Managing Conflicts of Interest: The Road Ahead

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Recent allegations have accused “respected experts” for purportedly promulgating information and opinions to physician-consumers while concealing their conflicts of interest (COIs) and commercial bias.1 The news blitz stemming from these transgressions has led to intense examination of the relationship between physicians and companies that sell medical products and devices. Universities, professional societies, and government agencies uniformly condemn such practices and endorse a variety of methods to reduce the likelihood of commercial influence on activities that are designed to be objective.2,3

In 2008, the American Society of Nephrology (ASN) created a committee to review the Society’s policies and practices regarding its interface with commercial interests. The committee submitted its ensuing report to the ASN Council and published a summary of its final recommendations—which were unanimously approved by council—in this issue of JASN.4

There are four largely separate but contiguous processes whereby commercial interests could influence how physicians provide treatment to patients: conducting research, publishing scientific information, educating practitioners, and developing policy. ASN’s educational efforts comprise the majority of the Society’s interactions with commercial interests and, not incidentally, draw the most national attention from the perspective of potential COI and commercial bias. Thus, ASN conducts its major activity squarely in the sights of those who seek to eliminate the possibility of commercial influence in the process of educating practitioners.5

The ASN Committee on Corporate Relations struggled with the meaning and definition of COI. It is widely recognized that everyone has some form of conflict. Although we did not develop a unique definition, we generally agree with the definition proposed by the Institute of Medicine (IOM).6 The practical consequence of this definition is that identifying COI should focus on financial conflicts because they are more objective and better suited to regulatory scrutiny. However, although the committee focused its analysis on financial entanglements, we recognize that professional conflicts should be considered when implementing the proposed recommendations.

This emphasis on financial conflicts transforms the focus of bias. We considered one definition of bias as “a conclusion or recommendation based on opinion unsupported by facts.” According to this definition as applied to medicine, almost no recommendation can be totally unbiased. The practical resolution of this matter is to focus on commercial bias, which the committee defines as “an inadequately supported judgment or recommendation about the use of a commercial product.”

The committee made no recommendation regarding the highly controversial issue of continuing medical education (CME) funding. However, the sentiment of the committee is more closely aligned with IOM’s recommendations rather than other recommendations directed at eliminating industry support for CME.5,6

The IOM report makes two important points. First, CME is essential to providing high-quality care to patients and, therefore, its importance is increasing. Second, there is no information on the consequences of making a dramatic shift in funding for CME. Making a major change in how CME is funded in the absence of data will have unforeseen consequences.8 The committee generally agrees that any changes should be subject to careful review and testing.

The committee strongly endorses the concept that there should be clear separation between the development of the content of educational programs and the generation of financial support. We are impressed with how well ASN has implemented this policy during the past few years.

Although virtually everyone can agree that there should be no commercial bias in CME activities, there is surprisingly little understanding of the practical implications of this policy. There are two processes for uncovering potential COI and commercial bias. The first is the process of disclosure. The second is the evaluation of presentations by designated observers and participants.

Disclosure is strongly endorsed by all groups. The Accreditation Council for Continuing Medical Education (ACCME) requires disclosure of accredited providers, including ASN. However, what should a speaker disclose? There is wide...
agreement that a speaker should disclose all financial relationships with commercial entities. In addition, some interpretations of ACCME regulations would require that speakers disclose financial relationships with governmental and not-for-profit organizations.

What should participants in CME events expect a speaker to disclose? We recommend that speakers be required to clarify at the beginning of their presentations all involvement with commercial interests. To further ensure transparency, moderators should highlight specific information about financial ties to organizations that make products that are relevant to the subjects discussed.

The committee attempted to understand how to identify commercial bias in a presentation. As we discovered, there are no widely accepted criteria for identifying commercial bias. ASN’s approach has included an independent review of all slides before a presentation and a (required) question on the CME evaluation form to be completed by all participants pursuing CME credit. In some circumstances, ASN has requested an independent evaluation by selected reviewers. The committee’s review produced no clear evidence of commercial bias in any presentation during ASN educational programs. However, we discovered that some participants may have perceived commercial bias when designated observers detected none.

Thus, we are in the unenviable position of trying to eliminate a practice that is evidently rare in ASN educational programs and for which there is no clear definition. Nevertheless, the committee made two recommendations that should heighten awareness of possible commercial bias and begin to assess criteria for its identification. First, ASN should increase its efforts to identify specific individuals to attend presentations and evaluate possible commercial bias. Second, ASN should educate participants about the expectations for disclosure, what constitutes commercial bias in practice, and how to identify potential bias.

