Integrity in Scientific Publishing

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This essay is in honor of Harold S. Luft, who, while heading up the Philip R. Lee Institute for Health Policy Studies, publishing important empirical and theoretical papers, and at the same time mentoring me, managed to perform his task as Senior Associate Editor and then Co-Editor-in-Chief of *Health Services Research* with distinction. No one could call me an economist nor a health services researcher, but I do know about peer review and editing scientific journals and that is why I have been asked to celebrate that aspect of his remarkable career. So in this essay, I give my personal reflections and an idiosyncratic view of some of the challenges that face editors of scientific journals, with particular attention to large journals reporting on clinical research.

In some ways I began to know Hal in 1979, 9 years before we met in person, because I had been the Deputy Editor of the *New England Journal of Medicine* when it published, “Should operations be regionalized? The empirical relation between surgical volume and morality” (Luft, Bunker, and Enthoven 1979). This wonderful article, rightly republished in recognition of its being a “classic” (Luft, Bunker, and Enthoven 2007), made me feel I knew Hal, which delusion in itself perfectly illustrates the strangely intimate but long-distance relationship editors have with authors. Handle a few manuscripts from an author, and soon you feel you know his or her soul. Given the importance of a manuscript to academic authors, it sometimes turns out that you do—in Hal’s case, only a fraction of it, but an important fraction nonetheless.

Editor’s note: This essay is based on an invited presentation at a “Festschrift” held on September 18, 2008 to honor Harold S. Luft upon the occasion of his retiring as Director of the Philip R. Lee Institute for Health Policy Studies, School of Medicine, University of California, San Francisco. It has been altered slightly for publication at *HSR*. This essay on peer review honors Dr. Luft’s roles as editor at *Health Services Research*.

It is characteristic of Hal's humility and sense of fair play that once he had become an editor himself, he contacted me several times to discuss issues of editorial policy. While he did so more because I had been an editor seemingly forever than because I had any useful ethical opinion, the issues he wished to discuss always involved ethical conundrums. In this, Hal was learning what the editors of large medical journals discover soon after their appointment, namely that most of the really troublesome problems they must confront are ethical ones. If Hal was like me, he learned that these are common, vexing, and give the editor the impression that he or she is being put in the position, not merely of trying to select and improve the scholarly work of his colleagues, but of policing a barrel-load of monkeys.

RESEARCH MISCONDUCT AND SCIENTIFIC EDITORS

I arrived at the *New England Journal of Medicine* in September 1977, at the same time as its new Editor-in-Chief, Dr. Arnold Relman. It took < 4 months before we met our first ethical issue. A physician wrote to point out that, on the same day that we had published an article to show that patients with chronic paranoid schizophrenia had low levels of monoamine oxidase in their platelets (Berger et al. 1978), another journal had published an article to show that levels in such patients were the same as in normals and other schizophrenics (Potkin et al. 1978). She also pointed out that though neither article referenced the other, they had two authors in common. When we challenged the authors, they justified their practice by asserting that it was not their custom to refer to unpublished work in a publication. (Wyatt and Murphy 1978). They, and no one else, had possessed information that completely undermined both their publications, so this disingenuous claim demonstrated at the very least a startling contempt for the process of publication.

It was, for me at the *New England Journal of Medicine*, the first of many. Adopting Jules Pfeiffer's phrase, I came to call such academic tricks "little murders"—not deserving to be hanging offenses, but destructive of the delicate web of trust between colleagues that keeps the whole enterprise functioning and afloat. By 1979, coincidentally the year of Hal's first great paper, I was already sufficiently concerned with the tricks being pulled by individuals I regarded as my academic colleagues to publish an article on the "Ethics of

medical publication.” Although slight, it had the merit of being the first publication on the ethics of publishing clinical research—a topic sharing many issues in common with health services research. Because I wrote it at the end of a series of such lectures I gave in Australia, I submitted it to the *Medical Journal of Australia*, with the result that, though that journal has since become an important publication, my article was effectively buried from my colleagues (Rennie 1979).

At the same time, much more serious academic bombs were exploding. During the late 1970s and all throughout the 1980s, well-publicized and sometimes dramatic cases of scientific misconduct, several (Darsee and Heymsfield 1981) involving papers published in the *New England Journal of Medicine*, were being reported in the media, and clinical researchers, their institutions, and the journals were being deeply embarrassed. Meanwhile the Congress, sensing blood, and justifying their intrusion by invoking their duty to protect the federal dollar, began hearings in 1981. We were all entertained to the ridiculous sight of our scientific betters testifying that scientific misconduct did not exist, despite the obvious existence of all the cases that had provoked the hearings. Some then claimed that, if it did exist, it was vanishingly rare, despite the total absence of data on its prevalence (Rennie and Gunsalus 1993).

