing demographic information on all US. physicians (living or dead, member or non-member, licensed or non-licensed). In 2005, database product sales, including an unknown amount from licensing Masterfile information, provided more than $44 million to the AMA [5].

Pharmaceutical companies are the primary customers for prescribing data, which are used both to identify "high-prescribers" and to track the effects of promotion. Physicians are ranked on a scale from one to ten based on how many prescriptions they write. Reps lavish high-prescribers with attention, gifts, and unrestricted "educational" grants (Table 1). Cardiologists and other specialists write relatively few prescriptions, but are targeted because specialist prescriptions are perpetuated for years by primary care physicians, thus affecting market share.

Reps use prescribing data to see how many of a physician's patients receive specific drugs, how many prescriptions the physician writes for targeted and competing drugs, and how a physician's prescribing habits change over time. One training guide states that an "individual market share report for each physician...pinpoints a prescriber's current habits" and is "used to identify which products are currently in favor with the physician

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in order to develop a strategy to change those prescriptions into Merck prescriptions" [6].

A *Pharmaceutical Executive* article states, "A physician's prescribing value is a function of the opportunity to prescribe, plus his or her attitude toward prescribing, along with outside influences. By building these multiple dimensions into physicians' profiles, it is possible to understand the 'why' behind the 'what' and 'how' of their behavior." [7] To this end, some companies combine data sources. For example, Medical Marketing Service "enhances the AMA Masterfile with non-AMA data from a variety of sources to not only include demographic selections, but also behavioral and psychographic selections that help you to better target your perfect prospects" [8].

The goal of this demographic slicing and dicing is to identify physicians who are most susceptible to marketing efforts. One industry article suggests categorizing physicians as "hidden gems": "Initially considered 'low value' because they are low prescribers, these physicians can change their prescribing habits after targeted, effective marketing." "Growers" are "Physicians who are early adopters of a brand. Pharmaceutical companies employ retention strategies to continue to reinforce their growth behavior." Physicians are considered "low value" "due to low category share and prescribing level" [9].

In an interview with *Pharmaceutical Representative*, Fred Marshall, president of Quantum Learning, explained, "... One type might be called 'the spreader' who uses a little bit of everybody's product. The second type might be a 'loyalist', who's very loyal to one particular product and uses it for most patient types. Another physician might be a 'niche' physician, who reserves our product only for a very narrowly defined patient type. And the idea in physician segmentation would be to have a different messaging strategy for each of those physician segments " [10].

In *Pharmaceutical Executive*, Ron Brand of IMS Consulting writes "...integrated segmentation analyzes individual prescribing behaviors, demographics, and psychographics (attitudes, beliefs, and values) to fine-tune sales targets. For a particular product, for example, one segment might consist of price-sensitive

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physicians, another might include doctors loyal to a given manufacturers brand, and a third may include those unfriendly towards reps" [11].

In recent years, physicians have become aware of—and dismayed by—script tracking. In July 2006, the AMA launched the Prescribing Data Restriction Program (see http://www.ama-assn.org/ama/pub/category/12054.html), which allows physicians the opportunity to withhold most prescribing information from reps and their supervisors (anyone above that level, however, has full access to all data). According to an article in *Pharmaceutical Executive*, "Reps and direct managers can view the physician's prescribing volume quantiled at the therapeutic class level" and can still view aggregated or segmented data including "categories into which the prescriber falls, such as an early-adopter of drugs, for example...." [12]. The pharmaceutical industry supports the Prescribing Data Restriction Program, which is seen as a less onerous alternative to, for example, state legislation passed in New Hampshire forbidding the sale of prescription data to commercial entities [13].

The Value of Samples

The purpose of supplying drug samples is to gain entry into doctors' offices, and to habituate physicians to prescribing targeted drugs. Physicians appreciate samples, which can be used to start therapy immediately, test tolerance to a new drug, or reduce the total cost of a prescription. Even physicians who refuse to see drug reps usually want samples (these docs are denigrated as "sample-grabbers"). Patients like samples too; it's nice to get a little present from the doctor. Samples also double as unacknowledged gifts to physicians and their staff. The convenience of an in-house pharmacy increases loyalty to both the reps and the drugs they represent.

