Soc
DOI 10.1007/s12115-009-9259-9

COMMENTARY

JAMA, Free Speech, and Conflicts of Interest

Jonathan Leo

I recently co-authored a letter to the *BMJ,* pointing out an author's undisclosed conflict of interest related to a study (http://jama.ama-assn.org/cgi/content/full/299/20/2391) published in the *Journal of the American Medical Association* (*JAMA*). Our letter (http://www.bmj.com/cgi/eletters/338/feb05_1/b463) was really little more than an observation based on a fifteen-second Google search plus some minor comments. It was definitely not a groundbreaking piece of investigative journalism based on top-secret files, and anyone with access to the World Wide Web could have done the same. The study we wrote about examined the use of Lexapro, an SSRI, in stroke patients. The author of the study, a psychiatry professor, had not disclosed that he had served on the speaker's bureau of Forest Pharmaceuticals, the manufacturer of Lexapro. Compared to the recent revelations about academic psychiatrists and their unreported side deals worth hundreds of thousands, in some cases millions, of dollars with pharmaceutical companies, what we wrote about was minor. Although our letter said nothing negative about *JAMA*, and under normal circumstances would likely have been read by only a handful of people, the editors were extremely upset and their subsequent comments (http://blogs.wsj.com/health/2009/03/13/jama-editor-calls-critic-a-nobody-and-a-nothing/) to a *Wall Street Journal* reporter that I was a "nobody" and "nothing" thrust the issue into the headlines.

The ultimate goal of the research group who authored the study is to prevent depression from developing in stroke patients not *treatment* of depression but the *prevention* of depression, an important distinction. While it would certainly increase the market share for Lexapro, the idea of prophylactically medicating a large group of people with no psychiatric diagnosis so that a minority of them will not develop depression later on is an initiative worthy of vigorous debate. In this trial they looked at three groups: Lexapro, problem solving therapy, and placebo. Both Lexapro and therapy beat placebo. Considering that there are about 6 million stroke patients in the United States, and that, according to several data sets, about 37%, or 2.2 million people, will develop depression, this represents a large market for the pharmaceutical companies, especially when you consider it involves prescribing a medication for people who do not have a diagnosis of depression. Following its publication, the authors were quoted (http://www.usatoday.com/news/health/2008-05-27-stroke-depression_N.htm) in the media as saying that every stroke patient who could tolerate the medicine should be started on an SSRI. At the very least, the slippery slope comes to mind at this point. If we are going to try and prevent depression in one high risk group by treating everybody in the group before they are clinically depressed, then what about other high risk groups? Where do we stop? Should we medicate all the returning veterans (a 20% rate of depression), every pregnant woman (10% to 20%), the entire population of foster children (80% rate of psychopathology), and all the medical students in the country (20% rate)?

A week after their "Dr. Nobody" comment, the editors published an editorial, in which they spilt a considerable amount of ink cataloguing my sins, and they used my case as the impetus for a new policy that puts restraints on what people can say about *JAMA.* Whereas their initial comments could have been brushed off as having been made in "the heat of the moment," and would have been quickly forgiven in the blogosphere and op-ed pages, this was not the case with the editorial, which clearly required more time

J. Leo (✉)
Lincoln Memorial University,
6965 Cumberland Gap Parkway,
Harrogate, TN 37752, USA
e-mail: jonathan.leo@lmunet.edu

Published online: 01 September 2009

and thought to prepare. The initial comments could also have been attributed to one or two people, but the subsequent *JAMA* editorial took on an institutional stamp of approval. Their editorial has raised several issues that I think are important to clarify. Most importantly, I believe that there are two distinct sources of disagreement between the *JAMA* editors and me. The first issue, which I consider relatively minor, is simply a disagreement about the tone of the wording used by the editors when they contacted me following the publication of the letter in the *BMJ*. Rather than engage in an ongoing argument regarding their tone, I would prefer to grant the *JAMA* editors their version of the events. I hope this will prevent readers from being distracted from the more important issue.