Having shown they had a better grasp of scientific realities than the scientists, and having proved, yet again, that no profession could be trusted to self-regulate, the politicians in Congress demanded, and in 1989 put in place, regulations defining scientific misconduct and procedures for investigating, adjudicating, and sanctioning it. During the 1990s these were refined as case law built up, and in 2000 they became government wide (Rennie and Gunsalus 1993, 2008). Research misconduct was restricted to, as far as the government was concerned, falsification, fabrication, and plagiarism, and institutions were free to define and sanction any other types of ethical lapses—that is little murders—as they saw fit, and to try to separate the insufferable behaviors of mere jerks from the illegal actions of bona fide crooks (Gunsalus 1992).

Over the past decade, the rhetoric has died down, as handling of allegations of misconduct has become routine. Cases still occur, of course—whoever claimed that a degree in science bestowed saintliness? Recently, for example, Eric Poehlman went to prison not for merely falsifying his data in many published articles, but (of greater concern for the federal government) using those falsified articles to support his applications for government grants (Sox and Rennie 2006).

The policy messages for me were these. First, scientists were at sea when asked to render judgments about whether their colleagues' behaviors were either guilty or innocent, but they seldom recognized or understood the bases of their ignorance. However, they discovered that lawyers had long dealt with this problem, using a system called "the law." Secondly, along with their inability to self-regulate, the self-serving defensiveness of scientific associations was, and remains, hard to exaggerate. For example, when the 1995 Commission on Research Integrity suggested a list of whistle-blower protections (U.S. DHHS, Public Health Service, Commission of Research Integrity 1995), one prominent academic leader called it "an attack on science" (Letter from Ralph A 1996). Over several years, in the 1980s formal meetings between the professions of law and science allowed both sides to become educated about the ethical and practical need for explicit definitions and procedures. Finally, the adoption of rules that could stand up to legal challenge allowed the whole process to become routine, and editors, when they receive accusations against authors in the United States, now know who is responsible for handling them.

PEER REVIEW

Editors, of course, have to orchestrate journal peer review, and this more than anything seems to put them at the center of their specialties. They find themselves spending a good deal of their time preserving the integrity of the network that is peer review. The fact that manuscripts are "peer reviewed" is frequently used to advertise a journal, and no scholarly journal (online or in print) can hope to be recognized as such without some sort of peer review system in place.

However, editors too must actively engage in the business of peer review, that is, the assurance of evaluating and improving the science reported in their journals. Instead, while demanding ever-higher standards from their authors, editors themselves have only too often been content to operate in an evidence-free zone concerning their own outcomes, while at the same time asserting the virtues of their procedures. In 1986, appalled by the sad state of the scientific literature, I wrote that whether in spite of, or because of, the peer review system: "There seems to be no study too fragmented, no hypothesis too trivial, no literature citation too biased or too egotistical, no design too warped, no methodology too bungled, no presentation of results too inaccurate, too obscure, and too contradictory, no analysis too self-serving, no argument too

circular, no conclusions too trifling or too unjustified, and no grammar and syntax too offensive for a paper to end up in print” (Rennie 1986).

To combat this lacuna and with the strong support of my current journal, *JAMA*, I started a succession of international Congresses, their sole mission being to stimulate research into the processes of selection and improvement of scientific articles. Held at 4-year intervals, the first was in 1989 and the sixth in 2009 (see <http://www.ama-assn.org/public/peer/peerhome.htm>). One effect has been to increase the number of publications reporting such research on editorial peer review from about 5 to around 150–200 a year (Rennie 2002). However, despite all this work, the evidentiary basis for the merits of editorial peer review has been spotty (Jefferson et al. 2002), perhaps because research, beyond relatively simple audit (Kassirer and Campion 1994), is often directed at looking for the wrong thing in the wrong place. It tends to focus on the results of the process, rather than examining the decision making processes of the reviewers and editors.

The fact remains, however, that while every journal finds the business of creating and maintaining a vigorous peer review system exhausting, expensive and contentious, the scientific and academic community is voting for it with their time and money, and justifying it on the general basis that—like democracy—it is, despite its flaws, the best system there is. As no comparative effectiveness studies have as yet been done against other systems, this assertion is itself entirely unscientific (Rennie 1994).

REVIEWERS

My own view is that, regardless of whether peer review improves the selection and quality of articles, when editors bring in others to assist their journal as peer reviewers, they are in effect democratizing the editorial process. This has the healthy result that more people feel involved, more are educated about the professional values that undergird the system, and the widespread paranoia that exists when authors offer up their precious reports to the tender mercies of journal editors may be lessened.