Some physicians use samples to provide drugs to indigent patients [14,15]. Using samples for an entire course of treatment is anathema to pharmaceutical companies because this "cannibalizes" sales. Among the aims of one industry sample-tracking program are to "reallocate samples to high-opportunity prescribers most receptive to sampling as a promotional vehicle" and "identify prescribers who were oversampled and take corrective action immediately" [16].

Studies consistently show that samples influence prescribing choices [14,15,17]. Reps provide samples only of the most promoted, usually most expensive, drugs, and patients given a sample for part of a course of treatment almost always receive a prescription for the same drug.

Funding Friendship

While it's the doctors' job to treat patients and not to justify their actions, it's my job to constantly sway the doctors. It's a job I'm paid and trained to do. Doctors are neither trained nor paid to negotiate. Most of the time they don't even realize that's what they're doing...

—Shahram Ahari

Drug costs now account for 10.7% of health-care expenditures in the US [18]. In 2004, spending for prescription drugs was $188.5 billion, almost five times as much as what was spent in 1990 [19]. Between 1995 and 2005, the number of drug reps in the US increased from 38,000 to 100,000 [20], about one for every six physicians. The actual ratio is close to one drug rep per 2.5 targeted doctors [21], because not all physicians practice, and not all practicing physicians are detailed. Low-prescribers are ignored by drug reps.

Physicians view drug information provided by reps as a convenient, if not entirely reliable, educational service. An industry survey found that more than half of "high-prescribing" doctors cited drug reps as their main source of information about new drugs [22]. In another study, three quarters of 2,608 practicing physicians found information provided by reps "very useful" (15%) or "somewhat useful" (59%) [23]. However, only 9% agreed that the information was "very accurate"; 72% thought the information was "somewhat accurate"; and 14% said that it was "not very" or "not at all" accurate.

Whether or not physicians believe in the accuracy of information provided, detailing is extremely effective at changing prescribing behavior, which is why it is worth its substantial expense. The average annual income for a drug rep is $81,700, which includes $62,400 in base salary plus $19,300 in bonuses. The average cost of recruiting, hiring, and training a new rep is estimated to be $89,000 [24]. When expenses are added to income and training, pharmaceutical companies spend $150,000 annually per primary care sales representative and $330,000 per specialty sales representative [25]. An industry article states, "The pharmaceutical industry averages $31.9 million in annual sales spending per primary-care drug...Sales spending for specialty drugs that treat a narrowed population segment average $25.3 million per product across the industry." [25]

Conclusion

As one of us (SA) explained in testimony in the litigation over New Hampshire's new ban on the commercial sale of prescription data, the concept that reps provide necessary services to physicians and patients is a fiction. Pharmaceutical companies spend billions of dollars annually to ensure that physicians most susceptible to marketing prescribe the most expensive, most promoted drugs to the most people possible. The foundation of this influence is a sales force of 100,000 drug reps that provides rationed doses of samples, gifts, services, and flattery to a subset of physicians. If detailing were an educational service, it would be provided to all physicians, not just those who affect market share.

Physicians are susceptible to corporate influence because they are overworked, overwhelmed with information and paperwork, and feel underappreciated. Cheerful and charming, bearing food and gifts, drug reps provide respite and sympathy; they appreciate how hard doctor's lives are, and seem only to want to ease their burdens. But, as SA's New Hampshire testimony reflects, every word, every courtesy, every gift, and every piece of information provided is carefully crafted, not to assist doctors or patients, but to increase market share for targeted drugs (see Table 1). In the interests of patients, physicians must reject the false friendship provided by reps. Physicians must rely on information on drugs from unconflicted sources, and seek friends among those who are not paid to be friends. ■

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Note Added in Proof

Reference 26 is cited out of order in the article because it was added while the article was in proof.

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