

Conflict of Interest and Medical Journals

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Conflict of interest (COI) affects every aspect of medicine, including clinical care, teaching, and research. According to one definition, “A conflict of interest exists when profes-



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sional judgment concerning a primary interest (such as patients' welfare or the validity of research) may be influenced by a secondary interest (such as financial gain). Perceptions of conflict of interest are as important as actual conflicts of interest.”¹ Over the past decade, there has been increasing attention to virtually every aspect of COI in medicine, including reports from authoritative national committees,² federally mandated reporting of industry payments to physicians,³ enhanced policies and procedures governing COI at academic medical centers and research institutions, and efforts to harmonize reporting of COI overall⁴ and in scientific publications.⁵

This theme issue of *JAMA* is devoted to presenting new information on the evolving nature of COI. The issue includes 23 scholarly Viewpoints that represent the multifaceted aspects and complexity of COI from numerous perspectives, ranging from academic medical centers and industry to patients and the public. Harvey Fineberg, MD, frames the theme issue by emphasizing that understanding, dealing with, and continually improving what is known about COI is critical if physicians are to retain the trust that patients have placed in the profession.⁶ William Stead, MD, provides an overarching editorial on the various multidisciplinary aspects of COI covered in the Viewpoints and suggests that a systematic approach is needed in which all stakeholders in the health professions and biomedical sciences work together to protect professional judgment and integrity while ensuring medical progress.⁷

In addition, 2 research reports in this issue of *JAMA* present findings on COI involving physicians. In one study, Tringale and colleagues⁸ analyzed data from the Open Payments reports of industry payments to physicians in 2015 and found that 449 864 (approximately 48%) US physicians were reported to have received a total of \$2.4 billion in industry-related payments, with a higher likelihood and higher value of payments to physicians in surgical specialties than those in primary care specialties and to male physicians than female physicians. In another study, Larkin and colleagues⁹ used information from a data set that included more than 16 million prescriptions and compared prescribing by 2126 physicians at 19 academic medical centers that implemented policies between January 2006 and June 2012 that restricting pharmaceutical representative sales visits to physicians (“detailing”) with prescribing by a control group of 24 593 matched physi-

cians who were not subject to such policies. Introduction of academic medical centers' detailing policies was associated with a 1.67-percentage point decrease in the market share of detailed drugs (representing an 8.7% relative reduction in market share following the intervention) and a 0.84-percentage point increase in the market share of nondetailed drugs (representing a 5.6% relative increase in market share).

COI is a critically important issue for biomedical journals and editors. This editorial reviews journal policies governing COI and discusses important decisions and issues editors must address regarding COI related to research reports and opinion articles, resolving undisclosed COIs, and safeguarding against COI in the editorial decision process.

Journal Policies on COI

Effective evaluation and transparent management of COI are essential to ensure the integrity and credibility of published articles and to promote public confidence and trust in the scientific process and the credibility of published articles.¹ Accordingly, all authors of all manuscripts submitted for consideration for publication in *JAMA* and the *JAMA* Network specialty journals (including research reports, reviews, opinion articles, and letters to the editor) are expected to provide detailed information about all relevant financial interests, activities, relationships, and affiliations including, but not limited to, employment, affiliation, funding and grants received or pending, consultancies, honoraria or payment, speakers' bureaus, stock ownership or options, expert testimony, royalties, donation of medical equipment; or patents planned, pending, or issued.^{10,11} As stipulated in the International Committee of Medical Journal Editors (ICMJE) disclosure form, these disclosures should include “Any potential conflicts of interest involving the work under consideration for publication” (during the time involving the work, from initial conception and planning to present), any “relevant financial activities outside the submitted work” (over the 3 years prior to submission), and any “other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing” what is written in the submitted work (based on all relationships that were present during the 3 years prior to submission).^{1,10}