Regarding the major issue, the editors were at odds with me and virtually everyone else who had eventually written about it. In short, the editors felt that it was entirely appropriate, as long as they were polite, to contact me and my dean, and demand that I withdraw an accurate letter written with publicly available information. Drifting into First Amendment issues, they essentially argue that I had no right to write about *JAMA* without *JAMA*'s permission. I, on the other hand, thought I had the academic freedom to write about matters in the public record. I think most people believe that once a written body of work, such as a scientific article, is in the public record, it is fair game for others to write about it. Isn't this idea essential to the free exchange of ideas? By creating new stipulations regarding the content of comments made on its papers, as well as when those comments could be made, *JAMA*'s editors essentially separated themselves from the rest of the intellectual world, placing themselves in a unique class with their own set of rules. If other organizations ever adopted this *JAMA* policy and applied it to themselves the free exchange of ideas would be sharply curtailed.

Throughout this entire matter I repeatedly said that if anyone could point out a factual error in the *BMJ* letter I would promptly retract it and issue an apology. Interestingly, no one, including the *JAMA* editors, who had every opportunity to do so, ever claimed that my letter contained inaccuracies. When faced with demands to retract the article I was in a quandary, as I thought it would be academically dishonest to withdraw a letter that had no factual errors. Wouldn't retraction of the truth be a lie? The *JAMA* editors also expressed their disapproval (again, surprisingly, in writing) with the *BMJ* for publishing the letter. Given that there were no inaccuracies in the letter, it appears that their condemnation of the *BMJ* was based upon the idea that one journal should not publish criticisms of papers published in another journal.

The editorial stated that the publication of my letter was "a serious ethical breach of confidentiality." Ironically, the editor's charge about me came in an editorial in which the editors released my email correspondence, something I never did. I was never under any confidentiality agreement and statements which imply that I violated a confidentiality agreement or interfered with an investigation are untrue and impugn my reputation. Interestingly, there seems to be a double standard regarding *JAMA*'s own policy regarding the confidentiality of emails. While they had no qualms in releasing my emails, they have told other letter writers (http://www.healthyskepticism.org/news/correspondencewithJAMA.htm) that a dialogue related to letters is confidential (Healthyskepticism.com).

New Revelations About the Study

JAMA has claimed that their investigation was more comprehensive than our *BMJ* piece. I only ask that readers actually compare the material published in *JAMA* with that published in *BMJ*. Granted there were some other undisclosed conflicts, but the correction published in *JAMA* does not include any analysis of the context or potential implications. For instance, it does not point out that the undisclosed conflict with Forest is significant because they are the same company that manufactures the study drug, Lexapro. I believe our *BMJ* letter presents a more complete (and troubling) story. However, in light of more recent allegations (http://www.healthyskepticism.org/news/2009/Jun09.pdf), apparently both of our investigations only scratched the surface. Additional allegations have been raised by Laura Boylan, a neurologist, including: faulty clinical trial registration; conflicts of interest that occurred before *JAMA*'s required 5-year reporting window; and questions about the investigators' decision to switch from Celexa to Lexapro (see www.healthyskepticism.com).

The typical clinical trial generates an enormous amount of data. Once the trial is concluded, there is the potential problem of researchers selectively picking and choosing the data that puts the drug in the best light, while at the same time ignoring the problematic data. This has happened before with dire results for patients. To prevent this potential abuse, or even the appearance of abuse, the editors of the world's leading medical journals now require researchers to register their study with a publicly available clinical trial registry. A key component of trial registration is that researchers, before they start gathering the data, document the endpoints that they consider the most important. The Robinson post-stroke trial was registered in a timely fashion at http://www.clinicaltrials.gov/ but, according to the registry site, which posts all drafts of the registration, the primary endpoints were not posted until August 2008—4 months after the study was published in *JAMA*. This appears to be a direct violation of *JAMA*'s own stated policy. Even a clerical error would seem to be

problematic, as it is the editor's responsibility to verify the accuracy of the registration. In her article (http://meds.queensu.ca/medicine/obgyn/pdf/Is_This_Clinical_Trial_Registered.pdf) describing successful clinical trial registry, the editor-in-chief of *JAMA* stated, "Every trial participant and every investigator should be asking: 'Is this clinical trial fully registered?'" It appears that the *JAMA* editors ignored their own advice (See *JAMA*, Vol. 293, p. 2927). While our original letter to the *BMJ* pointed out that an author violated a *JAMA* policy, this new revelation points to *JAMA* disregarding its own published policy. I would like to have inquired of *JAMA* if this trial was correctly registered, but it is unclear to me if my questions would have qualified as allegations that needed to be investigated with me being subject to an indefinite gag order during the process.

