

The Influence of Money on Medical Science

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WHILE ON VACATION RECENTLY, I HAD THE OPPORTUNITY to contemplate the sometimes unethical influence of money on medical science, a very serious issue, which has become more evident over the past year or so. It seemed ironic that this wonderful time of contemplation was aided by the soothing, normal flow of the Delaware River in Pennsylvania, which just a week before had deluged roaring destructive flood waters well beyond its normal banks. Such is the nature of Nature, which very much mimics the pattern of my thoughts over the past few weeks as I experienced what happened as a result of trying to address a serious problem.

There can be no doubt that editors of peer-reviewed medical journals must always place the interest of patients above all else. Every published article eventually can and should affect patient care. Therefore, all articles that we publish must be ethically sound, valid, reliable, and credible (ie, reflective of work that is performed, written, reviewed, and edited in a manner that is unencumbered by financial pressure). With that in mind, it is important to discern the necessary and honest interests of for-profit companies from the potentially corrupting influence of commercial interests.

The influence of commercial interests on medical science is far-reaching but, to a great degree, essential. The discovery of new medications, devices, and techniques is funded primarily by for-profit companies¹; testing new modalities of treatment is funded primarily by for-profit companies; and the manufacture and profitable marketing aspects of these modalities appropriately falls in the purview of this industry.

Two basic goals of for-profit companies are the discovery, testing, and production of products (the scientific goal) and the sale of products to garner profits, thereby generating returns to the shareholders (the marketing goal). Profits are a logical expectation of the companies that fund the discoveries. Ideally the products discovered, tested, and produced will be beneficial to many individuals for whom the products will be prescribed and who will purchase them, returning a healthy profit for the company.

Now comes the potential problem. In some instances, the marketing goal of a company dominates the scientific aspect of the company-funded research. There have been a number of high-profile examples of such research irregu-

larities involving for-profit companies, such as the refusal to provide all study data to the study team,² reporting only 6 months of data in a trial designed to have 12 months of data as the primary outcome³; incomplete reporting of serious adverse events^{4,5}; and concealing clinical trial data showing harm.⁶

For-profit companies also can exert inappropriate influence in research via control of study data and statistical analysis, ghostwriting, managing all or most aspects of manuscript preparation, and dictating to investigators the journals to which they should submit their manuscripts. For example, I have been told that in response to *JAMA*'s policy requiring an independent statistical analysis by an academician for industry-sponsored studies in which the only statistician who analyzed the data is employed by the study sponsor,^{7,8} some companies are insisting that the researchers not submit those studies to *JAMA*. That tactic risks not only the perception that the company may have something to hide, but the reputation of any researcher willing to accede to such a company demand. Since the announcement of our policy requiring an independent statistical analysis,⁸ only one company has refused to obtain this second analysis of the submitted manuscript, and that decision came only after full review and evaluation by *JAMA*. When we indicated that *JAMA* would not publish the paper without the required independent statistical analysis, the authors and sponsor withdrew the paper from *JAMA*; that paper was published elsewhere shortly thereafter and has received much media coverage. I can only hope that the decision by the sponsor was based on something other than not wanting an outside analysis of data that might have uncovered flaws in the original analysis.

Individual clinicians or medical scientists may also exhibit inappropriate or unethical behavior perhaps influenced by money or other factors. All would agree that it is dishonest for clinicians and medical scientists to falsify data or data analysis; to provide negative peer reviews of other's submitted but not yet published manuscripts because they do not want to be "scooped"; or for an editor of a medical journal to participate in the editorial review and decision to publish a review article authored by himself or herself and for which financial imbursement from the sponsor was obtained. These are obvious problems, but in other situa-

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tions, the concerns about potentially unethical financial influence on individuals are more difficult to identify.

If for-profit companies are to make medical advances, it is essential for them to have the best (ie, the most intelligent, creative, and experienced) individuals working on a medical problem either as employees of a for-profit company or as consultants. Who is better to conduct the clinical research necessary to test a product? Who should teach clinicians about the benefits and adverse effects of the product? The majority of these intelligent, creative, and experienced individuals are academicians. Surely these individuals cannot be expected to provide such expertise without compensation or to perform clinical studies without funding. So what is appropriate compensation? That is a difficult issue faced by the administrators and faculty at academic medical centers⁹ and even at government agencies, such as the National Institutes of Health. However, these same academicians publish most of the research, reviews, editorials, commentaries, and perspectives in medical journals.

How do editors preserve the integrity of their journals while ensuring that they serve as vehicles for dissemination of scientific information that could help clinicians provide better care for their patients? First and foremost is to ensure that all published articles are scientifically sound and as objective and unbiased as possible by using rigorous peer review and careful editorial evaluation. Another important aspect is to ensure that readers are aware of the authors' financial relationships and potential conflicts of interest so that these readers can interpret the article in light of that information.