Although many universities and other institutions and organizations have established policies and thresholds for reporting financial interests and other COIs, *JAMA* and the *JAMA* Network journals require complete disclosure of all relevant financial relationships and potential financial COIs, regardless of amount or value. For example, authors of a manuscript about hypertension should report all financial relationships they have with all manufacturers and owners

of products, devices, tests, and services used in the management of hypertension, not only those relationships with entities whose specific products, devices, tests, and services are mentioned in the manuscript. Authors also should report all financial and material support for the research and the work (such as sponsor support and source of funding) clearly and completely in the Acknowledgment section of the manuscript. If authors are uncertain about what constitutes a relevant financial interest or relationship for an individual author or relevant support for the work being reported, they should err on the side of complete disclosure or contact the editorial office for clarification.¹⁰ In a Viewpoint in this issue of *JAMA*, Joseph Thornton, JD, editorial counsel for the Editorial and Publishing Group, emphasizes the ethical and legal importance of complete and accurate reporting of COI by authors.¹²

For all accepted manuscripts, disclosures of COIs and relevant financial interests, activities, relationships, and affiliations and declarations for each of the authors are published in the Acknowledgment section of the article, and thereby disclosed to readers. In addition, all financial and material support for the research and the work also is reported in the published article along with the specific role of the funding organization or sponsor in each of the following: “design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.”^{10,11}

The purpose of requiring detailed reporting of COIs and financial support and making this information available to readers (either in the published article or as some journals do, by posting the submitted financial disclosure forms online along with the published article) is to enable readers to evaluate the authors’ COI disclosures and the financial aspects of the published article and to interpret the information in the article accordingly in light of those disclosures.

As part of the editorial assessment process, editors evaluate the COI disclosure information reported by the authors and the financial support for the study and also consider potential COIs involving peer reviewers. Reviewers are expected to disclose potential COIs (financial or otherwise) to the editors at the time they are invited to review a specific manuscript and notify the editors to determine if the conflict should disqualify the reviewer from completing the review.¹¹ Not all COIs necessarily preclude an individual from reviewing a manuscript. In some cases, depending on the nature and extent of the COI and if the editor and reviewer agree that the reviewer can provide meaningful substantive comments related to the subject matter of the manuscript, the editor may request that the reviewer complete the review and disclose any COI and will evaluate the content and objectivity of the review in light of the reviewer’s potential COI. In addition, all peer reviewers are required to disclose any potential COIs or disclose no COIs when they complete and submit a review. In all cases, however, any information peer reviewers or potential reviewers receive about a manuscript must be kept strictly confidential, is not to be shared with any third parties, and must not be used to further their own interests or the interests of any others.¹¹

Research Reports

The potential for COI to result in bias can occur in any manuscript, although research reports ordinarily provide less concern regarding the influence of COI on the reporting of the results. In addition to requiring detailed reporting about COI from each author and detailed information about research funding and support, at *JAMA*, these articles are subject to both external peer review and in-depth internal editorial evaluation. For many reports, including randomized clinical trials and meta-analyses, standards have been established for reporting of the results. Although reporting standards do not eliminate COI, they provide a blueprint for what should be expected in a research report.

Several issues regarding COI and research reports require additional attention. Research reports funded by industry are either those in which industry supports the research project but has no involvement in the analysis or preparation of the manuscript for publication or those in which industry has key involvement in the study design, collection and analysis of data, and preparation of the manuscript for publication. Because of the inherent COI that industry sponsors have with publishing research reports that are favorable regarding their products, in general, it is preferable in studies with industry support for these sponsors to have a limited role that is prospectively defined and detailed.

In addition, some trial protocols and agreements with investigators include statements about the rights of the funder to review a manuscript prior to submission and in some cases to delay publication (for instance, up to a year). Delaying publication of any manuscript at the request of any funder (beyond a reasonable time for its review) is unacceptable, and no investigator or institution should engage in a contractual arrangement in which the funder can delay publication or has rights to veto publication.