Another point of interest concerns the original study protocol (http://www.researchgrantdatabase.com/g/1R01MH065134-01A1/Prevention-of-post-stroke-depression-treatment-strategy/), approved in 2002, which called for the use of Celexa, an SSRI manufactured by Forest Pharmaceuticals. A year later, in 2003, the authors switched from Celexa to its close cousin, Lexapro, another Forest product. Why the switch? Some background information is necessary. In 2002, as Forest's patent on Celexa was getting close to its expiration, the company received patent approval for Lexapro, also an SSRI. With a generic version of Celexa available, Lexapro was now five times more expensive than Celexa. Although the clinical trial data showed little difference between the two medications, Forest's introduction of Lexapro involved one of the largest marketing programs in the history of antidepressant advertising. (See Melody Petersen's, Our Daily Meds http://www.amazon.com/Our-Daily-Meds-Pharmaceutical-Prescription/dp/0374228272 for a more in-depth discussion of the marketing of Lexapro.)

All of a sudden, in 2003, Celexa was passé and Lexapro was the drug of choice. In their 2008 *JAMA* paper, the stroke study authors cite two papers as justification for the 2003 decision to switch from Celexa to Lexapro. The evidence they cite for this decision seems problematic. The first citation is a thought piece, whose author list ironically includes three former chairmen of psychiatry departments who resigned from their positions following problematic media attention–two because of undisclosed conflicts of interest (http://www.cbsnews.com/stories/2008/08/14/politics/uwire/main4351669.shtml) and one because of an ethical violation (http://www.boston.com/news/local/articles/2007/10/14/a_doctors_downfall_mcleans_fallout/). And I'm the bad guy? The second citation is a study funded by a subsidiary of Forest and published in 2005—two years after the authors actually made their decision to switch. Yet, this switch was not strictly up to the authors. Ultimately, the switch from Celexa to Lexapro was approved by NIMH, the organization that funded the study. It is unclear why NIMH, which is supposed to be acting in the best interests of both patients and taxpayers, allowed government funds to be spent to investigate the use of the more expensive on-patent medication instead of the cheaper generic medication. In her discussion of these issues, Boylan—in much stronger wording than we ever used—stated, "I look to institutions like *JAMA,* the NIH, universities, and the peer review process to keep the public interest at the fore and maintain information integrity. It seems to me there is much room for improvement." Interestingly, both Dr. Robinson and two of the former psychiatry chairmen mentioned earlier co-authored a 2005 review which promoted the increased use of psychotropic drugs for patients with medical illnesses, such as cerebrovascular disease and alzheimer's disease. The acknowledgement section of their article acknowledges editorial support from a ghost writing company (http://userwww.service.emory.edu/~jdbremn/papers/evans_mooddisorders.pdf).

Conflicts of Interest in Medicine

One of the assumptions that the *JAMA* editors have built their new policy on is that they can do a better job than anyone else when it comes to investigating undeclared conflicts in *JAMA*. I think this is a questionable assumption. As the following example shows, just requiring professors to list their affiliations is setting the bar fairly low. In a 2006 study (http://jama.ama-assn.org/cgi/content/full/295/5/499) published in *JAMA,* the authors concluded that pregnant women with a history of taking antidepressants should continue taking their medication. Following the publication of the study, an outside source revealed to *JAMA* that several of the authors, who were psychiatry professors, had not revealed all the companies they were affiliated with (*JAMA*, vol. 295, p. 499). The issue received significant media attention (http://www.post-gazette.com/pg/06192/705022-114.stm), with an editorial (http://www.nytimes.com/2006/07/23/opinion/23sun2.html?_r=2), *Our Conflicted Medical Journals*, in the *New York Time*s (7/23/06) bluntly stating: "Their financial ties were not disclosed to *JAMA* on the preposterous grounds that the authors did not deem them relevant."

JAMA subsequently performed an investigation and published a correction consisting of a simple listing of the authors' company affiliations, which in the editors' eyes was sufficient information for the *JAMA* readers. At this point, neither the general public nor the *NYT* editors knew the full extent of the financial relationships involved. It has recently come to light, according to *The Atlanta Journal Constitution* (http://www.ajc.com/services/content/printedition/2009/06/11/emory0611.html) that one of the authors, Dr. Zachary Stowe, a Professor of Psychiatry at Emory University, was

paid $253,000 in 2007 and 2008 by Glaxo Smith Kline alone. Keep in mind that while *JAMA* provided a simple listing of the companies involved, the public learned about the true extent of undisclosed conflicts by virtue of our free and open press; they did not learn about them by reading *JAMA*. And judging by the fairly extensive media attention given to the conflict, the *amount* of money was an issue for the general public.

