

# Conflict of Interest and Cost-effectiveness Analysis

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**M**ORE THAN 30 YEARS AGO, BRONOWSKI, WHO SPOKE so poetically about the ethos of science, wrote that “the body of scientists is trained to avoid and organized to resist every form of persuasion but the fact.”<sup>1</sup> The values of science, he argued, are “inescapable conditions for its practice.”<sup>1</sup> But the practice of science, especially the biomedical sciences, has changed significantly since Bronowski made his observations. Increasingly, academic biomedicine has become commingled with corporate interests. Spurred by the burgeoning commercial opportunities of new discoveries such as those in genetics, the growth in academic-industry collaborations has created uneasiness among some observers who suspect that conditions beyond the pure facts of science can influence its outcome.

During the mid-1980s, several medical journals, including *JAMA*, adopted policies on conflicts of interest.<sup>2,3</sup> According to 1 survey conducted in 1994-1995, nearly 50% of US medical journals with a circulation greater than 1000 had written policies regarding conflicts of interest.<sup>4</sup> Those who support policies on author disclosure of financial interests in scientific publications generally do not assume that such policies will improve the quality of science. They recognize that transparency of interests is not an antidote to bias or misconduct in science but believe it can foster public trust. Others, skeptical of the emphasis given to financial interests as opposed to other potential sources of conflicts of interest, see no justification for requirements that raise suspicions without contributing to the scientific agenda.<sup>5,6</sup> As noted by Rothman, conflict-of-interest policies are “ethically questionable, because they impugn authors with the implied accusation of wrongdoing without evidence and without recourse.”<sup>7</sup> Thus, without an empirically established connection between conflict of interest and scientific outcome, many scientists and journal editors who favor financial disclosure are inclined to view it as sound public relations or as a gesture of moral correctness. The journal *Nature* explained in an editorial that until there is evidence that “undeclared interests led to any

fraud, deception or bias in presentation” the journal will continue “in its stubborn belief that research as we publish it is indeed research and not business.”<sup>8</sup>

Specific cases of industry-funded science and their relationship to bias and misconduct were investigated by Congress in 1988.<sup>9</sup> The report of the investigating committee, however, brought no additional clarity to the influence of funding sources and conflict of interest on scientific results.<sup>10</sup>

Subsequently, several studies have shown that clinical decisions are affected by physicians’ financial incentives or their interactions with drug companies.<sup>11,12</sup> Other studies have explored the effects of industry funding on scientific outcomes. In a retrospective analysis of 107 trials in 5 leading medical journals with regard to outcome and sources of funding, Davidson<sup>13</sup> found that studies sponsored by pharmaceutical companies were much less likely to favor traditional therapy over new drug treatment. Stelfox et al<sup>14</sup> found that authors who had a financial association with manufacturers were much more likely than those who did not to have a favorable published position on the safety of calcium channel antagonists as a treatment for cardiovascular disorders. That study reported that 96% of the authors who were supportive of calcium channel antagonists had financial relationships with manufacturers compared with 60% who were neutral and 37% who were critical. Only 2 of the 70 articles included in the study disclosed the authors’ potential conflicts of interest. After reviewing these and other results, the editor of *BMJ* wrote, [these studies] “begin to build a solid case that conflict of interest has an impact on the conclusions reached by papers in medical journals.”<sup>15</sup>

In this issue of *THE JOURNAL*, Friedberg et al<sup>16</sup> have focused the question of conflict of interest on health economics. With the increasing importance of managed care, studies of cost-effectiveness and cost-benefit analyses of

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pharmaceutical agents have become key factors in health reimbursement decisions. Today, the financial success of a pharmaceutical product depends on meeting not only standards of safety and efficacy but also cost-effectiveness.

Friedberg et al questioned whether there was an association between industry-favored outcomes of cost-effectiveness studies for high-profile, expensive oncology drugs and corporate funding of the research. The sample of articles used in the study was well balanced between those funded by pharmaceutical companies and those funded by nonprofit organizations. The most noteworthy finding is that studies funded by pharmaceutical companies were nearly 8 times less likely to reach unfavorable qualitative conclusions than similar studies funded by nonprofit organizations. These results are consistent with the hypothesis that private funding sources can bias outcomes of pharmacoeconomic studies. However, as the authors point out, there are other hypotheses that can account for the results, including the plausible conjecture that pharmaceutical companies may perform in-house prescreening of cost-effectiveness studies before they are contracted out to independent scientists. If only the drugs that screen favorably on cost-effectiveness are contracted by companies for external analyses, the likelihood of association between the outcome and the funder's interests is increased without the specter of bias.

Another finding of Friedberg et al<sup>16</sup> that is less favorable to an interpretation other than bias related to conflict of interest is that industry-sponsored studies were more likely to contain qualitative overstatements of quantitative results. However, the statistical power of this result is low and the methods for correlating quantitative and qualitative outcomes are not explained.

The primary challenge raised by this study is to distinguish among several plausible explanations for the apparent biases in cost-effectiveness analyses. This effort would be aided by a comparative study of several pharmacoeconomic assessments of a single drug under different funding arrangements that includes an analysis of how the analytic framework is selected and an examination of the assumptions used in studies funded by for-profit and nonprofit organizations. Such studies could determine whether any differences in outcome can be explained by structural elements in the modeling or other subtle biases related to conflicts of interest.

Most important, the field of pharmacoeconomic analysis must continue to pursue higher levels of professionalization. Standardized methods of analysis should be developed and adopted by health economists through their professional societies. There has been some progress in establishing consensus-based recommendations on cost-effectiveness analyses.<sup>17</sup> However, without a standard set of methods it is not possible to make comparisons across studies to assess the factors that account for varying outcomes. The differences observed between studies funded by industry and nonprofit organizations may be a result of methods chosen, prescreening, or bias due to the source of funding. By following the traditions of professional societies, such as those of engineering<sup>18</sup> and psychiatry,<sup>19</sup> in setting guidelines of prac-

tice, pharmacoeconomists can attain a special role in the health care policy community in developing independent studies that are based on accepted canons that meet the highest standards of their profession. Government agencies that depend on such studies to set health care reimbursements can contribute guidelines that will help in promoting standards of professional practice. Canada and the United Kingdom have developed national guidelines for cost-effectiveness studies.<sup>20,21</sup>

Biomedical journals should consider developing guidelines for the submission and review of cost-effectiveness studies.<sup>22</sup> Under such guidelines, for instance, authors would be required to clearly describe their assumptions, provide sound justification of the choice of methods, and fully disclose any financial relationships that exist between them and the company that manufactures the product, including whether the sponsor required written approval of the manuscript before submission. Although such an approach does not completely eliminate the potential for bias related to conflict of interest, clearly defined guidelines should foster more transparent reporting of pharmacoeconomic analyses and should enable clinicians and policymakers to better interpret and more appropriately apply the results to patient care decisions.

#### REFERENCES

1. Bronowski J. *Science and Human Values*. New York, NY: Harper; 1965:59.
2. Reiman AS. Dealing with conflicts of interest. *N Engl J Med*. 1984;310:1182-1183.
3. Southgate MT. Conflict of interest and the peer review process. *JAMA*. 1987;258:1375.
4. Glass RM, Schneiderman M. A survey of journal conflict of interest policies. Presented at: the Third International Congress on Peer Review in Biomedical Publication; September 18, 1997; Prague, Czech Republic.
5. Rothman KJ. Conflict of interest: the new McCarthyism in science. *JAMA*. 1993;269:2782-2784.
6. Davidoff F. Where's the bias? *Ann Intern Med*. 1997;126:986-988.
7. Rothman KJ. Journal policies on conflict of interest. *Science*. 1993;261:1661.
8. Avoid financial "correctness" [editorial]. *Nature*. 1997;385:469.
9. *Federal Response to Misconduct in Science: Are Conflicts of Interest Hazardous to Our Health?* Washington, DC: US Government Printing Office; 1989. A report of the 100th Congress, 2nd session, September 29, 1988.
10. *Are Scientific Misconduct and Conflicts of Interest Hazardous to Our Health?* Washington, DC: US Government Printing Office; 1990. A report of the 101st Congress, 2nd session, September 10, 1990.
11. Hillman AL, Pauly MV, Kerstein JJ. How do financial incentives affect physicians' clinical decisions and the financial performance of health maintenance organizations? *N Engl J Med*. 1989;321:86-92.
12. Chren MM, Landefeld CS. Physicians' behavior and their interactions with drug companies. *JAMA*. 1994;271:684-689.
13. Davidson RA. Source of funding and outcome of clinical trials. *J Gen Intern Med*. 1986;1:155-158.
14. Stelfox HT, Chua G, O'Rourke K, Detsky AS. Conflict of interest in the debate over calcium-channel antagonists. *N Engl J Med*. 1998;338:101-106.
15. Smith R. Beyond conflict of interest. *BMJ*. 1998;317:291.
16. Friedberg M, Saffran B, Stinson TJ, Nelson W, Bennett CL. Evaluation of conflict of interest in economic analyses of new drugs used in oncology. *JAMA*. 1999;282:1453-1457.
17. Russell LB, Gold MR, Siegel JE, Daniels N, Weinstein MC. The role of cost-effectiveness analysis in health and medicine. *JAMA*. 1996;276:1172-1177.
18. American Public Health Association, American Water Works Association, Water Environmental Federation. *Standard Methods for the Examination of Water and Waste Water*. 19th ed. Washington, DC: American Public Health Association; 1996.
19. American Psychiatric Association. APA Online. Clinical Resources, Practice Guidelines. Available at: <http://www.psych.org>. Accessed September 17, 1999.
20. Simonich WL. Cost-effectiveness analysis. *N Engl J Med*. 1995;332:124.
21. Pausjensen AM, Detsky AS. Guidelines for measuring the costs and consequences of adopting new pharmaceutical products: are they on track? *Med Decis Making*. 1998;18(suppl):S19-S22.
22. Kassirer JP, Angell M. The journal's policy on cost-effectiveness analyses. *N Engl J Med*. 1994;331:669-670.