American Journal of Gastroenterology

Published by Blackwell Publishing

ISSN 0002-9270
doi: 10.1111/j.1572-0241.2008.01843.x

ETHICS IN GASTROENTEROLOGY

Conflicts of Interest in Clinical Practice and Research

Larry D. Scott, M.D., M.A.
Professor of Medicine, Division of Gastroenterology and Hepatology, The University of Texas Medical Branch, Galveston, Texas

(Am J Gastroenterol 2008;103:1075–1078)

CASE REPORT

A new device for endoscopic management of gastroesophageal reflux disease has recently been approved by the U.S. Food and Drug Administration (FDA); it employs a novel suturing system that allows the creation of a dead space in the gastric cardia that, at least in the animal model of reflux, in which it was tested, appeared to reduce the likelihood of reflux by 50%. Because it was similar to devices already on the market, it was approved by the FDA under a 510K exemption and did not undergo clinical trials. After meeting with the company president and physician consultant, you find the device interesting and promising; it would seem to offer a greater chance for a durable benefit in patients with medication-dependent reflux who wanted an alternative to long-term use of antisecretory agents than the currently available endoscopic treatments, with which you have had some experience, albeit with uneven success. The company is offering a week-long training course in an animal lab at their expense, and, in addition, an opportunity to purchase a 1% equity interest in the company. Once the device is in use in your practice, the company is offering $1,000 per patient in whom the device is used in order to gather postmarketing experience. What should be your response?

COMMENT

A number of questions can be generated in contemplating this situation. Perhaps first and foremost is the appropriateness of using new technology in patients in whom there has been only limited experience thus far, a circumstance created in part by loopholes in the federal device regulations. But even if this was a tried and true intervention, what problems would these financial arrangements create, if any? Could the possibility of financial reward or perhaps just the lure of having an early experience with a novel technology bias decision making in an individual patient for whom this device might be beneficial? This, in essence, is what conflict of interest is all about—a circumstance in which the prospect of personal gain influences medical decisions that, in turn, conflict with the best interest of the patient. Such gains are often financial, but may be nonfinancial as well, such as personal esteem. Most conflicts of interest probably never materialize, but the appearance alone is often enough to undermine trust in a specific physician, if not the medical profession as a whole. Furthermore, they are pervasive in medicine today and are of increasing concern to the public (1). Our fee-for-service health-care system, which rewards physicians for doing more, is something we deal with on a daily basis, particularly in subspecialties such as gastroenterology in which expensive interventions are a major part of our practice. Little thought is given to this when we recommend, for example, a colonoscopy for colorectal cancer screening, but a recent analysis of colonoscopy practice has suggested that these procedures are recommended in excess of what the guidelines suggest. While there are many possible explanations for this phenomenon, personal financial gain is, nonetheless, on the list (2).

CONFLICTS IN RESEARCH

Dramatic examples of conflicts of interest in medicine have occurred in the research arena and many of these have been detailed in the print media. The *Seattle Times* was a major driving force in the litigation involving investigators at the Fred Hutchinson Cancer Center, who had a major financial take in a bone marrow transplant trial that went awry (3). In 1999, the death related to multiorgan failure of 18-year-old Jesse Gelsinger, who had taken part in a gene transfer trial at the University of Pennsylvania for ornithine transcarbamylase deficiency, was highly publicized (4). Both James Wilson, the principal investigator, and the institution stood to gain financially had the trial been successful. When the FDA cited 14 violations, including failure to meet entry criteria, the possibility that financial gain had influenced decision making generated much discussion at the time. While unlikely to have occurred, the perception that it might have was enough to raise serious questions about trust and outside influence in clinical research.

With decreasing funding for research, technology transfer has become an increasingly common outlet for financial gain for both institutions and investigators. The Bayh-Dole Act in 1980, along with other legislative products, permitted institutions to seek intellectual property protection for inventions developed with federal funding (5). Prior to this time, patents were held by the granting agency, often the National Institutes of Health, which had little interest in licensing these for commercial development. While the purpose of this legislation was to accelerate the transfer of research-derived benefits for the public good, it also created a novel opportunity for new sources of income for academic centers. Re-

sulting commercial ventures, involving science and industry almost by definition, created conflicts of interest and, in turn, spurred the development of conflict of interest committees at research institutions. While financial gain is the most obvious conflict that could potentially affect decision making in research, there are other nonfinancial conflicts, including fame and notoriety, which could affect the research effort anywhere from the experimental design to hiring of staff.

