Conflict of Interest in Psychiatry: How Much Disclosure Is Necessary?

November 01, 2006 | Major Depressive Disorder [1]  
By Daniel Carlat, MD [2]

Just how “hot” is the topic of conflict of interest in psychiatry? The answer was brought home to me dramatically this past May at the APA meeting in Toronto. During the meeting, I had the opportunity to chair a symposium titled “Pharmaceutical Industry Influence in Psychiatry.” My copresenters and I showed up well ahead of time to meet and prepare introductions. As we gazed out at the empty seats, we joked that there would be at least 5 people in attendance since, after all, there were 5 presenters.

How wrong we were. As the time to begin approached, a slow trickle rapidly became a rush of attendees. Every available seat filled quickly, and a large crowd stood in the rear and hovered in the hallway outside the room.

In retrospect, I shouldn't have been surprised. Over the past several months, psychiatry has been subject to several embarrassing exposés related to conflict of interest. These events provided painful lessons on what constitutes financial conflict of interest and what should be disclosed.

In this article, I will begin by discussing the notion of conflict of interest in medicine and then zero in on 2 examples of conflict of interest in psychiatry. These examples provide good jumping-off points for delving into major controversial issues concerning how much authors and researchers should disclose regarding their financial relationships with commercial enterprises.

Defining “conflict of interest”

The New England Journal of Medicine published the classic article defining conflict of interest in medicine in 1993. A clinical ethicist at Harvard University, Dennis Thompson, defined conflict of interest as "a set of conditions in which professional judgment concerning a primary interest (such as a patient's welfare or the validity of research) tends to be unduly influenced by a secondary interest (such as financial gain)."¹

In medicine, a typical scenario involves the physician who receives money from a pharmaceutical company for research, consulting, or speaking. The conflict is between 2 different interests or desires. One desire is to produce scientifically valid research or, in the case of a speaker, to communicate accurate and relevant medical educational material. The potentially conflicting interest is the desire to make money from the pharmaceutical company.

Obviously, there are times when these 2 interests coincide. Often, for example, speakers will choose to speak strictly on behalf of medications that they sincerely believe are superior. Even if this is true, however, a potential conflict of interest still exists because the audience will never know whether the promise of a check at the end of the dinner program has altered the speaker's opinion of the featured product.

We usually focus on financial conflicts of interest (hereafter referred to as COI) because they are easy to identify and quantify. Other common COI in medicine include the desire for academic advancement and for media coverage. In all cases, COI can bias the content of research articles, review articles, and educational lectures. In recent years, several studies have been conducted, both in psychiatry and in medicine at large, that documented the ways in which financial COI appear to influence the outcome of medical research.

Recently, for example, Perlis and colleagues² examined all clinical trials that were published in 4 of the major psychiatric journals from 2001 to 2003. Of 162 randomized placebo-controlled studies, those that reported COI were 4.9 times more likely to report positive results for the sponsored
Conflict of Interest in Psychiatry: How Much Disclosure Is Necessary?

How credible is this response? The core question here is whether the authors' relationships with associations with industry.

concluded that there was no inherent conflict of interest with respect to any of our financial money from drug companies, but the published study was not a clinical trial of any particular drug, research, they pointed out, was not funded by industry.

But did conflict of interest really exist?

Antidepressants and pregnancy: an embarrassment for JAMA

In retrospect, the issue of antidepressant use in pregnancy is so rife with controversy that the Journal of the American Medical Association (JAMA) should have seen this one coming a mile away.

In February 2006, JAMA published a study on depressive relapse during pregnancy. Conducted and written by major luminaries in the field of perinatal psychiatry, this naturalistic multisite study tracked depressive symptoms and antidepressant use in 201 pregnant women, all of whom had histories of depression but who were euthymic and taking antidepressants at the beginning of the observation period. The results were striking: 68% of women who stop taking antidepressants relapsed during the pregnancy, whereas only 26% of those who continued their medication did.