The generation of new information must be conducted in an objective fashion. Such objectivity is the foundation of scientific advancement and the development of effective medical therapies. The committee determined that ASN’s journal editors follow well-accepted practices for requiring authors to report conflicts. We recommend that the ASN Publications Committee and the journal editors continue to assess developments and adjust their policies and procedures as new opportunities arise. However, we believe the Society must pay more attention to the possibility of commercial bias in the review process.

We recognize that reviewers might have positive or negative predispositions to the conclusions emanating from a given set of data. Some of these predispositions might be influenced by commercial interests. Given the considerable importance of decisions for publication, and that relatively few people are usually involved in such decisions, we recommend that ASN reassess this process. In particular, we recommend that ASN reviewers abide by the same disclosure requirements as the authors they review. This requirement also applies to abstract reviewers. During our evaluation, we realized that the presentation of an abstract reporting the effects of a new product could influence the stock price of the sponsoring company.

All ASN members who participate in the Society’s committees, boards, and advisory groups are required to complete a disclosure form. The committee appreciates that different groups might require different kinds of information on potential conflicts. We recommend that ASN’s process for reporting and evaluating potential conflicts reflect the specific needs of each group (which includes policy development, education, publications, and grants review) within the context of the Society’s overall policy. The committee favors making the disclosure process as simple as possible for each member. To require all members to complete extensive disclosure forms risks an overly bureaucratic process with consequent disincentive to participate in Society activities.

To whom should COI disclosures be made? Disclosed information that resides in a vacuum has no value. Thus, a critical component of disclosure is appropriate review by Society leaders with decision-making authority. These leaders must also inform group members of participants’ potential conflicts. The entire process may be group specific, will need to evolve, and should not be imposed by executive fiat.

The process of managing COI is an ongoing activity and will evolve over the next several years and beyond. It will continue to be an important activity irrespective of how national policies of funding CME activities emerge. We live in an age where COI is seemingly encouraged and discouraged. Universities, government agencies, and the public encourage entrepreneurship as a part of our responsibility to develop solutions for medical diseases. However, these same groups, together with professional societies, rightly insist that COI be managed with optimal transparency.

Threading the needle of fairness, transparency, and appropriate privacy in managing conflicts is a daunting task. For this reason—and the fact that this will continue to be a rapidly evolving area—we recommend that ASN develop a group to regularly review the Society’s policies and practices for evaluating and managing potential COI and make recommendations for their modification.

ASN’s mission is to lead the fight against kidney disease. Members can be assured that there is healthy attention to the process of managing COI and that our Society will be in the forefront of developing ways to evaluate its success.

DISCLOSURES

As is the case with all editorials, the opinions reflected here are the authors and not necessarily the policy of the ASN.

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Signaling at the Slit: Podocytes Chat by Synaptic Transmission

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Glomerular podocytes are unique in form and function. With a highly organized cytoskeleton to counteract transmural distending forces, they serve as part of a molecular sieve that establishes the permselective properties of the glomerular filter. Podocytes consist of a voluminous cell body, which bulges into the urinary space, and highly branched foot processes.1 The foot processes of neighboring podocytes regularly interdigitate, leaving meandering filtration slits between them that are bridged by the slit-diaphragm.3

In addition to the common structural organization of podocytes and neurons, both cells share several highly tissue-specific proteins such as nephrin-neph proteins, which drive the formation of slit-diaphragms in the kidney and synapse formation in Caenorhabditis elegans motorneurons,4 amino acid transporters such as CAT3 or EAAT2,5 ion channels such as BKCa,6 catecholamine receptors,7 and axonal guidance factors.8

The slit-diaphragm is linked to and tightly regulates the actin dynamics of foot processes.9 Strikingly, among these actin-linking proteins, an increasing number of “neuronal” proteins have been identified as crucial determinants of actin-based cell processes, such as synaptotagmin, dendrin, or its interacting partner KIBRA—a protein recently associated with learning and memory.10 These findings emphasize the hypothesis that foot process dynamics and neuronal synaptic plasticity are regulated by an analogous set of molecules.11–14

Recent studies have changed our conception of the glomerulus from a relatively static structure to a dynamic one, whose integrity depends on signaling mechanisms at the filtration barrier.15 Typical epithelial cell layers often use gap junctions to rapidly and efficiently exchange chemical and physical signals. However, epithelial podocytes, being kept apart by slit-diaphragms, are probably not able to form gap junctions under physiologic conditions, implying a role for alternative communication pathways between cells. Thus far, very little is known of the intercellular signaling that might dynamically fine tune the complex three-dimensional foot-process network.

