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Full Disclosure: Where is the Evidence for Nefarious Conflicts of Interest?

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Background

Recent years have seen increasing focus on relations between physicians and industry, particularly pharmaceutical and device companies, and the conflicts of interest (COIs) that might arise from them.¹ Specific abuses of such relationships have often garnered national attention through scholarly journals and public communications media.^{2,3}

In May 2009, the American Association for Thoracic Surgery (AATS) and the Society of Thoracic Surgeons (STS) jointly adopted a report establishing standards for proper relationships between individual cardiothoracic surgeons and industry.^{4,5} One of the standards addresses the question of disclosure: "Members should disclose their own or their institutions' financial relationship with the manufacturer of a drug or device whenever clinical research or experience with a particular procedure or device is presented at a meeting or is published."

This standard is stated in broad terms, and the precise meaning of "disclose" is not spelled out. The AATS and the STS require that all authors must disclose relationships with companies that could constitute a COI before their papers can be presented at annual meetings.^{6,7} Both organizations report only the name of the possibly conflicted author, the company with which he has a relationship, and the nature of the relationship. No other details are published in the annual meeting program.

The AATS and STS official journals, *The Annals of Thoracic Surgery* (ATS) and the *Journal of Thoracic and Cardiovascular Surgery* (JTCVS), respectively, have specified the details of industry relationships that must be disclosed before a paper will be published. If a conflict is disclosed, The ATS places a text box on the title page of the published article: "Dr. X discloses that he/she has a financial relationship with company Y." No additional details are provided.⁸ The JTCVS Disclosure Statement requires reporting not only the name

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of the company with which a conflict exists and the nature of the relationship, but also the dollar amount received by the author—other details, such as the duration of the relationship, are omitted.⁹

The *published* disclosures of COIs for these annual meetings and journal publications include neither dollar amounts nor duration of the reported relationships.

Should Full Disclosure Include Dollar Amounts and Relationship Duration?

Cardiothoracic surgeons are familiar with the requirements of disclosure of COIs in presentations and in publications, as they are ubiquitous in presentations at meetings and papers in journals. In answer to the question of whether increased levels of disclosure are needed, J. Peter Murphy responds in the affirmative in the accompanying article, and argues that we should add dollar amounts and duration of relationships to current requirements.¹⁰

Most scholarly discussions of this issue as well as deliberations within organizations and revelations by the media embellish a paucity of facts with unsupported assumptions and sometimes hyperbolic assertions that intuitively seem either true or false, depending on the reader's pre-existing biases. Murphy's presentation contains some unsupported assumptions: "Without full and absolute transparency regarding these potential conflicts, we are in danger of losing the trust that the public has in our profession." "... [I]nvariably our patients will demand more information as they become increasingly aware of the extent of physician/industry relationships." "Collaboration has been valuable, but full transparency is critical to open, unbiased scientific dialogue and exchange." Where is the evidence that these assumptions are true? The article also contains hyperbole, for example, claiming certainty for assertions that are far from certain: "Can disclosure absent these critical details truly be considered 'Full Disclosure?' Certainly not." "It is rational that we attempt to manage conflicts of interest internally, and certainly if we do not, the Federal government will become even more intrusive than they are presently." One might believe this statement to be true, but what the Federal government will or will not do, in my experience, is rarely certain.

Unstated assumptions may be important as well. For example, Murphy assumes that listeners at conferences and readers of journals will pay attention to and be guided by additional relationship information. His case would be strengthened if he could provide evidence that listeners and readers put any thought into disclosures that are currently provided, because absent such evidence, why should we believe that providing additional disclosures will have beneficial effects?

Arguments Against Disclosure of Relationship Duration and Payments

Murphy makes several observations with which we agree: COIs are not related only to money, but also to non-financial considerations such as career advancement and academic achievement; the collaboration between industry and physicians has been highly productive and beneficial for patients in the past; some but not all financial interactions between industry and physicians are unseemly or worse; hard evidence for the existence or severity of the problem is in short supply; and, finally, the status quo is unsatisfactory.

In making the case for increasing disclosure requirements to include dollar amounts and duration of relationships, however, Murphy cites what he understands to be the two “legitimate” arguments against such a requirement: it is an intrusive, gratuitous invasion of privacy and collecting the data and reporting it are difficult and costly. These seem of minor importance, however, compared with two much more important counterpoints to the position he espouses: the real danger of slowing if not interrupting the highly productive research and innovation that has come from physician-industry collaboration over the last half-century, and the nearly complete absence of reliable evidence that this collaboration or any other interactions between physicians and industry poses a serious problem to patient safety. Indeed, it may be that the entire enterprise of requiring COI disclosures is a collection of solutions in search of problems.

Productive Research and Innovation

To appreciate the progress that has been made through physician-industry collaboration, one need only mention the pump oxygenator developed by Dr. John Gibbon collaborating with engineer Thomas Watson of IBM, the cardiac valve prosthesis developed by Albert Starr collaborating with engineer Lowell Edwards (resulting in the creation of the highly successful Edwards Laboratories), and external then implantable pacemakers developed by Dr. C. Walton Lillehei collaborating with engineer Earl Bakken, creator of Medtronic. Each of these pairs represent collaboration between a heart surgeon and commercial engineers, each of which led to a major advance in heart surgery; many others could be cited in most other surgical specialties, such as orthopedics and neurosurgery.

