The Impact of Conflict of Interest on Trust in Science*

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ABSTRACT: *Conflicts of interest have an erosive effect on trust in science, damaging first the attitude of the public toward scientists and their research, but also weakening the trusting interdependence of scientists. Disclosure is recognized as the key tool for management of conflicts, but rules with sanctions must be improved, new techniques for avoidance of financial conflicts by alternative funding of evaluative research must be sought, and there must be new thinking about institutional conflicts of interest. Our profession is education, and both the public and research professionals of all ages would benefit from greater understanding of how science should and does work.*

The relationship of conflict of interest and trust operates at several levels, with different kinds of trust and different kinds of conflict of interest. Conflict of interest is not a new topic, and it is difficult to say anything new on the subject; it has been well worked over in the last decade.[1] Steiner gave a fine summary of the topic at a prior meeting in Warsaw on research ethics in 1995, later published.[2]

Public Trust in Science

First, the most obvious and recognized kind of trust, that of the public in the science which provides medical treatments. This is an extension of the traditional deep trust which individuals have for their physicians. Next is trust of those who ask them to volunteer as subjects for experimental treatments. Sometimes this is the same person with whom they have an established trusting relationship, but in many cases it is a nurse or doctor acting for a research group carrying out a clinical trial.

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Many research subjects have to be begged to read their informed consent form before signing it; they trust the investigator they know; they believe he or she has their best interests at heart, even if they are aware of his or her various reasons for recruiting them for the research study and the risks spelled out in frightening but boring detail in the consent form. There is a paradox here. Perhaps the patient has a conflict between rationally looking out for his own personal welfare and optimistically hoping for improvement or relief of his condition, as well as being honored for participating in the research study. The inducement of free diagnostic tests and medication, which might be hard to afford otherwise, may also account for the ease with which patients are recruited in some cases.

Scientists other than physicians doing clinical trials are also dependent on public trust. In general in the U.S., although there is a traditional distrust of science and scientists, public financial support for research has continued to grow. Think of the advances in physics and chemistry of the last 50 years, and how much public investment in research has made them possible. Commercial interest and support of research have also contributed, but not to the extent that the biomedical industry has paid medical professionals, in and out of academia. Somehow, scientists and engineers have dealt with their mixed financing without arousing serious public questions about the integrity of their research or endangering their reputations. Perhaps it is a matter of scale, or because medicine and health are so much closer to home. Clearly we physicians have a strong interest in avoiding widespread public cynicism about biomedical research, and should have an equally strong interest in not deserving it.

Scientists also are trusting in doing their research. According to S. Shapin, historian and sociologist of science, speaking at a symposium at the University of California San Diego (UCSD) in 1990 and in his book in 1994,[3] scientists in the 17th century first advised against trusting authority, but in so doing, were mainly rejecting Aristotle, whose influence had prevented scientific observations for hundreds of years. Science was supposed to rely on evidence from experiment. In practice, scholars relied considerably on the words of other contemporary scholars. However, it was understood that the gentleman-scientists of the day were always truthful in their descriptions of what they had done. This meant that researchers could rely on the observations and, to a lesser degree, on the conclusions of other scientists in planning and carrying out their work. A justifiable trust of a scientist in another's work remains an essential element in modern research.

Whether today's science practitioners have the same moral standards as 17th century gentleman-amateurs is debatable, but the important point is that the trust of scientists can be damaged by appreciation of factors that limit the reliability of prior work. Reliance on the printed word is central to scientific trust, which is one reason that respect for the literature has particular importance in judging whether someone has violated the norms of science. Interestingly enough, a formal presentation at a meeting or even a printed abstract is considered less reliable. The justifiability of this opinion might be that only about half of abstracts are completed and eventually published as refereed papers. The dark side, of course, is that scientists are willing to stretch their results for a trip to a meeting but not quite so willing to put inadequate evidence before the entire scientific community in a publication.

Beyond the efficiency of relying on prior published experiments in planning one's work, today's science increasingly relies on the exchange of materials—vectors, agents, chemicals—between laboratories. This truly remarkable exchange depends on trust in both laboratories that the donor is not keeping something back and that the recipient will not take the gift and push ahead, especially without publicly acknowledging the source of the material. Further, the ability of research trainees from different laboratories to exchange experiences and knowledge, an important part of their education, depends on trust between their mentors.

