

DOCTORS AND DRUG COMPANIES: ETHICS AND EVIDENCE

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The Phenomenon

Prescription drug sales are growing at a rate of nearly 20% per year, accounting for a growing part of money spent on health care (as the proportion of spending on physician services falls). One half of the growth in prescription drug sales is due to increasing use of existing drugs, one quarter is due to increases in prices of existing drugs, and one quarter is due to new drugs.

Drug companies spend more than \$10 billion per year on marketing in the US – more than is spent on research and development or production. The sales force of pharmaceutical sales representatives has increased >50% since 1994, from 35,000 to 56,000 in 2001. Tales of lavish spending on physicians remain common, and several drug companies have been convicted of illegal marketing activities.

Ethical Considerations in Physicians' Relationships to Drug Companies

Three considerations relate to physicians' relationships to drug companies. The principle of distributive justice holds that benefits should accrue to those who bear the associated burden, suggesting that physicians should not benefit personally from patients' payments for drugs. The doctor-patient relationship is based on the principle of fiduciary trust, or benevolence, according to which the physician should act in the patient's best interest. To the degree that an external influence changes the physician's action in a way that is not based on the patient's interest, the influence and action violate this principle. Finally, an individual's character may be shaped by the individual's actions, and this change may be unseen and difficult to reverse, especially when the action involves balancing self-interest and altruism.

Evidence that Relationships with Drug Companies Affect Physician Behavior

Several lines of evidence are consistent with the hypothesis that relationships with drug companies affect physician behaviors.

First, it has been suggested that it is unlikely that drug companies would spend large sums of money on marketing to physicians if this marketing did not increase the sale of the marketed product.

Second, physicians' beliefs about particular drugs are often consistent with marketed messages but not with scientific evidence in the peer-reviewed literature.

Third, the prescription of particular classes of drugs (e.g., antihypertensives and perhaps antidepressants) are consistent with marketing but not with either evidence or guidelines.

Fourth, in studies of the content of CME lectures sponsored by a particular drug company, the company's drug has received a higher proportion of mentions and doctors attending the lecture have reported increased prescribing of that drug.

Fifth, in material presented by pharmaceutical sales representatives, 90% of material is accurate and biased towards the manufacturer's product. 10% of material is false. Few physicians can distinguish the true statements from the false ones.

Sixth, accepting money from a drug company to lecture, attend a meeting, or support research has been strongly associated with submitting a request to add a drug made by that company to the hospital formulary.

Seventh, there are noteworthy cases consistent with the hypothesis that professional organizations are influenced by companies upon which their revenues depend. Examples include the resignation of the editors of the *Annals of Internal Medicine* and the American Academy of Pediatrics actions in relation to a federal program promoting breast feeding.

Summary

Drug companies spend large amounts of money to influence physician prescribing. Substantial evidence indicates that marketing information presented by drug companies is biased and sometimes inaccurate, that bias and inaccuracies are not detected by physicians, and that relationships with drug companies influence physician behaviors, including information presented, prescribing, and submission to requests to formularies. The principle of benevolence, a basic tenet of medicine, holds that actions should be based on the patient's best interests, and that actions influenced by things external to the patient's interests are ethically questionable.

References

1. Chren MM, Landefeld CS, Murray TH. Doctors, drug companies, and gifts. *JAMA* 1989; 262:3448-3451.
2. Chren MM, Landefeld CS. Physicians' behavior and their interactions with drug companies; A controlled study of physicians who requested additions to a hospital drug formulary. *JAMA* 1994; 271:684-689.
3. Dana J, Lowenstein G. A social science perspective on gifts to physicians from industry. *JAMA* 2003; 290:252-255.
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5. The truth is out there. *Lancet Neurology* 2003;2:261.

Doctors and Drug Companies: Ethics and Evidence

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Objective

To develop conceptual and empirical frameworks that can inform our thinking about 2 questions:

- How should we, as physicians, relate to drug companies?
- What policies should we and our organizations adopt?

The Issue Is Not Just “Them”

- The issue is us.
- Dr. Harold Elliott: “Doctors fear drug companies the way bookies fear the mob.”
(American Prospect 9/24/2001)
- Hopkins Dean David Blake: “No conflict, no interest.” (Baltimore Sun 6/25/2001)

Topics

- An ethical framework for our relationships with drug companies and other organizations that offer us gifts
- Data:
 - Do these relationships affect our prescribing?
 - Do they affect our teaching and science?

The Party

- “It was doctors' night out last June at the world-renowned Museum of Modern Art in New York City, and the Saturday night party, put on by Pfizer Inc., was lavish.”

ABC News, 2/22/2002

Cash

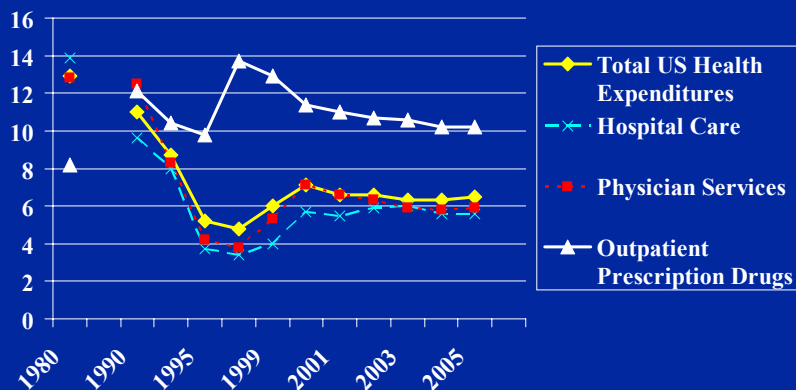
- Dr. Rudy Mueller: "It's very tempting and they just keep anteing it up. And it's getting harder to say no."
- A cash payment of \$2,000 for putting four patients on the latest drug for high cholesterol: Is it a “Clinical study” or “Bounty”?

ABC News, 2/22/2002

Drug Companies Spend >\$10 Billion/Yr on Drug Promotion in the U.S.

- More than is spent on R&D;
- More than is spent on the raw materials;
- More than is spent on medical school and residency training combined;
- ~\$10,000 for every practicing physician;
- Supports a growing sales force: 56,000 in 2001, up from 35,000 in 1994.

Annual Percent Increase in US Health Expenditures



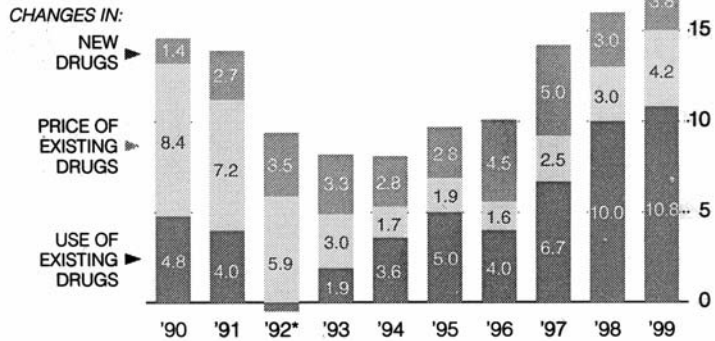
<http://www.hcfa.gov/stats/NHE-Proj/proj1998/tables/table2.htm>

BY THE NUMBERS

Explaining Increases in Drug Sales

In recent years, the growth in drug companies' sales has been driven more by increased use of drugs already on the market than higher prices for those drugs, a change from the trend earlier in the decade.

Percentage change in dollar volume of prescription drug sales from the previous year



Source: IMS Health

The New York Times

Money is Made by Mark-ups

<u>Drug</u>	<u>Company</u>	<u>Mark-up for Seniors*</u>
Synthroid	Knoll	1446%
Micronase	Pharmacia/Upjohn	363%
Zocor	Merck	144%
Prilosec	Astra/Merck	99%

*Compared to most favored customers. Committee on Government Reform, US House of Representatives, 10/20/98.

An Ethical Framework

1. Justice
2. The Doctor-Patient Relationship
3. Our Character

MM Chren et al. *JAMA* 1989;262:3448-51.

Distributive Justice

- Distribution of burdens and benefits should be fair – the one who bears a particular burden should gain the associated benefit.
- When we accept gifts from drug companies:
 - Patients or the public pay
 - We benefit
 - Drug companies believe they benefit
 - Do patients benefit?

The Doctor-Patient Relationship

- A “special relationship”
- We should act in each patient’s best interests:
Our role and duty is that of a fiduciary
- Does accepting a gift from a drug company affect my behavior independent of my patient’s interests?

Our Character

- We live in a profound moral paradox, balancing altruism and self-interest.
- The balance is precarious: gifts feed our human tendencies to self-interest, often in ways unseen by our patients.
- Is my character affected by accepting a gift?
Will I develop bad habits?

In the case of our habits, we are only the
masters of the beginning, ...
their growth by gradual stages being
imperceptible, like the growth of disease.

Aristotle, Ethics

How Should We Implement These Principles?

Does Accepting a Gift Affect Me?

Webster's Definition

“Something voluntarily transferred from one person to another without compensation.”