While the article did not ignore the potential perils of prenatal exposure to antidepressants, the authors concluded the abstract with a statement endorsing their use: "Women with histories of depression who are euthymic in the context of ongoing antidepressant therapy should be aware of the association of depressive relapse during pregnancy with antidepressant discontinuation."

At the end of the article, the funding source was reported as the National Institute of Mental Health and 2 of the 13 authors—Dr Newport and Dr Stowe—reported financial ties to drug companies. The following was associated with their names: "None of the other authors reported disclosures."

On February 8, Dr Adam Urato, an obstetrician/gynecologist and faculty member at Tufts University, read the article with interest and was struck with the disclosure. Since he frequently advises patients to conduct the large clinical trials that are needed to yield significant results. Indeed, in the Perlis study, industry-sponsored studies generally enrolled higher numbers of subjects than nonsponsored studies, implying greater statistical power to measure any differences between treatments.

On the other hand, a recent review of industry-sponsored studies of anti-psychotics detailed specific techniques used by companies to manipulate research design in order to ensure positive results.

The techniques included underdosing competitors' medications, devising study inclusion criteria so that the subjects enrolled were more likely to respond to the sponsor's product, and selectively reporting data so as to minimize the side effects.

Thus while still controversial, potential sponsorship bias is seen as an important issue in academic medicine. Over the past 2 decades, medical journals have responded to this problem by requiring authors to disclose their financial COI when they submit manuscripts. However, there continues to be much variation and debate about how much information authors should disclose and when they should disclose it.

By this time, the story was already out—the Wall Street Journal published a front-page story entitled "Financial Ties to Industry Cloud Major Depression Study." That article not only reported the missing disclosures, but detailed the many controversies about antidepressant use in pregnancy, including recent FDA warnings linking SSRI use with pulmonary hypertension, seizure risk, and—in the case of paroxetine—cardiac malformations. The implication was that antidepressant drug makers had influenced the most prominent researchers in the field to gloss over the risks of using antidepressants in pregnancy and to instead highlight the benefits. The fact that they did not disclose their relationships made them appear even guiltier of commercial bias.

But did conflict of interest really exist?

In a letter of response to JAMA, 4 of the authors explained why they did not submit disclosures. The research, they pointed out, was not funded by industry. Yes, the individual researchers receive money from drug companies, but the published study was not a clinical trial of any particular drug, so no particular company stood to benefit from the results. For these reasons, said the authors, "we concluded that there was no inherent conflict of interest with respect to any of our financial associations with industry."

How credible is this response? The core question here is whether the authors' relationships with...
industry might have influenced the way they designed, conducted, or interpreted their research. Did the researchers have a financial incentive to modify their research in any way? In order to answer this question, we would have to know whether their research results are likely to lead directly to future payments from the relevant companies.

In fact, there are several possible scenarios in which the authors could financially benefit from the results:

1. They may receive research funding from a range of drug companies wanting to demonstrate the value of their own products in preventing relapse during pregnancy.
2. They may be invited to serve as paid consultants. The role of "consultant" varies, but a major role is to advise companies about what sort of research studies might yield results beneficial to their future marketing efforts.
3. They may be invited by companies to conduct lucrative continuing education activities—such as giving lectures, participating in conferences, and authoring sponsored articles—in order to disseminate their research findings.

In fact, there is evidence that some of the authors of the JAMA article are already deriving additional income in this way. An industry-funded medical education enterprise, the Massachusetts General Hospital Psychiatry Academy, now offers a symposium titled "Psychotropic Drug Use During Pregnancy," which is conducted by some of the JAMA authors. The faculty discuss the results of their study and others and endorse the use of antidepressants in pregnancy (the videotaped presentation can be viewed online). Thus, it seems clear that in the case of the JAMA article, the following elements of potential COI were met:

- The researchers receive payments from companies that manufacture antidepressants.
- The research findings endorse the value of antidepressant therapy in pregnancy.
- The findings are likely to attract more money from industry to the researchers in the future.

Since the researchers stood to benefit financially from positive results, their judgments may have been, in the words of Thompson, "unduly influenced by a secondary interest (such as financial gain)."