Peer review is an extremely important part of modern science, both in research grant allocation and in selection of papers for publication. This is also a remarkable system, built on trust. The fairness and impartiality of the reviewers must be equalled by their reserve in not appropriating information to their advantage and the disadvantage of the individual whose work is being reviewed. This trust breaks down a bit with the "hottest" science; for example there was an interesting tale that the manuscript of the first breakthrough paper on new superconducting materials used as protection a simple substitution of the symbol for one element instead of another in the chemical formulas, to be corrected in the galleys before publication.

I should mention that physicians are also very trusting in their acquisition of knowledge after leaving their academic training. The private consultations offered by drug company detail men or the special lectures and trips to teach about new drugs are supported by the pharmaceutical and equipment manufacturers because they work.

The government also trusts its scientists, giving them both money and responsibility in its allocation. However, the government is more careful in checking freedom from interfering interests, not only in its disclosure requirements for peer reviewers, but in the regulations imposed on research institutions to be more demanding. Peer reviewers and conference speakers are required to be much less forthcoming by most journals and professional societies.

Conflict of Interest

A few words about definition are necessary. When we speak of a conflict of interest, we mean that an individual who has a fiduciary or public-serving duty or interest also has a personal interest in the outcome of what he or she is doing. As Lo *et al* described the fiduciary interest,[4] "Conflicts of interest may occur whenever a person is entrusted with acting on behalf of others or in the public interest." In any original or creative research, of course, the investigator has an "interest" in the outcome, although it is unlikely to be a financial interest, unless the scientist is really doing the research to support a private company.

In evaluative research, however, such as the large volume of clinical trials which dominates political concern, both financial and non-financial interests often play a role. These interests are not "potential;" they either exist or don't exist. Their potential is to damage research objectivity by causing bias, which induces deliberate or inadvertent error. The protection against either kind of error is scrupulously careful research, with experimental checks and balances. But if the reward for altering the research outcome

or rendering professional judgment in a biased manner becomes too great, then the scientist should not be left to his own devices to ensure objective research. This is where disclosure and oversight come in.

There are many conflicting interests in the world of science and medicine, but the conflicting interests of different parties do not constitute what we call conflict of interest. This was a relatively common misconception of speakers at this conference. Another problem is that many speakers relied on a flawed definition of conflict of interest. This unfortunate definition talked about conflicting interests as "especially" those that "tend" to "unduly influence" behavior. It doesn't matter whether the personal interest does influence behavior or not, and the words "unduly" and "especially" don't belong in any definition; if the person has an interest that clashes with the fiduciary interest, then a conflict of interest exists. Any conflict of interest has the capacity (potential, if you will) to affect the conduct of research, and this is what must be managed.

It's easy to adopt a euphemistic definition because it would be nice to deny the existence of a conflict of interest, but it is much more practical to accept it and go on from there. For example, in Steiner's definition,[2] "a conflict of interests exists when a secondary interest—a financial interest, in these cases—may influence or appear to influence the judgment of the university and the research scientist in carrying out their primary missions ..." But a conflict of interest exists whether or not judgment is influenced. Appearance becomes a serious issue when there is no conflict of interest at all but someone suspects there is; however, if there is a conflict, and it is apparent, then the institution must work much harder to overcome the presumption that judgment is affected. This is done by taking steps to manage the conflict and the research.

One more example: in the current survey of institutional rules on the conduct of research[5] it was reported that "most guidelines use variations of the following definition: 'Conflicts of interest are situations in which a University employee may have an opportunity to influence University administrative, business, or academic decisions in ways that could lead to personal gain or give improper advantage to others. The potential of real and perceived conflict exists when employees are simultaneously involved in more than one organization. Under all circumstances, actual conflict situations, as well as the appearance of conflict, should be avoided'." The tendency toward euphemisms is indicated by "may have an opportunity" in the first sentence. This should be "has motivation". The second sentence brings in that word "potential" that should modify "bias" but is used so often wrongly to modify "conflict" in a confusing context in which I suspect the authors meant "real or perceived" rather than what is written. And, as usual, the statement of how to deal with conflicts, the third sentence, is grossly overstated.[6] A refreshing number of speakers at this meeting recognized that "actual" conflicts of interest are ubiquitous, and cannot be wished away by clumsy semantics. Before you can assess the seriousness of a conflict of interest and strategize management, you have to acknowledge that it exists.