Webster's Collegiate Dictionary

Gifts Have Meaning

- Gifts are used to initiate and maintain relationships: the gift relationship.
- Gifts entail obligations beyond compensation:
 - grateful conduct
 - grateful use
 - reciprocation
- Gifts are rarely spontaneous and often not voluntary.
- Gifts can be dangerous.

Do Drug Companies Affect Our Prescribing?

You ... Not Me

- Most medical residents thought that accepting gifts from pharmaceutical sales representatives affected other physicians' prescribing.
- Few thought they themselves were affected.

MA Steinman et al. Am J Med 2001; 110: 551-57.

DrKoop.com

- Koop to Congress: pass legislation that would extend Schering-Plough's Claritin patent
- Schering-Plough to Koop Foundation: \$1 million earlier in the year

NY Times, 9/5/99, page 1,18.

DrKoop.com

- Koop: “I never disclosed the grant because I did not think it was an issue.... There was no quid pro quo.... There are people in my situation who could not receive a million-dollar grant and stay objective. But I do.”

NY Times, 9/5/99, page 1,18.

What Is the Relative Influence of Commercial and Scientific Sources on Prescribing?

- Random sample of 100 Boston physicians
- Factors that influence their prescribing
- Beliefs about cerebral vasodilators and propoxyphene

J Avorn et al. Am J Med 1982;73:4-8.

Factors Rated as “Very Important” by
Physicians in Influencing Their Prescribing

Patient preference	2 %
Drug ads	4 %
Detail men	20 %
Advice from colleagues	48 %
Scientific papers	62 %
Own training and experience	88 %

J Avorn et al. Am J Med 1982;73:4-8.

Many Physicians Had Mistaken Beliefs
Consistent with Commercial Sources

	<u>Physicians</u>
Impaired cerebral blood flow is a major cause of senile dementia	71 %
Cerebral vasodilators are useful in managing confused geriatric patients	32 %
Darvon is more effective than aspirin as an analgesic	49 %

J Avorn et al. Am J Med 1982;73:4-8.

Has Anything Changed?

Little Has Changed

Mail survey of 1,200 U.S. primary care physicians

Respondents incorrectly believed that:

- Thiazide diuretics were less likely to achieve normal BP than Ca-blockers, ACE-inhibitors, or beta blockers.
- Beta blockers are stopped twice as often as other drugs.
- Ca-blockers and ACE-inhibitors had been shown to reduce the risk of stroke in hypertensive patients.

Ubel and Adler. JGIM 1999;14(S2):125.

Did the JNCV Recommendations Affect Prescribing?

- “Because diuretics and β -blockers have been shown to reduce cardiovascular morbidity and mortality in controlled clinical trials, these two classes of drugs are preferred for initial drug therapy.”

Siegel and Lopez. JAMA 1997; 278:1745-48.

Drug Class	1992, No. (%)	1995, No. (%)
Calcium antagonist	57 324 (33)	66 819 (38)
ACE inhibitor	43 061 (25)	57 161 (33)
β -Blocker	31 752 (18)	19 564 (11)
Diuretic	27 396 (16)	13 417 (8)
α -Blocker	5 480 (3)	11 713 (7)
Central sympatholytic	3 888 (2)	3 110 (2)

*Percentages are from the total antihypertensive prescriptions in the sample and do not add to 100% because miscellaneous combination products were not included. ACE indicates angiotensin-converting enzyme.

- These data are consistent with the hypothesis that prescribing is influenced by commercial sources of information, perhaps more than by scientific sources.

Do Specific Relationships with Drug Companies Affect Physician Behavior?

- Case-control study of 40 MDs who had requested that a drug be added to the formulary and 80 MDs who had not
- Relationships:
 - meeting with pharmaceutical representatives
 - accepting money to attend or speak at symposia or to perform research

Chren & Landefeld. JAMA 1994;271:684-9.

Physicians Who Requested that Drugs be
Added to the Formulary Interacted with Drug
Companies More Often than Other Physicians

Odds Ratio (95% CI)

Accepted money from a drug company	5.1 (2.0-13.2)
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Chren & Landefeld. JAMA 1994;271:684-9.

... and Interacted with the Specific Manufacturer
More Often than Did Other Physicians

Odds Ratio (95% CI)

Met with a pharmaceutical representative from the company making the drug requested	13.2 (4.8-36.3)
Accepted money from the company making the drug requested	19.2 (2.3-156.9)

Chren & Landefeld. JAMA 1994;271:684-9.

What Are the Effects of Our Relationships to Drug Companies on Our Teaching?

