

Physicians and the Pharmaceutical Industry

Is a Gift Ever Just a Gift?

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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 study⁹ 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 Sub-

See also p 391.

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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ject 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 Marketing¹³ 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 quantita-

tive 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.

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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 Tallman, 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 studies¹⁴⁻⁴² 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 1¹⁷ 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 school²⁶ 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 al³⁰ 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 meals³⁹ and samples³⁹ decreases as they enter practice, while frequency of receiving honoraria,³⁹ conference travel,²⁵ and research funding²⁵ 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 controver-

sial. As many as 85% of programs had policies on interactions.^{21,23,33,35-37}

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 drugs²⁵ 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' welfare²⁵ 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 conference³⁷ and lunch rounds²⁷ 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 postinter-

action methods to assess the impact of particular interactions.

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 physicians³⁹ 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 gift²⁰ and the number of gifts received²⁶ correlated with the belief that pharmaceutical representatives have no

†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.

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

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 ³⁶	
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 ²⁹	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 drug³⁹ 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 examined¹² 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 of their drug		20% ²⁹ to 35% ²⁵ 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 (<i>P</i> = .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 ²⁴	LS, 3.4 (<i>P</i> = .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 (<i>P</i> < .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 iden-

tify 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 findings⁴³⁻⁴⁷ 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 ($\beta = .638$; $P = .02$) (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 ($r = 0.24$; $P < .04$) ²⁶ 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) ¹⁶
	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 theories⁴⁸ (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 non-generic 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 drug¹⁴; an increase in hospital prescribing rate of the conference travel sponsor's drug¹⁶; increased nonrational prescribing choice of the sponsor's drug after related resident teaching given by physician pharmaceutical representatives¹⁵; 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 Landefeld¹⁷ 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 programs,³⁷ 61% of US emergency medicine programs,³³ and 25% of Canadian

family medicine programs²¹) and fewer distribute these guidelines²¹ 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 percent³⁷ 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 subsidy⁴⁹; interaction with pharmaceutical representative (PR)⁵⁰⁻⁵²; research funding⁴³⁻⁴⁷; 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 program⁶² 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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