Given the existence of a conflict of interest, how do you decide the likelihood of bias affecting the result? The magnitude of the interest, financial or non-financial, is a well-recognized criterion. But the structure in which the research or judgment takes

place should not be ignored, either in assessing risk, or on taking steps to lessen it. Carefully controlled experiments, data monitoring boards, and frequent, open research meetings all can contribute to fight bias. The reward structure in academic research clearly increases the occurrence of non-financial conflicts of interest; these cannot be dealt with by mandatory financial disclosure, but by careful research protocols, designed to minimize subjective observations or choices.

The type of conflict of interest most likely to affect the public's trust, as reflected in institutional policies and regulations, is a financial conflict, where the scientist stands to gain financially as a result of a particular research outcome. Is the concern of the scientist for the patient or volunteer as strong if there is money to be made by proceeding with the research? It should be recalled that the undesirable risk of a conflict of interest is that the investigator's judgment may be biased, consciously or unconsciously, by a material interest. This judgment may be related to the circumstances of merely doing the research, or of interpreting the results. No one can trust scientific judgment as much if there is reason to suspect bias, regardless of an individual's prior reputation.

Institutional regulations increasingly require disclosure of financial conflicts, which can range from receiving grants from interested drug companies, to investigators doing double duty as advisors or even researchers for such companies, to owning stock or ownership interests in such companies. There is usually a threshold specified, such as $10,000, in such interests, that requires disclosure. Only a handful of institutions now require disclosure to patients or subjects,[7] as opposed to disclosure to the institution's administration, but this is evolving. A survey of medical schools found that 88% of the responders had policies that dealt with conflict of interest, and about half gave examples and exceptions, but relatively few required disclosure of conflicts when writing or speaking publicly or in seeking permission to use human subjects for research.[5]

Of course, there are lesser financial interests that are excused from these regulations: for example, trips and lectureships that in the aggregate do not exceed this amount, stock options that are not easy to value, and the "expense" money that comes with recruiting patients for clinical research. We should also note an interest in achieving research results that are worth publication, with increased likelihood of renewed competitive or drug research grants, a larger research laboratory, promotion, salary increases, and so on. No one seems to recognize that National Institutes of Health (NIH) money can have as much of an influence in inducing bias as any drug company money, and for much the same reasons. Despite this very real financial interest, conflict of interest regulations focus on relationships to profit-making organizations.

To make matters worse, one's enthusiasm for evidence-based medicine and practice guidelines must be tempered by awareness of the possibility of bias on the part of those who compile them for us.[8] Recent investigations have shown that favorable results in clinical trials are more likely in those cases in which the investigator has a financial interest in the study.[9,10] This should come as no surprise. Conscious or unconscious bias may result from a conflict of interest, without any deliberate

deception on the part of the investigator. The bad publicity given to science by the cases of research misconduct apparently motivated by a conflict of interest has colored the entire debate over conflict of interest, as pointed out by Korn.[11] The very definition of conflict of interest has suffered from confusion with misconduct or bias arising in a conflict situation.[6]

Unfortunately, investigative reporters in the media[12] tend to focus on any financial conflicts they can dig up on clinical researchers, to the exclusion of considering the roles of chance, error, ignorance, or other sources of bias. Someone with a historical perspective might observe that many errors and deceits have been the result of interests that were not financial in any sense, but probably from biases induced by other interests, such as being the originator of a theory, discoverer of a potentially useful drug, a skeptic about some other scientist's results, or someone susceptible to wishful thinking. Or, in some cases, someone whose fiduciary interest in the welfare of his patient or research subject was subordinated to a misguided scientific curiosity—I am thinking of terrible experiments such as the Tuskegee observations of syphilitic men, or the Nazis human experimentation, but also the more commonplace enthusiastic embrace of a novel treatment or diagnostic method that leads to rather casual care and selection of the individual patient.

But the factors that make a scientist lose trust in another are more likely to be the result of personal knowledge about conflicts of interest which are not disclosed to the public, but are in the realm of personal preferences, style, or choices. The details vary, from knowing someone is too dedicated to his theory to produce reliable data, to being suspicious about a rush to publish which often results in retractions and corrections. Eagerness for priority, a stimulating but certainly dangerous interest, is common among researchers but not usually recognized outside academia. It casts a shadow on the trustworthiness of a researcher among his fellows when it is recognized. Of course, a scientist's consequent withholding of trust reduces the efficiency of research since previous results must be repeated or challenged. Further, modern research requires ready exchanges of materials, specimens, and information. Mutual trust is an important element in this traffic, for reasons which must be evident.