- 2 CME courses on 3 calcium antagonists, each course sponsored by a different company
- Company drug was mentioned more often – (60% of mentions vs. 12% & 28%, respectively)
- Mentions of the company drug were more often favorable (50% vs. 35%)

M Bowman. *Mobius* 1986;6:66-69.

Drug-company Sponsored CME Affected Self-reported Prescribing

	<u>Before</u> <u>CME</u>	<u>After</u> <u>CME</u>
	prescriptions written	
Diltiazem	31%	50%
Nifedipine	43%	29%
Verapamil	26%	21%

J Cont Educ Health Prof 1988;8:13-20.

Can You Trust What You Hear?

- 106 statements about drugs in 13 presentations to MDs by pharmaceutical sales representatives

MG Ziegler et al. JAMA 1995;273:1296-8.

You Can't Believe Everything You Hear

	<u>#</u>	<u>Favorable</u>	<u>Neutral</u>	<u>Unfavorable</u>
Inaccurate about promoted drug	12	100%	0%	0%
Accurate about promoted drug	79	49%	32%	19%
Accurate about competitor drug	15	0%	40%	60%
Inaccurate about competitor drug	0	---	---	---

MG Ziegler et al. JAMA 1995;273:1296-8.

Most of Us Don't Sort the Wheat from the Chaff

- 74% of MDs attending the presentations did not recall a false statement

MG Ziegler et al. JAMA 1995;273:1296-8.

Can You Believe What You Read in the Ads?

- 109 full-page drug ads from the first 1990 issue of 10 leading medical journals
- Each ad was peer-reviewed by 2 MDs in the relevant clinical area and a clinical pharmacist, using FDA standards

MS Wilkes et al. Ann Intern Med 1992;116:912-919.

Reviewers Often Disagreed with the Ads

<u>Reviewers' judgement</u>	<u>Ads</u>
Incorrect ad claim that drug is the "drug of choice"	30%
Unbalanced presentation on efficacy and side effects	40%
Headlines misleading about efficacy	32%
Ad would lead to improper prescribing	44%

MS Wilkes et al. Ann Intern Med 1992;116:912-919.

What About Our Professional Organizations?

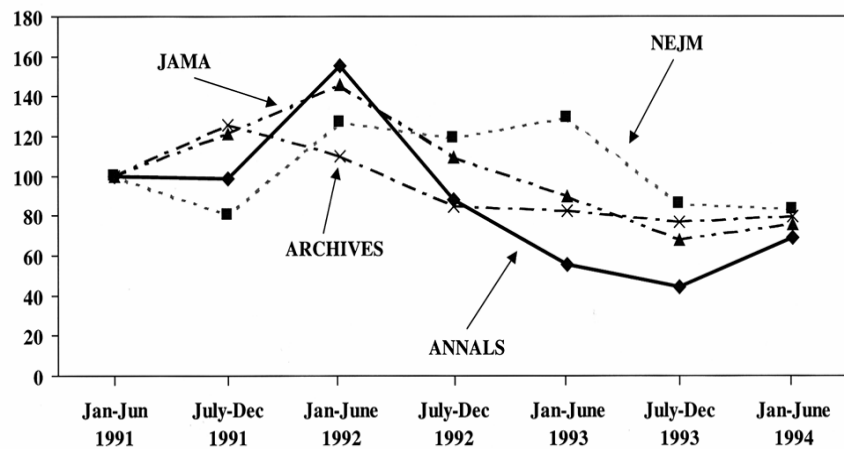
- Drug companies provide substantial parts of the budgets of many societies.
- Meetings make money.

“The American Psychiatric Association
Glaxo-Smith-Kline Convention”

- Exhibits
- \$50,000 sessions “to control which scientists and papers were presented and to help shape the presentations”
- What are the effects?

Washington Post, 5/25/2002

Figure 1



What Happened?

New York Times, 8/24/99:

- “Drug companies stopped advertising, costing the journal \$1 million to \$1.5 million”
- “... journals have increasingly become cash cows for the medical societies ..., with annual profits in the tens of millions of dollars, largely from drug company advertisements. [This] is changing how the journals do business....”

Conclusions

1. The legal drug business is big, getting bigger, sophisticated, and powerful.
2. Doctors' behaviors are sometimes influenced by relationships with drug companies, perhaps more than they know.
3. Information from drug companies is biased, and this bias is rarely detected by doctors.

Conclusions

4. An ethical framework for evaluating relationships with drug companies (and other health care ventures) might include:
 - justice
 - the doctor-patient relationship
 - effects on one's own character.