CONFLICTS IN PRACTICE

The structure of the health-care system in the United States, by necessity, creates a potential conflict of interest with every patient we see, but it is obvious and virtually unavoidable. Beyond daily encounters with patients, however, less obvious are the so-called joint ventures in which physicians buy ownership in health-care facilities, particularly the ones at which they do not practice. Examples include free-standing laboratories or radiology facilities for which available evidence has linked more imaging and overutilization with financial incentives (6, 7). Joint ventures in radiotherapy facilities not only resulted in increased use of services with increased costs, but quality appeared to suffer as well (8). It was these kinds of ventures that led to the evolution of federal oversight and restriction of physician-owned health-care facilities, most evident in the so-called Stark laws, named for Congressman Pete Stark from California, who introduced the legislation in the early 1990s. More recently, the evolution of ambulatory surgical centers (ASCs), of which the ambulatory endoscopy center is an example, has raised concerns among regulators. While ASCs effectively facilitate the efficient practice of gastrointestinal endoscopy while optimizing the patient experience, the major investors are the physicians using them; the higher the throughput, the higher the payout to investors. However, these centers are considered an extension of one's practice, in contrast to the aforementioned joint ventures for which self-referral was not a part of practice. Moreover, as a practice site, physician–owners are in perhaps the best position to provide quality assurance. As such, they are generally considered exempt from federal restrictions. Nonetheless, when viewed from the perspective that the more patients scheduled, the more the financial return, the concern over competing priorities or conflicts between patient welfare and physician financial gain is almost inescapable. While there are no studies addressing this issue in gastrointestinal endoscopy, at least in radiology, imaging is more often ordered when the physician has a financial interest in the facility performing the study, be it in his or her own office or a free-standing facility outside the practice site (6).

RELATIONSHIPS WITH THE PHARMACEUTICAL INDUSTRY

The other major arena in which potential conflicts of interest commonly arise is the relationship of medical practice to the drug and device industry, of which the case presented here is an example. Ninety-four percent of physicians have some type of relationship with industry, of which gifts (83%) and drug samples (78%) are the major examples (9). Other relationships include reimbursement for costs associated with attending professional meetings, consulting, joining a speaker's bureau, and enrolling patients in clinical trials. What is bothersome about these virtually ubiquitous relationships is that a physician's medical decision making might be influenced, either overtly as a *quid pro quo* or less obviously, if a drug comes to mind simply because it appeared on a note pad or as a logo on a wall clock. And if this drug is chosen over a less costly but equally effective agent, or of more concern, chosen for a questionable indication, then the conflict of interest has materialized because the best interest of the patient would have become secondary. The problems are magnified when devices are involved because the installation or deployment of the device often involves an invasive procedure that has its own set of risks and adverse events.

Concerns about industry influence in continuing medical education (CME) has also become an issue. While disclosures of personal conflicts of interest by individual speakers has become the rule in accredited educational programs for practicing physicians for which CME credits are offered, industry support of CME remains commonplace. Nearly two-thirds of CME expenditures in 2005 were derived from industry (10). Other educational venues are less regulated, however, and this includes the drug company-sponsored speaker who is brought to town and escorted to various sites by the local representative, over a 1- or 2-day period, and private, for-profit companies, largely funded by industry, that provide CME through speakers and written materials. While such programs are designed to influence those attending, the physician speakers or writers, often from academic institutions, are provided honoraria for these educational programs and are thus confronted with their own conflicts of interest. While the idea of industry support for CME is not intrinsically unethical, the extent to which it is designed to influence medical decision making and the extent to which it actually succeeds are problematic.

Can physicians be influenced by these types of activities? There seems to be little doubt that physician behavior, in fact, is influenced by a relationship with industry (11). Furthermore, the most obvious testimony to its success from the industry perspective is the dollars expended to establish and maintain these relationships—$19 billion annually, according to a recent commentary (12). An increasing number of academic health centers and some community hospitals have now restricted or eliminated access by industry representatives; how prevalent this response might be in private offices is unclear.

SOLUTIONS AND MANAGEMENT

Attempts to regulate medical practice using managed care have largely been unsuccessful. Precertification programs

were designed to restrict certain diagnostic and therapeutic interventions to those indications that were most appropriate, and thereby provide some control over potential conflicts. While the concept made sense, the programs were unpopular in both medical and lay circles. Further, they were subject to gaming, which in turn rendered them invalid. And of course health plans—businesses that need to make money—had a conflict of interest themselves in wanting to maximize their bottom line. An alternative—prepaid medical contracts or the so-called capitation plans—left the burden on providers and, as such, created a negative incentive to use resources such that needed services were at risk or foregone. In looking for alternatives, recent efforts by health plans have involved more extensive credentialing for specific interventions and initiation of quality assurance guidelines that are linked to reimbursement (6). Implementation of pay-for-performance models that attempt to correlate physician interest with patient interest addresses conflicts of interest indirectly (10). Still, individual physicians, when making decisions that affect patient welfare, must be cognizant of the potential competing interests that are intrinsic to our health-care system and the widespread perceptions of misuse that exist (13, 14). And while financial conflicts are the most obvious and the easiest to measure, there are other nonfinancial influences—personal acclaim, unique experience, and coercive technology—that could also bias decision making. Reliance on physician integrity is generally safe, but in uncertain or questionable circumstances, discussion with colleagues, presentation of challenging patients at medical staff conferences, and formal second opinions are all methods to maximize quality care that is less susceptible to outside influences.