In discussions with investigators at biopharmaceutical companies, it is clear that in some cases, they are involved in the design and conduct of randomized clinical trials. Some of these investigators have expressed concern that they may be excluded as authors or have been encouraged to add academic authors to ensure that their study would be fairly assessed during the review process. This is disturbing and unfair. Although the COI for these investigators is apparent, numerous safeguards are in place, such as those based on availability of trial protocols, statistical analytic plans, and trial registration information that should allow objective evaluation of the study. *JAMA* and the *JAMA* Network journals require authors of clinical trials to submit trial protocols, statistical analytic plans, and trial registration information with manuscripts to allow review by editors and peer reviewers, and for all accepted reports of clinical trials, this information is published with the articles.¹⁰

Over the past few years, it has become clear that a number of governmental agencies are providing greater oversight for manuscripts that are either prepared by their employees or funded with resources from those agencies. In some cases, even though this review process may be part of the legislative mandate of the agencies, this level of oversight of research manuscripts raises concerns. Just as industry sponsors should

not be able to delay or affect the submission of a manuscript or publication of an article, nor should governmental agencies. It is not clear how often manuscripts have been delayed or changed because of these reviews. However, all authors should be afforded the protection and academic freedom to publish the results of studies regardless of the interest of the funder, whether a governmental agency, foundation, or for-profit company.

Viewpoints, Editorials, and Invited Commentaries

Opinion articles represent a challenge for editors, and some journals indicate that they do not permit authors with any COI to write such pieces. In *JAMA* and the *JAMA Network* journals, Viewpoints are opinion pieces that are submitted independently of a research report (in contrast to Editorials or Invited Commentaries, which usually are solicited by the editors), and COI is considered in the review of the submission. Editorials and Invited Commentaries are opinion articles that usually accompany a published research report, and COI is always considered prospectively when selecting an author and soliciting the editorial.

For Viewpoints, Editorials, and Invited Commentaries, judgment and discretion are necessary, and issues related to COI and authorship are evaluated on a case-by-case basis. For instance, if it is clear that authors may directly benefit from publication of an opinion article, for example, if the authors own stock in a company that manufactures the product they are writing about, *JAMA* would be unlikely to publish such an article. In contrast, authors who have a consulting arrangement with or received a research grant from a company that makes a specific product would not automatically be excluded from writing a Viewpoint, Editorial, or Invited Commentary.

All opinion articles are reviewed for concerns about bias, such as when an author expresses strongly held opinions that appear not to reflect the data or evidence. This is particularly an issue in Editorials, for instance, when the author only emphasizes some results of a research report and does not accurately reflect the totality of the evidence. At *JAMA*, all Editorials are reviewed by the editor in chief and executive editor, as well as by the deputy editor or associate editor managing the research article, to ensure that the Editorial accurately reflects the research report.

There is subjectivity in the decision regarding who can and who cannot write Viewpoints, Editorials, or Invited Commentaries, and what represents a disqualifying COI. Many experts have various relationships with industry, such as consulting arrangements, grant support, or serving on data and safety monitoring boards, and automatically disqualifying such experts from expressing their opinion might represent a form of bias. It is the obligation of journal editors to ensure that these articles accurately reflect the evidence.

Undisclosed COIs

Even though *JAMA* requires authors to provide full and complete disclosure of their COIs, journal readers or other interested individuals often notify the editors that a particular author has not accurately declared his or her COIs. These concerns can be broadly categorized into 3 groups.

First, the allegation is determined to be correct. This may be based on, for instance, a search of the literature or Internet and comparing declarations of COI in previous articles with the current one, a search of databases that report industry payments to physicians, or by documentable previous knowledge of an individual's COI. In these cases, it is clear that there is an undeclared COI; the author acknowledges the error and a letter of explanation and a correction are published.