Looked at in this way, there appears to be no question that the potential for COI existed and that full financial disclosures should have been made. Does this mean that the authors actually altered the research design to make sure the results favored antidepressants? Of course not. These are all highly ethical scientists who conduct clinical studies to answer important questions about psychiatric care. However, requiring full financial disclosure would not have invalidated the results of their research. It simply would have provided readers with information that might be relevant in their own evaluation of the research design and conclusions.

Was JAMA's response to this controversy adequate?

Even before this controversy, JAMA had a clear policy about financial disclosure. The relevant section of the authors' instructions reads as follows:

"All authors are required to disclose all potential conflicts of interest, including specific financial interests and relationships and affiliations (other than those affiliations listed in the title page of the manuscript) relevant to the subject of their manuscript. Authors should err on the side of full disclosure and should contact the editorial office if they have questions or concerns."

This is the section that the authors of the antidepressant article presumably read. The crucial phrase in this excerpt is: "relevant to the subject of their manuscript." This phrase allows authors to make their own decisions about what is important to disclose. As discussed above, the JAMA authors used this latitude to decide that their financial relationships were not relevant to the subject of their manuscript.

JAMA's response to this situation was to publish an update on their COI policy: the new policy requires authors to report disclosures in the body of their manuscript at the time of submission rather than in a separate authorship form, which is sometimes received well after the manuscript review process.

Unfortunately, this policy update does not get to the core of the problem. The core defect in the JAMA policy is that authors are allowed to decide when a financial tie is relevant; the policy revision does nothing to fix this. All it does is make it more likely that journal editors will review the disclosure statement in a timely fashion. If JAMA were serious about preventing further similar controversies, it would require authors to
disclose all financial ties to any health care-related company, whether seemingly relevant or irrelevant to the topic of the article. It would then be up to the readers to decide whether these ties represented true conflicts.

A more definitive solution to the problem of missing disclosures would be to establish an online national "clearing house" that would list the financial ties of all physicians and research grant recipients so that journal editors and readers would be able to check this instantly. Physicians would be man dated to update this every 6 months, and it would be monitored by their respective Boards of Registration in Medicine (I thank Ronald Pies, MD, for this suggestion).

Because *JAMA* failed to implement a requirement of complete disclosure, the publication got "burned" again, only 6 months after the previously described article was published. In this instance, the journal published an article on the relationship between mi graine headache and cardiovascular disease. This epidemiologic study showed a significant association between migraines and morbidity and mortality from cardiovascular disease. None of the 6 authors reported that they receive fees from manufacturers of headache and cardiac medications, a story that also received national attention.

According to news reports, Dr Tobias Kurth, the lead author of the study and a Harvard Medical School faculty member, said that the financial ties were irrelevant because the study did not explicitly promote drug treatment for migraines. However, Dr Catherine DeAngelis, the editor-in-chief of *JAMA*, disagreed with the authors' assessment and told reporters that she would have published the ties if she had known about them. Again, the litmus test is whether authors might gain financially from results that benefit the companies with which they have ongoing financial relationships. This study highlighted the lethal dan gers of untreated migraines, a finding that would be expected to increase pre scriptions of analgesics and increase profits of the relevant companies. The authors, in turn, potentially stand to benefit from future consultancies or speaking engagements based on the results.

It appears that as long as decisions about the relevance of financial ties are left up to authors, further high-profile embarrassments are in store for our major journals. This is the first part of a 2-part article. In Part 2, which will appear in a future issue of *Psychiatric Times*, I will describe a recent event in academic psy chiatry that has been termed "the perfect storm" of conflict of interest. The article at the center of this controversy provides a good starting point for discussing whether journal editors should require disclosure of authorship and compensation.

Dr Carlat is assistant clinical professor of psychiatry at Tufts University School of Medicine in Boston and is editor-in-chief of The Carlat Psychiatry Report. He reports no conflicts of interest regarding the subject matter of this article.

References:


Source URL:
http://www.psychiatrictimes.com/conflict-interest-psychiatry-how-much-disclosure-necessary

Links: