Journal of the American College of Cardiology
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Published by Elsevier Inc.

Vol. 61, No. 11, 2013
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2012.12.030

EDITORIAL COMMENT

Conflicting Information About Conflict of Interest*

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Conflict of interest occurs when circumstances create a risk that a person's professional judgment or actions regarding a primary interest will be unduly influenced by a secondary interest. This has recently become a focus of attention for physicians and physicians' groups as well as for the lay press and some politicians—particularly financial conflict of interest (FCOI), which occurs when monetary or material inducements have (or are perceived to have) the potential to influence impartial judgment. However, the paper by Aneja et al. (1) in this issue of the *Journal* presents findings that may prove surprising to some. In an analysis of randomized

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clinical trials whose results were published in 1 of 3 high-impact journals (*The New England Journal of Medicine*, *Lancet*, and *JAMA*), Aneja et al. (1) found that authors with an acknowledged FCOI in addition to the primary research grant or contract (i.e., payments for consultancies or lectures, stock ownership, or employment) did not produce study manuscripts that were more likely to show positive results for the experimental therapy. This finding remained consistent even when FCOI reporting increased directly with the level of industry funding of the trial. The type of FCOI and the use of a surrogate endpoint in the relevant clinical trial were not statistically associated with greater likelihood of positive result reporting, although the p value for surrogate versus clinical endpoint was 0.051.

These are provocative findings, but their generalizability is limited by the methods used in the study. First, the articles examined by the authors were restricted to randomized trials published in 3 very high-impact general biomedical journals. Such journals are hardly representative of the general medical literature, because they are highly selective and typically publish findings from large, adequately powered trials that tend to be clinically interesting regardless of whether the results are positive or negative. We know that many clinical trials are not reported at all (2–4), and it is likely that even for most trials that are reported, the less prestigious journals in which they are published would be less likely to insist on accurate characterization of the results than the 3 prestigious journals that formed the substrate for the present investigation.

There is a significant body of literature indicating that self-reported FCOI is inaccurate (5), and as noted above, there is reason to believe that such inaccurate reporting may be more the case in less authoritative medical journals. Unfortunately, the authors did not interrogate the authors or the public record independently to clarify this issue. They would have made a much more convincing case if the veracity of the self-reports had been validated.

The National Institute of Medicine's ClinicalTrials.gov registry could play an important role in this regard by serving as a key instrument for research concerning publication bias and FCOI reporting. As of September 2007, there is a legal requirement to register almost all clinical trials relevant to United States practice; as of 2008, reporting of trial results is required. Given this level of available detail, the 3 critical dependent variables in such an investigation would be: 1) whether the results were published; 2) whether the results were positive, neutral, negative, or inconclusive for the new treatment; and 3) whether the interpretation in the publication was accurate, inappropriately more favorable than the results would warrant, or inappropriately less favorable than the interpretation coming from an independent review. Here again, it is likely that if biased interpretation exists, it may be more likely to be found in less prestigious journals, because the journals investigated in the study by Aneja et al. (1) provide robust editorial oversight of the introduction and discussion sections of the manuscript. However, recent work suggests that retractions are at least as common in more prestigious journals, although the underlying reasons for such findings are not yet clear (6,7).

One important step that would help to unravel this issue would be more uniform reporting of conflicts of interest, both to provide more understandable information and to reduce the burden on authors and investigators. Lichter and McKinney (8), building on a recommendation from the

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

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Institute of Medicine, recently suggested an approach for creating a central mechanism for reporting FCOI.

The complexity of this issue can be appreciated in the context of discussion about a manuscript purporting to show that FCOI among Food and Drug Administration Advisory Committee members led to inappropriately positive votes regarding new therapies, because conflicted members more often voted for approval (9). Although the authors found that this relationship pertained only to competitor drugs for the drug undergoing evaluation, the authors de-emphasized this aspect, leading to the study being cited as supporting an industry bias. However, when the Food and Drug Administration looked more closely, it emphasized the key finding that conflicted members actually were not more likely to vote for approval of the product for which they had a conflict, but they indeed were more likely to vote positively for a competitors' product (10). Unfortunately, the *JAMA* reference is still widely quoted for the general finding, whereas the more nuanced interpretation by the Food and Drug Administration itself is buried on its website.

An additional factor that should be considered is nonfinancial conflict of interest. Investigators who hold strong beliefs or who are engaged in competing work often can affect the interpretation of a study's results or the editorial perspective taken by a journal. These types of conflicts are well described, but they are not evaluated as often because they are less overt and are harder to quantify than FCOI.

As is the case in many other arenas, the field of biomedical ethics could benefit from more empirical investigation. Suppositions and news reports can raise issues, and in many cases anecdotal accounts and opinions serve a vital function. But all too often, they give misleading impressions that would be dispelled by a dispassionate and comprehensive view. Despite the flaws in the study by Aneja et al. (1), they have performed a valuable service by pointing out that, at least in the restricted setting of 3 top-tier general biomedical journals, the existence of reported FCOI is not correlated with significant differences in positive or negative study outcomes. The comprehensive availability of journal contents, combined with the increasingly granular data available via the ClinicalTrials.gov registry, could enable both the clinical community and patient advocates to monitor bias—including bias arising from less obvious sources than financial conflicts. A systematic approach to interrogating this issue, coupled with increasingly comprehensive sources for data analysis, has the potential to reduce the amount of conflicting information about conflicts of interest.

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Key Words: clinical trial ■ conflict of interest ■ FCOI.