The contributions to human welfare by cooperative work between physicians and industry—both pharmaceutical and device companies—have been enormous. In the last few decades, fully half of the reduction in deaths due to coronary artery disease can be attributed to collaboration that has led to improvements in evidence-based therapies.¹¹ Indeed, such advances would not have been possible without the merging of knowledge and skills of businessmen, engineers, and technical experts in industry with the clinical expertise of physicians, whose knowledge of clinical needs and the ways in which drugs and devices interact with the human body was indispensable to innovation. The higher the barriers that are erected between the creative minds of industry and of medicine, the less innovation and improvement of human health are likely to occur. Admittedly, there is little clear and convincing evidence that physician-industry collaboration has been harmed by current disclosure requirements, but given the amply proved benefits of such collaboration and the absence of scientific evidence of harm caused by that collaboration, the burden of proof rests on those who wish to impose additional regulation.

Absence of Evidence

The facts underlying the national debate on relations between industry and physicians are seen to be meager when stripped of assumptions grounded in intuition and unsupported assertions. Murphy clearly substantiates that there has been much negative publicity in the media, some emanating from Congress, about disturbingly high levels of payment from industry to some physicians. Beyond that, very little hard evidence indicates that physician

COIs vis-à-vis industry pose a serious threat to health care. Nearly all of the experimental research underlying this concern comes from the psychology and sociology literature, from which physician behavior is projected from investigations carried out in non-medical contexts. Most of the remaining evidence comes from surveys of the views and experiences of physicians, residents, and patients.¹⁰ Both of these data sources have low probative value.

The ranking and relative value of evidence types has been investigated and described by several groups, such as the US Preventive Services Task Force (USPSTF)¹² and the GRADE Working Group.¹³ Rankings of the relative value of different kinds of evidence may be helpful in thinking about the question at hand. (Table 1) All of the evidence supporting the need for a high level of scrutiny and regulation of physician-industry relations falls into Code D, Quality of Evidence = Very Low, suggesting that existing data are far from dispositive of this issue. Moreover, the lowest of five ranks on the USPSTF effectiveness of evidence scale is authoritative statement: “Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.”¹⁴ We ought to exercise extreme care in using currently available information, all of which is of low quality, to make important policy decisions.

Murphy admits that the data supporting his position is weak and points to the difficulty of carrying out randomized controlled trials in this area, implying that the only alternative to anecdotes, surveys, expert opinions, and extrapolations from experiments in unrelated fields is a randomized controlled trial. There are many other kinds of evidence, however, such as nonrandomized prospective and retrospective studies of various types. In fact, one particular study that is both feasible and relevant to the debate has not been done. It is related to the critical central issue, the reason why anyone cares about physicians’ COI: the possibility that COIs cause harm to patients. The variable of harm to patients should be the primary outcome measure in studies of the concerns about COI, disclosures, and conflict management. Yet, *no study, retrospective or prospective, has been carried out to examine the effects of physicians’ COIs on the outcomes of patient care.* In the absence of this critical information, no rational policy to regulate physician-industry relations is possible.

This writer recently undertook an extensive search of the biomedical literature and was able to find only a single paper that addressed, albeit indirectly, COI and clinical outcomes. It is a meta-analysis of patient outcomes after autologous chondrocyte implantation, comparing commercially funded with independently funded studies.¹⁵ The authors found no difference in patient outcomes between the two groups. Although this evidence is from meta-analysis, therefore of only intermediate quality, it does not support a need for intensified regulation of physician-industry relations.

Until we have well-designed and executed studies of physician-industry COI that use the outcomes of patient care as the primary outcome measure, we will not be able to weigh the benefits to patients (known and documented medical innovation and improved health outcomes) against the harms (as yet undocumented compromise of health outcomes caused by physicians’ biases in prescribing and using drugs and devices due to COI). Without such studies, we cannot create rational policy and law on physician-industry relations—that is, we cannot rationally decide whether optimal health care can be achieved most reliably by

strengthening disclosure requirements, as Murphy argues, or by encouraging collaboration between physicians and industry by breaking down barriers rather than building them. At this time, the latter, although politically unpopular, seems the more reasonable course.

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Table 1
Levels of evidence and need for further research

Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Code	Quality of Evidence	Definition
A	High	Further research is very unlikely to change our confidence in the estimate of effect. • Several high-quality studies with consistent results • In special cases: one large, high-quality multi-centre trial
B	Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. • One high-quality study • Several studies with some limitations
C	Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. • One or more studies with severe limitations
D	Very Low	Any estimate of effect is very uncertain. • Expert opinion • No direct research evidence • One or more studies with very severe limitations

Source: GRADE (Grading of Recommendations Assessment, Development and Evaluation) Working Group 2007 ¹ (modified by the EBM Guidelines Editorial Team)¹⁶