Scientific misconduct committed by reviewers during review (e.g., plagiarism) and misbehavior (such as blocking publication for personal gain) are the chain-saw massacres of research misconduct because they strike at the most tender part of the scientific process (Rennie 1999). But I believe that the major ethical problem with the customary system of review is a much more general one. Peer review is usually a black box. There are two ethically

balanced systems: either complete blinding of everyone to the name and institution of the author and reviewers, or complete openness so that the reviewers know who the authors are, and vice versa. My experience is that reviewers who sign their reviews invariably act responsibly, perhaps because their signature implies accountability (Ingelfinger 1974; Rennie 1994). Those journals, which include the *British Medical Journal*, that use this open system find none of the problems predicted by those unwilling to try anything new. Finally, we have a long history to tell us that secrecy is the enemy of justice (Rennie 1994).

AUTHORS AND THEIR CONTRIBUTIONS

Joshua Lederberg (1993, p. 10) bluntly summed up the importance of the written scientific report, "Above all, the act of publication is an inscription under oath, a testimony." Only when a piece of work is published is it possible for others to examine it fully, criticize it and attempt to replicate it (Rennie, Yank, and Emanuel 1997). For myself, I always assumed that my submitted manuscript was my best shot and I would have to stand behind what I had committed to paper and then to print. So the sort of behavior I described at the start seemed astonishing in its implicit contempt for the journal and its readers as well as depressing as a statement about the state of scientific integrity of at least some of its practitioners.

Publications are, of course, the coins that enable researchers to proceed along the road of academic advancement, but only too often, the researchers forget that the coins have two sides: credit and accountability (Rennie and Flanagan 1994). A common factor in cases before the 1995 U.S. DHHS, Public Health Service, Commission of Research Integrity was an eagerness on the part of authors to enjoy the credit associated with publication, coupled with a failure to accept responsibility for what they published when it was questioned. Indeed, a frequent experience for editors is to find out that the paper that had brought the authors so much attention had, in the face of a couple of hard questions, become an orphan. Time and again, the colleagues of gross fabricators plead ignorance of any direct knowledge of the data behind manuscripts despite signing forms indicating they were authors and previously taking public credit in the media (Stewart and Feder 1987).

In order to tie credit more closely with public accountability, my colleagues and I at *JAMA* attempted to challenge would-be authors to think

in terms of what each had contributed rather than their formal position in the hierarchy, and we devised and put into operation a simple method whereby authors disclosed this to the journals, and the journal in turn to the readers (Rennie, Yank, and Emanuel 1997). After more than a decade of persuasion, disclosure of roles as contributors has become the standard, adopted by the International Committee of Medical Journals and the large editors' organizations. It gives credit where it is due, increases transparency, which should surely be in the tradition of science, and allows us all to see who did the work.

Anyone who doubts the necessity for such a system should look at the problems faced by the committee investigating the American co-author of the South Korean scientist Hwang Woo-suk, who was later convicted of embezzling funds associated with false claims and faked data about his stem cell research (Summary Investigative Report on Allegations of Possible Scientific Misconduct on the Part of Gerald P. Schatten 2006, http://www.msnbc.msn.com/id/33476693/ns/health-cloning_and_stem_c). The journal *Science* had published some of Hwang's work in 2004, and in the report of the committee looking into the systems *Science* had adopted to prevent fraudulent publications (and the need for retractions) in the future, *Science* was advised to adopt just such a system of disclosure of contribution (Brauman 2006).

By the simple expedient of disclosing to the readers what individual authors claim to be their contributions, a considerable advance has been made in increasing accountability for published work. All journals should adopt this policy. (*Editors note*: In 2006, begun under the co-editorship of Harold S. Luft, *HSR* adapted this form and has since required all its authors to disclose conflicts as well as declare their roles as authors; this material is now published for all accepted manuscripts; Luft, Flood, and Escarce 2006.)

THE BIGGEST THREAT TO INTEGRITY: FINANCIAL CONFLICTS OF INTEREST

For the editors of large clinical journals publishing trials supported by industry money, their worst nightmare is the corruption of the entire process by money from the commercial sponsors. Enormous amounts have been written about financial conflicts of interest over the past 25 years, and numerous studies have confirmed what we all know: money talks (Bero, Galbraith, and Rennie 1992; Bero and Rennie 1996; Wazana 2000) What is, perhaps, surprising, is the

extent to which these studies show that, while we know that others can be and are corrupted by money, we also “know” that we ourselves are impervious to its influence (Dana and Loewenstein 2003). Even though pharmaceutical companies would not spend vast sums of money trying to influence doctors if they did not have evidence that it worked, researchers manage to convince themselves that they are personally immune to such tactics.