What about relationships with the drug and device industry? Clearly the case presented here is problematic and the best option is transparency and complete disassociation with the company. Still, complete isolation of industry from medical practice is not realistic and, moreover, clinical needs, particularly in procedure-oriented specialties such as gastroenterology, often translate into novel or improved technology that benefits patients. But while such interactions will and should continue, physician providers should also resist opportunities for personal financial gain, unless that gain can somehow be isolated from their own clinical practice. In situations in which that has not or cannot happen, transparency and disclosure are the most often applied management tools. However, disclosure has limited value and from the patient perspective, when a clinical need is at stake, such information may only confuse an individual and possibly raise questions about physician trust.

In the practice setting, opportunities to benefit from industry largesse are ever present. And in academic health centers, such opportunities also flourish. The chance to join a pharmaceutical company speaker's bureau for a physician scientist–investigator is often viewed as a perquisite not only because it would seem to identify that individual as an expert, but it also provides additional personal income that usually is not shared with the institution. But if physicians uniformly declined offers for any industry-sponsored activity for which they were paid, or if they refused to attend such events, commercially sponsored education would cease. Likewise, if physicians declined gifts or free samples, many of the concerns about the influence of pharmaceutical and device manufacturers on medical practice would diminish, if not disappear. While such a dramatic change is not likely to happen, it is, nonetheless, a sobering thought, and a movement in this direction may already have begun, as championed by leaders in American medicine and as more academic health centers have restricted industry presence on campus (11).

OUTCOME

In the case presented here, the physician involved decided not to accept the offer of training with the new device, and, in doing so, would not participate in the financial arrangements. After discussing the issues with colleagues, concern was raised not only about the absence of any meaningful data about safety and efficacy, but also the offer of financial reward. As presented, it appeared designed to bias medical decision making and thus create an obvious financial conflict of interest—or at least it would likely be perceived as such. He was also concerned about violation of possible federal regulations. In declining to participate, he urged the company to evaluate the technology in an appropriate clinical trial before making the device available for marketing.

Reprint requests and correspondence: Larry D. Scott, 301 University Blvd., Rt. 0764, Galveston, TX 77555.

REFERENCES

1. Editorial: Falling short of professional standards. The New York Times, December 24, 2007. Available at: http://www.nytimes.com/2007/12/24/opinion/24mon2.html. Accessed January 3, 2008.
2. Krist AH, Jones RM, Woolf SH, et al. Timing of repeat colonoscopy: Disparity between guidelines and endoscopists' recommendation. Am J Prev Med 2007;33:471–8.
3. Heath D. Trial to open in deaths of cancer patients at Hutch. The Seattle Times, February 1, 2004. Available at: http://community.seattletimes.nwsource.com/archive/?date=20040201&slug=hutch01. Accessed January 3, 2008.
4. Shalala D. Protecting research subjects—what must be done. N Engl J Med 2000;348:808–10.
5. Gelijns AC, Thier SO. Medical innovation and institutional interdependence. Rethinking university-industry connections. JAMA 2002;287:72–7.
6. Kouri BE, Parsons RG, Apert HR. Physician self-referral for diagnostic imaging: Review of the empiric literature. AJR Am J Roentgenol 2002;179:843–50.
7. Moore NJ. Regulating physician self-referrals and other physician conflicts of interest. HEC Forum 2003;15:134–54.
8. Mitchell JM, Sunshine JH. Consequences of physicians' ownership of health care facilities—joint ventures in radiation therapy. N Engl J Med 1992;327:1497–501.

9. Cambell EG, Gruen RL, Mountford JMD, et al. A national survey of physician-industry relationships. N Engl J Med 2006;356:1742–50.
10. Tonelli MR. Conflict of interest in clinical practice. Chest 2007;132:664–70.
11. Brennan TA, Rothman DJ, Blank L, et al. Health industry practices that create conflicts of interest. A policy proposal for academic medical centers. JAMA 2006;295:429–33.
12. Campbell EG. Doctors and drug companies—scrutinizing influential relationships. N Engl J Med 2007;357:1796–7.
13. Krugman P. Drugs, devices, and doctors. The New York Times, December 16, 2005. Available at: http://select.nytimes.com/2005/12/16/opinion/16krugman.html. Accessed January 3, 2008.
14. Carlat D. Diagnosis: Conflict of interest. The New York Times, June 13, 2007. Available at: http://www.nytimes.com/2007/06/13/opinion/13carlat.html. Accessed January 7, 2008.

CONFLICT OF INTEREST

There is no conflict of interest.