Second, there is an allegation of an undeclared COI, but the author disputes that the undisclosed information represents a relevant COI. In these cases, journal editors often have to adjudicate the dispute, which may be complex and may involve substantial time and effort. For example, an author consults with a company that makes various products that are unrelated to the published article. However, presumably unbeknownst to that individual, the company owns a wholly owned subsidiary, and the allegation is that given the company's ownership of a subsidiary with a financial interest in the content of the article, the author should have been aware of that issue and declared a COI. Another example might involve an author who consults to a nonprofit group, and that group receives substantial funding from industry. The allegation may be that although the author received funding from the nonprofit entity, given that the funding was a "pass-through" from a company and is related to the content of the article, that relationship should have been declared. There are other examples, many of which require adjudication by journal editors. In general, since the goal is to declare potential COI, authors should declare all COI, recognizing whether a reasonable person might perceive the relationship as a COI.

Third, apparent undisclosed COI may occur because of different time windows for reporting COI used by different journals. For instance, journals that follow the ICMJE policy and many other journals require reporting of all relationships that were present during the 3 years prior to manuscript submission, whereas other journals and entities may have longer or shorter time windows for potential COIs that need to be declared. These timelines are arbitrary, but may create the appearance of discrepancies for reported and unreported COI information among various sources.

COIs of Editors

Journals have various decision-making structures. At most journals, final decisions regarding acceptance of a manuscript for publication are made only by the editor in chief (often in consultation with other deputy, senior, or associate editors), whereas at other journals, other editors may make final decisions on manuscripts, usually regarding rejection of a manuscript. In virtually all instances, peer reviewers are considered consultants and although their opinions are important and influence the decision of editors, the recommendations of peer reviewers are advisory and not binding.

At *JAMA*, manuscripts are managed by associate editors, senior editors, and deputy editors, as well as the editor in chief and executive editor. These editors decide if a manuscript should be sent for peer review, assign peer reviewers if appropriate, and then after completing the initial review

process, present the manuscript to a group of editors for discussion about whether to proceed with inviting authors to submit a revised manuscript for further consideration. Decisions about the manuscript (such as revise or transfer to a JAMA Network specialty journal) are made following a discussion at a manuscript meeting.

Final decisions regarding manuscript publication are made by the editor in chief or a designated editor who does not have any relevant COIs.^{10,11} The journal has a formal recusal process in place to help manage potential COIs of editors. This COI could be financial, or the COI could be professional, such as may occur with familiarity with a research project, for instance, if an editor had served as a consultant to the project or had collaborated with the authors. In the event that an editor has a COI with a submitted manuscript or with the authors, the manuscript, review, and editorial decisions are managed by another designated editor without a COI related to the manuscript.^{10,11} In a Viewpoint in this issue, Neil Bressler, MD, editor in chief of *JAMA Ophthalmology*, details situations in which editors should be recused from making decisions about manuscripts and describes the policies and procedures involved.¹³

In part because of concern about possible COI of handling editors, *JAMA* and the JAMA Network maintain an appeals policy, whereby authors can appeal a decision made by the journal. Each year, *JAMA* receives approximately 30 to 35 appeals regarding editorial decisions; these appeals are adjudicated by the editor in chief and executive editor in consultation with the editor involved with managing the manu-

script, unless the appeal was based on concerns about COI of the handling editor. During the past 5 years, no appeals have been based on concerns about possible COI of a handling editor. However, *JAMA* remains committed to the appeals process for various reasons, including possible COI of the handling editor.

Conclusions

As the articles in this issue of *JAMA* demonstrate, there has been substantial attention to and significant evolution of various aspects regarding COI in medicine. With respect to research, this is in part because of several factors: the enormous and important resources that industry provides to support clinical investigation, with industry funding far exceeding National Institutes of Health funding for clinical research; the increasingly complex relationship between academic medical centers, individual faculty, and industry; the increasingly recognized potential COI that individual physicians have with respect to tests and procedures they may recommend; and the commercialization of medicine with start-up companies, various devices and apps, patents and ownership, and other intellectual property issues. Journals have a responsibility to respond to this changing environment. Accordingly, *JAMA* continually reviews its policies and procedures for evaluating and reporting COI to ensure that all published information represents valid results, that information about potential COI is reported clearly and transparently, and that the journal maintains the trust of physicians and the public.

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