The problem scientifically, and from the point of view of patient care, is that the independent thought of the clinical researchers is hobbled by such practices, and they do not know it. Richard Feynman, the physicist, addressed the issue in his autobiographical sketches, “Surely You’re Joking, Mr Feynman!” (1985, p. 341 quoted from his 1974 address to Caltech students; Feynman and Leighton 1985). Discussing the frank and fair reporting of science, Feynman said it must be based on “. . . scientific integrity, a principle of scientific thought that corresponds to a kind of utter honesty—a kind of leaning over backwards. The idea is to try to give all of the information to help others to judge the value of your contribution; not just the information that leads to judgment in one particular direction or another. . . . The easiest way to explain this is to contrast it with advertising.”

It has been clear for at least two decades that, when clinical researchers have a financial stake in the results, it opens the door to a pervasive distortion of science (Rennie 2007). When a drug company sponsors a trial, the company employees usually select the drug tested, its dose, and the comparison drug. Company employees design the trial, often to produce the result they desire rather than to answer a scientific question. They have a powerful and fateful role in managing the trial, sometimes stopping it for reasons unrelated to science and despite any commitment to the trial participants (Psaty and Rennie 2003). They may even suppress the results completely (Rennie 1997). Company sponsors may parcel out tiny parts of the trial to hundreds of practitioners to accustom those physicians to prescribing the drug (“seeding trials”) (Hill et al. 2008; Sox and Rennie 2008). In addition, they collect and analyze the data, and write up the report. In other settings, companies may “ghost-write” favorable meta-analyses of clinical studies. Only after the design, methods, and results are completed may the academic “authors” be selected and paid to have their names on the byline, thus joining in all but name the marketing arm of the sponsor. And authors frequently ignore the requests of editors to disclose their financial ties.

Readers who seek more information about these practices are urged to study the extensive published correspondence following articles by Hill et al. (2008) and Ross et al. (2008) on guest authorship and ghostwriting, based on materials garnered from rofecoxib litigation (Hill et al. 2008; Ross et al. 2008).

Given these widespread practices, it is no surprise that the big medical journals are no longer willing to publish cost-effectiveness studies from industry simply because the editors cannot give full credence to claims of authorship, both named and unnamed, and can rarely access the data (Rennie and Luft 2000).

For journals publishing reports directly applicable to the care of patients, which is the editing world I inhabit, the distorting effect of money represents by far the single biggest challenge to the system's integrity (Rennie 2007). Meanwhile, the situation has been made worse by a political climate that favored stripping regulators of the power to regulate. For example, the Federal Drug Administration (FDA) has been emasculated. As a major new stream of funding for the FDA's critical roles of oversight and protection of the public's safety and health, the FDA has, since 1992, charged a pernicious user fee, which requires that companies seeking FDA approval pay the FDA to evaluate their drug applications. Congress has continued to reauthorize the relevant act. Predictably, this has had the effect of guaranteeing that the FDA, set up to protect the public, ends up beholden for its operating budget to the very industry the agency is supposed to regulate.

The health industry is vast and expanding. Money for health services research flows from government, and from innumerable commercial sources, very many of whom have a stake in the outcome of, say, comparative effectiveness studies. I have mentioned the wretched experience general medical journals have had with industry-funded cost-effectiveness studies. My expectation is that the editors of *Health Services Research*, given the vast sums of money at stake, will discover that the relevant pharmaceutical or insurance companies and the researchers they fund, will not all prove to be better behaved than the ones with whom I and my colleagues have been tangling ever more frequently for the past three decades. In other words, it seems to me certain that there will be health services researchers who will prove to be just as human, and just as venal, as the rest of us.

CONCLUSIONS

I have mentioned a few of the threats to the integrity of publication of clinical research, seen from the point of view of an editor of a general medical journal, whose job it is to buttress that integrity. Thirty-three years ago, when I began at the *New England Journal of Medicine*, research misconduct was almost unheard of, and certainly not defined; peer review was almost completely unstudied; authorship had not been seriously questioned and we had not come to think in

terms of contributions made; and, since academic researchers were not then allowed to profit from their inventions, financial conflicts simply never entered into editorial discussions. The FDA had the respect of the public and regulation seemed to offer a sensible brake on unrestrained capitalism.

To balance this sad litany, during these three decades, research techniques, not just in the clinical, therapeutic, and diagnostic sciences, but notably in the fields of trial design, in statistics and epidemiology, have made enormous leaps forward. It seems deeply ironic that as researchers produce more and more perfectly described reports, editors should be given more and more reasons to be skeptical, or even downright suspicious, of their results.

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