At one point Dr. Robinson replied to our letter, saying that my critical take on psychotropic drugs, which I have never denied, should have disqualified me from publishing a letter in the *BMJ.* He seems to equate thinking critically about psychotropic drugs with an "ideologically based mission." Considering that I have a track record of writing about the problematic marketing of psychotropic drugs, I think that he would have been better off criticizing me on something specific instead of just accusing me of being biased. I would welcome any comments from him about what I have written.

In short, over the past decade, I have written several articles pointing out that the benefits of the SSRIs (http://www.airplanecrash-lawyer.com/CM/IntheNews/SSRI%20Trials.pdf), and other psychotropic medications (http://www.springerlink.com/content/p0acb7nvrdxdr9br/) are often overstated, while their side-effects (http://direct.bl.uk/bld/PlaceOrder.do?UIN=159563673&ETOC=RN&from=searchengine) are downplayed. I have also noted that there is a disconnect (http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.0020392) between the scientific literature and the media when it comes to discussing the chemical imbalance theory of depression, and, furthermore, that there are significant conflicts of interest involving key opinion leaders in the field. Recently, several important scientific studies (http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.0050045) and (http://www.sfgate.com/cgi-bin/article.cgi?f=/c/a/2009/06/17/MN7N188GO6.DTL) have confirmed my views on the science behind the SSRIs and other psychotropic drugs. And in light of all the recent revelations about just how extensive the financial conflicts are, one critical view of my track record is that I was too naive and never understood the true extent of the problem. Ten years ago I questioned the use of stimulants in 3-year olds. At that time I never imagined that we would soon be using atypical antipsychotics for toddlers. In Florida alone, in 2006, more than 18,000 children on Medicaid were prescribed antipsychotic medications, and 367 of them were younger than 3-years old.

Aftermath

The initial disagreement between *JAMA* and me had about a 2-week life span in the media. Another journal editor commented: "This story has what journalists call 'legs' with some way to run" (*BMJ*, 3/28/2009). After initially telling the *WSJ* reporter that I was yelled at by the *JAMA* editors, I really did not do much of anything, other than to sit back and watch the daily events unfold. It seemed that at every turn the editors' efforts at damage control just led them deeper into trouble. For instance, while I was initially in a state of shock when I saw the March 11 editorial, I felt that in the long run the editorial would prove to be very problematic for *JAMA* and that it would ultimately harm *JAMA*'s reputation in a way that our letter to the *BMJ* never did and was never meant to do. I could not fathom how the editors themselves could not see that it was problematic. How could they have ever imagined that the press would support a gag order? And, as events transpired, the media dealt harshly with the editorial. Following the *JAMA* editorial, multiple newspaper editorials and commentaries were highly critical of *JAMA*'s new policy. I did not see a single major organization, medical editor, or news outlet that agreed with the new policy.

The American Medical Association (AMA) eventually stepped into the fray and asked the *JAMA* Journal Oversight Committee (JOC) to investigate the matter. Over the next several months the JOC, the editors, and the AMA all conducted various meetings about the matter. In my mind, the major question was would the JOC members stand behind the on-line editorial? When the answer finally came it was apparently "No."

Erasing the Scientific Literature

On July 9, 2009 the new policy came to an end when the *JAMA* editors published another editorial—this time in the print edition (*JAMA,* Vol. 302, p. 198). They never disavowed the first editorial or retracted it. (*JAMA* has also never retracted the CLASS study which led to the widespread use and inappropriate use of Celebrex.) Given the new editorial's sharp deviation from the original version, the only conclusion I can draw is that the JOC did not support the on-line version. The new editorial deletes all references to me and takes a much softer stance on handling people who bring undeclared conflicts to the attention of the *JAMA* editors. Rather than require people to maintain silence during *JAMA's* investigation, the print editorial states, *JAMA* will *request* that they maintain silence. While the on-line editorial accuses me of "breaking a confidentiality agreement," the newer editorial simply maintains that "the investigation is likely to be enhanced by maintaining confidentiality." Yet, the status of the original editorial is unclear. While there is no official retraction per se, the original editorial has been removed from the *JAMA* website. The editors appear to have taken the stance that it never

existed. Apparently, the ink they split earlier was of the vanishing kind. However, the fact remains that numerous people wrote about the on-line editorial. If the editorial never existed then what did they write about? I think the original editorial should still be part of the literature.

