

ADVANCES IN DRUG DEVELOPMENT

Current Developments in Oncology Drug Research

Section Editor: Mark J. Ratain, MD

Ethics in Medicine: Avoiding Conflicts of Interest in Prescribing



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H&O What are some potential sources of conflict of interest that physicians may encounter in prescribing?

GVN The main conflict of interest is the one that occurs when a physician has a vested interest in a particular drug or device they are going to prescribe. That vested interest can mean that the physician owns the company, works for the company, is a researcher for the company, writes for the company, or serves as a speaker for the company. The conflict can be financial, with bias being either conscious or subconscious. The conflict can also be emotional; for example, physicians may have friends in the company whom they trust and wish to support.

Another source of conflict is being an academic physician who needs to demonstrate productivity by being published. Publication often requires doing research, which in turn may require obtaining grants from commercial entities. These entities naturally have an interest in seeing positive results published, and they may require a researcher to sign a contract allowing them to direct which results are submitted for publication. In one case dating back to 1990, the now-defunct pharmaceutical company Knoll suppressed a study for 6 years because it showed that its branded thyroid replacement medication was no more effective than several other, less-expensive agents.¹ Researchers need to read the contracts that they sign with pharmaceutical companies carefully; the companies are unlikely to attempt to block publication at this point, but they still may insist on reviewing the results and providing their own spin on them before publication.

H&O What special concerns exist regarding speakers' bureaus?

GVN Becoming a speaker for a speakers' bureau involves a financial relationship between someone who should be an independent researcher and a commercial entity. Companies will often recruit young academics for speakers' bureaus, who find these opportunities appealing because they can pay a sizable amount of money. Decades ago, when I was a young academic, I was offered \$2000 plus travel expenses simply to give a one-hour speech. One of the problems is that even if you are not directly promoting the company's product, you are lending credibility—through the name of your institution and your own credentials—to a targeted meeting that is meant to promote certain products.

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Another problem with speakers' bureaus is that they can be used to promote off-label uses of a drug. Companies are aware that they cannot advertise off-label uses for an approved drug, but the US Food and Drug Administration (FDA) does allow studies that were not used in the FDA approval process and have been published in a peer-reviewed journal to be presented

at academic meetings. Doing this is considered an exchange of information rather than drug promotion. What physicians may not realize is that as many as 70% to 75% of postmarketing studies are written by the drug company itself.^{2,3}

The ghost author, whose name does not appear on the published paper, is often a drug company employee or someone who is paid indirectly by the drug company via a medical communications agency. The guest author is an academic who agrees to have their name appear on the paper after the study has been conducted and the manuscript has been written. Guest authors can earn a considerable amount of money for this service, even if they had nothing to do with conducting the research or writing the results. In these cases, the people writing the articles are not the unbiased researchers you think they are, and the authors whose names appear are not the ethical academics you think they are.

Making use of ghost authors and guest authors is highly unethical, but studies show it happens in most commercially sponsored studies. Although many of these commercially sponsored studies are well conducted, research shows that the likelihood of publications showing positive rather than negative results is much greater when the studies are sponsored by a company than when they are not.

For example, dozens of articles about the anti-inflammatory agent rofecoxib were found to be ghost-authored,⁴ and at least one of these studies omitted the deaths of several study patients and underestimated the incidence of cardiovascular deaths.⁵ Rofecoxib was withdrawn from the market in 2004. Unfortunately, most cases of ghost and guest authoring go undetected.

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After a company has conducted a study, written the manuscript, recruited a guest author to put their name on it, and seen the piece appear in a peer-reviewed publication, it can hire speakers to present the findings at a conference. The company has essentially circumvented the FDA by creating a drug promotion that looks like an academic paper. The results may be presented at standard trade conferences as well as at company-sponsored conferences.

H&O How much of an effect do corporate perks have on prescribing patterns?

GVN As a group, physicians are easy to influence. Give them a free trip or a free lunch, and prescription rates go up—often for a considerable period. In one study, physicians were sent to a conference at which a specific drug was mentioned.⁶ When researchers tracked the prescribing behavior of these doctors before and after the conference, they found a significant increase in the prescribing rate for that drug, even 2 years later. The influence was not only strong but also enduring. I once had to query a fellow at my institution who had substituted a \$1400 drug for the \$200 drug we had been using just because a drug company representative had come by a few days earlier with pizza and a presentation. Because of cases like this, the Department of Anesthesiology here at the University of Washington no longer allows drug representatives on campus.

The influence that promotions have on a prescriber is not limited to a single patient or a single prescription. Selling a prescriber on a particular drug that offers minimal benefit in comparison with the standard but costs 10 times as much means that the prescriber may be writing prescriptions for the expensive agent for hundreds of patients who may be filling that prescription a dozen times a year. So, a single free lunch can turn into hundreds of prescriptions for life.

H&O What is your advice regarding Continuing Medical Education (CME) credits?

GVN I always advise physicians to obtain their CME credits from noncommercial sources, such as an academic institution. CME activities from professional societies are more credible than those directly sponsored by pharmaceutical companies, but they still are not free from commercial influence because the societies depend so much on support from industry. It bothers me that wealthy professional societies do not just fund their own meetings or charge tuition. Nobody likes to write a \$500 or \$1000 check to attend a meeting, but as a doctor, I can afford it better than many. So, I try to stick with educational opportunities that have little or no commercial involvement. But I do not harbor any illusions that I have not been exposed to some influence.

The more professional societies and universities support the approach of not allowing commercial sponsorship of education, the better off we are. One way that physicians can help reduce conflicts of interest is by participating on committees that shape the policies of their institutions, suggesting rules against certain types of sponsorship and against ghost or guest authorship. In

addition, sanctions are needed when these rules are broken to put some teeth into them.

H&O What other sources of conflicts of interest should physicians be aware of?

GVN Physicians are aware that direct kickbacks from drug companies are illegal, but subtler forms of kickbacks are emerging. One example is a company sending a nurse ambassador to your office to educate patients about the drugs or devices you prescribe. That setup can make a lot of sense in certain cases, such as when glucose monitors first came out and manufacturers sent nurses to educate patients and staff on their proper use. The idea is that the nurses eventually leave, and the clinic staff takes over. However, some companies send nurse ambassadors permanently or semi-permanently, having them function as office staff and perform tasks such as insurance approvals. This is a form of influence because the clinics come to rely on that extra staffing. Studies show that this practice saves clinics substantial costs, which can create a sense of obligation to the commercial entity.

Another subtle form of influence is patient-assistance programs, which are tax-deductible initiatives that make it possible for underserved patients to access expensive drugs

at minimal cost. They are essentially coupon programs that allow a drug company to receive tax deductions for its most expensive drugs. Because the availability of these coupons increases the number of prescriptions overall, the drug companies get plenty of full-pay patients as well. I generally avoid these types of programs unless I can be convinced that the expensive new drug truly offers a clinically significant advantage over a well-studied generic agent.

Disclosures

Dr Van Norman has no relationships to disclose.

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