In this issue of JASN, Giardino and colleagues demonstrate an exciting form of intercellular signaling by podocytes using neuronal glutamatergic transmission systems to regulate the maintenance of the foot process network.16 Previously, these authors found podocyte-specific expression of the small GTPase, rab3A, and its effector, rabphilin 3a; both proteins play an important role in Ca2+-dependent exocytosis of synaptic vesicles.17,18 Interestingly, synapses of neurons form a cleft of 20 to 50 nm, which is quite similar to the ~40 nm width between foot processes. Earlier electron microscopy studies also showed the presence of “synaptic-like” vesicles in the secondary foot processes of podocytes and the expression of a functional glutamatergic synaptic transmission system, providing a clear hint that podocytes not only exhibit synaptic plasticity but also execute synaptic-like communications.

Giardino et al.,16 now perform an elegant in vivo study by using rab3A-null mice and pharmacologic antagonists of N-methyl-D-aspartate (NMDA) receptors to block the glutamatergic signaling system. They observe rab3A deficiency as well as the blockade of NMDA receptors results in increased albuminuria. In vitro experiments using cultured podocytes reveal the inhibition of the NMDA receptor rearranges the actin/myosin cytoskeleton and the loss of rab3A causes uncoordinated exocytosis of glutamate-containing vesicles. Taken together, the authors uncover in their pioneering work a functional synaptic transmission system that seems to bridge the slits for interpodocyte communication, supporting the idea that podocytes share not only morphologic features but also use cell communication networks similar to neuronal cells.
ASN COMMITTED TO MANAGING CONFLICTS OF INTEREST
ASN Publishes Policy on Conflict of Interest

Washington, DC (August 21, 2009) — Twenty-six million Americans suffer from kidney disease, and for decades nephrologists in academia, practice, and industry have enhanced their quality of care. To ensure that partnerships between the American Society of Nephrology (ASN) and industry continue to improve kidney health, ASN leaders convened the Committee on Corporate Relations in 2008. Publications resulting from this committee’s efforts set will help guide medical societies and industry in their efforts to advance patient care, research, and education.

In an upcoming issue of the Journal of the American Society of Nephrology (JASN), ASN publishes the “ASN Policy on Managing Conflicts of Interest” and presents 10 recommendations that guide best practices on how to “design, monitor, and enforce regulations that insure appropriate Society’s interactions with industry.” Drawn from ASN’s long history of responsible partnerships with industry as well as extensive research and self-assessment, this article provides compelling guidelines for ethical approaches to these important partnerships.

These recommendations “are based on the premise that societies can develop beneficial partnerships with commercial interests as long as the Society’s leaders, staff, and members appropriately and responsibly manage their relationships with these entities.” The ASN Council unanimously approved all 10 of the committee’s recommendations.

In coordination with the online release of the article and an accompanying editorial entitled, “Managing Conflicts of Interest: The Road Ahead,” ASN will launch a webpage on August 27 that provides information about managing conflicts of interest on the Society’s website (www.asn-online.org) that includes:

1. Links to the above mentioned JASN article and the “Final Report of the ASN Committee on Conflict of Interest”;
2. A timeline that includes links to important resources on conflicts and bias; and
3. Information about congressional legislation related to conflicts and bias.

ASN will also address this topic during its upcoming annual educational meeting, Renal Week 2009, which will take place from October 27-November 1 in San Diego, CA. Bernard Lo, MD, who chaired the IOM panel that produced “Conflicts of Interest in Medical Research, Education, and Practice,” will present the Christopher R. Blagg Endowed Lectureship on “Conflicts of Interest in Medicine” on October 29 during the Public Policy Forum from 1:30 p.m. – 3:30 p.m.

In the conclusion of “ASN Policy on Managing Conflicts of Interest,” ASN invites other medical societies to “join together to articulate national standards for managing relationships with commercial interests.” The Society continues to lead the fight against kidney disease by attempting to address complex areas of significance, such as the management of conflicts of interest.


Founded in 1966, the American Society of Nephrology (ASN) is the world’s largest professional society devoted to the study of kidney disease. Comprised of 11,000 physicians and scientists, ASN continues to promote expert patient care, advance medical research, and educate the renal community. ASN also informs policymakers about issues of importance to kidney doctors and their patients. ASN funds research, and through its world-renowned meetings and first-class publications, disseminates information and educational tools that empower physicians.

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