Institutional Conflict of Interest

This topic, mentioned briefly in my discussion of definition a decade ago,[6] and analyzed provocatively in 1995,[13] has reached the national stage, with a major, clear-headed report from the Association of American Universities (AAU).[14] If individual conflicts are a difficult problem for administrators and government, then institutional conflicts are now almost insoluble. The investments of universities in the commercial ambitions of their entrepreneurial faculty are applauded by those in the government eager to let academic research pay its own way, and by those businessmen who have found their way into academia disguised as administrators, but deplored by everyone else. How can faculty members compete on a level playing field if some of them are personal favorites of the coaches? And how can the critical oversight functions of a university be exercised if they might compromise the budget's bottom line? A single entity cannot maintain research integrity while administering an institution's financial interests in research-related investments.

Implications for Management

Everyone seems to agree that the first step in management of conflicts of interest is adequate disclosure.[2] Since 1995 the NIH has allowed its grantees, the research institutions, to define the parameters of the problem and its management with the unfortunate result that most institution's policies are incomplete or unbalanced.[5,7] Since scientists' personality traits are hard to change, there is perhaps not much that can be done about many non-financial conflicts. However, management priority should be on research that affects people, and this requires more honest and careful implementation of disclosure requirements. This means well-written and disseminated policies, with clear rules and penalties described. This does not necessarily mean that faculty will be prevented from a range of research activities, but that oversight and accountability must both be increased.

Universities do not wish to discharge innovative faculty who have commercial ties,[9] and it should not be necessary to make them renounce any or all financial interests or take leaves of absence. Oversight of research projects by faculty committees was a promising alternative, but it is difficult to implement in practice. Substitution of "independent" scientists for critical data-gathering and analysis would be alright if the money paying for the research were not also paying their salaries. But what untainted source of funds would pay individuals to work on specific research projects?

I discussed this problem some years ago,[15] recommending a way to insulate the investigator from any company with a strong interest in the research turning out a certain way (that is to say, any company funding research!), by funding evaluative research through an independent private agency. This is done in motor vehicle emissions research, which shows it can be done. While this would attack only a limited part of the spectrum of conflict of interest, that in which the pharmaceutical industry is involved, this is a significant chunk of the issue of public trust in science. Representatives of the ethical pharmaceutical industry say that they have no desire to get falsely favorable results from researchers, but even if they believe this, do the researchers? However, insulation or buffering between the source of money and the medical investigator has yet to be tested.

The problem with a conflict of interest, it must be reiterated, is bias in planning, performing, or analyzing the research, not the potential enrichment of the researcher. Research protocols must be scrutinized carefully, to eliminate as much as possible the flexibility that could allow bias to creep in. Independent careful review of protocols, procedures, and statistics in the proposed research might be an effective and significantly beneficial way to deal with conflict of interest. More uniform policies for disclosure of interests would also help, although this leaves untouched the non-financial conflicts of interest that the public is hardly aware of.

Institutional conflicts of interest also deserve further consideration, with the idea of insulation or buffering, between the parties. If the investments of institutions are owned by their Foundations, as is typically the case, then there should be a strong wall built between the parent University and each foundation. The deans and college presidents should not sit on the foundation boards. It would be even better to have a consortium of

institutions create an independent private organization to manage the investments that come to the institutions. Clearly, the officials responsible for running the academic institution should not have to watch how personnel decisions affect the income flow from business entities. Investment in the outside companies of faculty should be a business decision by a corporation or foundation, not by a university or medical school.

One other area of action should be considered, something that we should be very good at, namely, education. Training of future researchers in the ethics of human subjects research as well as the formalities of disclosing conflicts of interest is necessary, and being undertaken with increasing enthusiasm. Educating the public is also necessary, since some of the disaffection that must concern us is due to unrealistic expectations of what science can and should do. Scientists trying to justify themselves are responsible for some of the hype which has led to excessive expectations. Increasing the public's understanding how science really works may show many the imperfect way we arrive at working truths, and the positive role of investment and industry in stimulating that search. Trust is better engendered by knowledge of how scientists work than by blind faith.

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