Since 1985, *JAMA* editors have requested¹⁰ and since 1989 have required¹¹ all authors to sign a specific statement disclosing the financial interests they have that might be perceived as influencing the article they have written. In 1990, *JAMA* began publishing these disclosures.¹² In 1999, *JAMA* began requiring authors to report any role the financial sponsor played in either the study or the resulting article. In 2005, we once again drew attention to these policies in an editorial.⁸

However, a number of authors still lacked a clear understanding of what was required in these financial disclosures. Therefore, in late spring of 2006, we began working on an even stronger statement and requirement that was published July 12, 2006.¹³ In addition, when several authors failed to disclose their potential conflicts of interest, rather than quietly publishing a correction, we made public (via the journal) announcements by publishing letters from these authors with an apology to the readers¹⁴⁻¹⁶ and, in 1 case, with an editorial response.¹⁷ In 2 cases in which we became aware of failure to report financial disclosures after the article was in print but before it was distributed, we published the detailed corrections in the online issue of *JAMA* simultaneously with the publication of the article.^{16,18} This action was meant to emphasize the seriousness of the failed disclosures.

Because we are so adamant and open about disclosure of financial interests, it is not surprising that we are being made aware of nondisclosures by authors and by readers. Somewhat surprising was that 3 consecutive cases of nondisclosures, all of which raised the interest of the mainstream press, involved authors from Harvard Medical School. To his credit, the dean of Harvard Medical School has informed me of his plan to send a letter enclosing the disclosure requirements for *JAMA* (plus our July 12, 2006, editorial)¹³ and those for the *New England Journal of Medicine* to all 8000 Harvard Medical School faculty members. In addition, he indicated that he will work with his faculty to enhance Harvard Medical School's current policies on financial relationships with for-profit companies (Joseph B. Martin, MD, PhD, oral communication, July 18, 2006).

It would be an understatement to say that I have been disappointed by the reaction of several would-be pundits to our initiative to increase transparency around the issue of disclosure of financial interests. They have misinterpreted, misrepresented, or misunderstood the meaning and results of our policy and our ability to manage the problem of authors' failure to disclose. Specifically, failure of the authors to fully disclose their financial ties does not automatically translate to the article being flawed. For example, the *JAMA* articles cited in this editorial as examples of authors' nondisclosure were all peer reviewed and editorially evaluated and no one has questioned their validity. Moreover, publication of our updated policy and editorial¹³ was not a reaction to any published newspaper articles as has been insinuated; the policy and editorial had been prepared weeks before any such media reports appeared.

Most important, there simply is no way to guarantee that all financial relationships and arrangements of all authors are disclosed. It is not feasible to independently investigate the financial relationships of every author, as no comprehensive, up-to-date source of this information exists. Calling every author (for *JAMA*, that involves thousands of individuals annually) offers no advantage over our current requirement that every author sign a document attesting to his or her financial relationships or lack thereof. Misrepresentation of or failure to completely disclose financial interests on the telephone or in person is not much different than doing so in writing—in fact, one might argue that requiring a signature better encourages honesty.

Leveling sanctions against an author who fails to disclose financial interests by banning publication of his or her articles for some time period would only encourage that author to send his or her articles to another journal; it cleans our house by messing others. So what about all editors, or at least a group, such as the International Committee of Medical Journal Editors, agreeing to share the information and jointly to ban the offending authors? Those who suggest this approach have not considered the risk of an antitrust suit.

Finally, the degree I hold is an MD, not an MDeity; I have no ability to know what is in the minds, hearts, or souls of authors. Furthermore, I do not have, nor desire to have, the resources of law enforcement agencies, but I do know that the accuracy of lie detector tests is questionable.

So what other tools are left to editors in their effort to enforce policies on full reporting of financial disclosures? The most potent—both in enforcement and education—is the instigation of a full investigation by the deans of the authors' institutions. In 2006, I have resorted to this approach twice, resulting in thorough investigations and appropriate corrective actions for the authors who were faculty members at the Mayo Clinic College of Medicine and the University of Nebraska School of Medicine, respectively. Furthermore, in both cases, the investigating committees found that many members of the faculties were not fully cognizant of the implications of financial ties and responsibility to disclose. Both deans have enacted conflict of interest education via such methods as grand rounds, mandatory educational modules, expansion of mandatory annual financial disclosures, and development of standard disclosure templates to be used by all faculty who submit manuscripts to professional journals or make presentations at professional meetings. This sort of intervention by academic administrators concerned about the integrity of medical science and faculty has a much more profound impact than other proposed methods.

Like these deans, I have also tried to enhance the education of authors via *JAMA's* expanded disclosure rules.¹³ As part of this process, we have made no attempt to conceal the episodes of failure to disclose in a simple correction published in *JAMA*, and we will continue this approach until it becomes unnecessary. Although our efforts to educate authors about the importance of full disclosure of relevant conflicts of interest and to enforce compliance with tightened rules have not always been received as we might hope, we do see a silver lining—even in the harshest scrutiny. The intensity of public discussion is invaluable, not only for raising the visibility of *JAMA's* requirements, but also for increasing awareness of the potential influence of money in science as well as for increasing appreciation for the role that full disclosure of potential conflicts of interest plays in en-

surging that physicians and patients can properly interpret, and more importantly trust, what they read in *JAMA*.

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