The new policy also seems to put some burden on the press. Under the new policy, an investigative reporter who notices a problematic unreported conflict-of-interest in *JAMA* needs to first contact *JAMA* before writing about it. There are already other examples (http://alison-bass.blogspot.com/2009/07/conflicts-galore-authors-of-big-statin.html) in the literature of reporters writing about undisclosed conflicts without obtaining prior permission from journal editors. Is it in the public's best interest for news organizations and journals to broker secret deals about when to write about something? Isn't this just another conflict of interest? In a society that prizes freedom of the press, a policy that puts constraints on the open and free exchange of publicly available information needs to be carefully evaluated.

The New Accountability

With every new chapter in the saga I kept wondering who could possibly be advising *JAMA* on its course of action. What if the editors had followed a different strategy, perhaps issuing a statement such as: "Authors Beware! We do not have the ability to police all our contributors' conflict-of-interest declarations. In the past we have relied upon the honesty of the authors, but now in the age of the Internet we can also rely upon our loyal readers. As this case shows, our readers are checking up on you." Case closed. The editors had multiple opportunities to issue such a statement. They could have done so at the very start of these events, or later, in conversations with the *WSJ* reporter, or when speaking with other reporters. And, in contrast to what did happen, the media would have praised *JAMA* for once again being in the forefront when it comes to handling conflicts of interest.

Even better, no one would have ever heard of me.

Acknowledgement I would like to thank my Dean, Dr. Ray Stowers, and the rest of the administration and students at Lincoln Memorial University for their support during this time. I would like to thank Jeffrey Lacasse and Colleen Salomon for their editorial support.

Conflict-of-Interest Declaration Since conflicts of interest are the catalyst behind this firestorm, it is only appropriate for me to be forthcoming. While I do not have a *financial* conflict of interest, my ideological conflict is that I believe that the relationship between academic medicine and the pharmaceutical industry is not healthy and the clinical trial process has become tainted by marketing pressures. I also believe that, unfortunately, medical journals shoulder part of the blame for this situation. This state of events has resulted in patients being given only a partial presentation of the science behind many of the medications they take. While I look at all of these problems as ideas worthy of debate, some see this viewpoint as a declarable conflict of interest. I am a member of the Society of Neuroscience, the Association of Clinical Anatomists, and I am a newly enrolled member of the American Civil Liberties Union.

Further Reading

Armstrong, D. 2009. AMA requests probe of *JAMA* charges. *Wall Street Journal*.

Boyle, L. Beyond the *JAMA* flap. 2009. Healthy Skepticism. Available at: http://www.healthyskepticism.org/news/2009/Jun09.pdf.

DeAngelis, C. D., & Fontanarosa, P. B. 2009a. Resolving unreported conflicts of interest. *JAMA*, *302*, 198 Available at: http://jama.ama-assn.org/cgi/content/full/302/2/198?home.

DeAngelis, C. D, and Fontanarosa, P. B. 2009b. Conflicts over conflicts of interest, *JAMA*. Available at http://jama.ama-assn.org/misc/jed90012pap_E1_E3.pdf.

Editors. Jammed by *JAMA*. *Chicago Tribune*, March 28, 2009.

Leo, J, and Lacasse, J. 2009. Clinical trials of therapy versus medication: even in a tie medication wins. *BMJ,* Rapid Responses. March 5. Available at: http://www.bmj.com/cgi/eletters/338/feb05_1/b463.

Robinson, R. G., et al. 2008. Escitalopram and problem-solving therapy for prevention of poststroke depression: a randomized controlled trial. *JAMA*, *299*(20), 2391–2400.

Jonathan Leo, AKA Dr. Nobody, is Professor of Neuroanatomy at Lincoln Memorial University-DeBusk College of Osteopathic Medicine. He is co-editor of the recently released book: *Rethinking ADHD: From Brain to Culture*, published by Palgrave Macmillan.