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# EDITORIAL POLICIES

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## The New England Journal of Medicine



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## Introduction



**F**or the convenience of authors who wish to submit material for publication in the *New England Journal of Medicine* and other interested parties, we have compiled 10 editorials written since 1991 that spell out the *Journal's* editorial policies.

This series of policy editorials also can be found on the *Journal's* World Wide Web site at <http://www.nejm.org>.

**Jerome P. Kassirer, M.D.**

**Marcia Angell, M.D.**

# The Ingelfinger Rule Revisited



The *Journal* has long had a policy, known as the Ingelfinger Rule, of considering a manuscript for publication only if its substance has not been submitted or reported elsewhere. This policy was promulgated in 1969 by the editor, Franz J. Ingelfinger,<sup>1</sup> to protect the *Journal* from publishing material that had already been published and thus had lost its originality. The policy was maintained by Ingelfinger's successor, Arnold S. Relman,<sup>2,3</sup> who saw it as a way to discourage the public announcement of research findings before publication in a scientific journal, as well as to discourage the growing practice of redundant publication. Both Ingelfinger and Relman acknowledged that the Ingelfinger Rule also protects the freshness and interest of the articles we publish. The Ingelfinger Rule has always had strong detractors, who believe it unreasonably slows the reporting of research results to the profession and the public. In particular, many reporters in the popular media insist that they and their expert sources can distinguish valid from flawed work as well as the peer-review system can. With the recent change in the editorship of the *Journal*, it is appropriate to revisit this issue.

How fast *should* news of medical research, particularly research with important clinical implications, be publicly disseminated? And by what route? Should investigators or their institutions call a press conference as soon as they have finished looking at their data? Can any delay be justified? What are the trade-offs between immediate public release of research results by investigators and release only after peer review and publication in a scientific journal?

Under ordinary circumstances researchers do not simply announce their conclusions to the media after finishing a study. The traditional, orderly process of science involves more than that.

Investigators are expected to describe their work in a manuscript, submit it to a scholarly journal for review by other experts in the field, and revise it when appropriate. To be sure, this process takes time, but it has important functions. Even the most honest investigators cannot be expected to judge their own work dispassionately. They are likely to be enthusiastic about their hypothesis and, almost by definition, not aware of flaws in the design of their study and interpretation of their data. The process of interpreting data is seldom clear-cut, and it is easy to be unaware that the data are inadequate to support the conclusions. Without the discipline of organizing and presenting their evidence, and without the criticism and revisions stimulated by the peer-review process, investigators may unconsciously misrepresent their work or exaggerate its importance. To reduce the effect of any possible biases, other experts must independently evaluate the validity of the evidence and the inferences drawn from it. Furthermore, practicing physicians should also have the opportunity to evaluate the evidence before they change the way they treat patients. Doctors should not practice medicine on the basis of newspaper or television reports. For all these reasons, the traditional, orderly — and often time-consuming — process of organizing, reviewing, revising, and reporting medical research in full detail is more than just a ritual; it is an integral part of clinical research, essential to quality control.

The delay necessary to complete the peer-review process usually presents no problem. Most research, even clinical research, does not have urgent practical implications. Instead, the results usually constitute one of a series of steps leading in a particular direction and suggesting lines for further research. Even results that do have immediate implications for patient care almost always need to be confirmed before practices are changed. Indeed, the failure to appreciate this fact underlies the current popular perception that the public is somehow being misled by contradictory research findings.<sup>4</sup>

Increasingly, however, there are pressures on researchers to take their conclusions directly to

the media, even before a manuscript has been prepared or reviewed. This is particularly true of research on AIDS, although the pressures are not unique to this disease. News of medical research is in great demand in our health-conscious society. Furthermore, some argue that because the enormous medical-research enterprise is largely subsidized by public funds, the public owns the information at all stages and has a right to hear about it at any time. On occasion this sense of urgency has been fueled by members of the popular media who have hinted darkly at the suppression of information by journals for competitive reasons. It has also been fueled by researchers and institutions who themselves increasingly seek out media attention for its prestige value and potential for enhancing funding.

Why shouldn't investigators go directly to the media, as long as the work is later submitted for peer review and publication? As we see it, the risk is that consumers will be receiving misinformation as well as valid information, and that they and their doctors will find it difficult to tell which is which. Misinformation is not innocuous. Much is made of the value of early news of research; too little is made of the risks.

Let us look at some examples of misinformation propagated by the premature release of research findings. In 1985 three physicians in Paris, in conjunction with the French Ministry of Social Affairs, held a press conference to announce that cyclosporine was effective in the treatment of AIDS.<sup>5</sup> This announcement was reported widely in the American press; the *Wall Street Journal* chided the American research community for not informing the public of new results with the same alacrity.<sup>6</sup> The evidence for the French claim was not published, and within a few weeks it was clear that there was no basis for it. Two years later, ICN Pharmaceuticals, Inc., manufacturers of the antiviral agent ribavirin, called a press conference to announce that they had found the drug to be effective in slowing the progression of infection with the human immunodeficiency virus (HIV). Data were said to be forthcoming. The hopes of patients with

HIV infection were raised, as was the stock in ICN Pharmaceuticals. Subsequently the Food and Drug Administration found the claim to be unwarranted.<sup>7</sup> Science by press conference is not limited to the field of medicine, of course; Pons and Fleischman engaged in a spectacular example when they announced that they had achieved cold fusion. Their institution, the University of Utah, was promptly voted substantial funds by the state legislature to further the research.<sup>8</sup> Once again, the work was not published. It is not clear whether the announcements about cyclosporine and ribavirin shortened lives, but they did raise false hopes and contribute to indiscriminate cynicism about the validity of medical research.

There is an inevitable tension, then, between the orderly process of science and the public's right to know, between quality and speed, between doing it right and doing it fast. This tension exists to some extent at all stages of the research process — almost from the inception of a study until publication in a journal — and there is no absolutely clear point along this continuum at which the dissemination of news of the research should occur. Optimally, each case would be considered individually, but that is not practical.

Both the Ingelfinger Rule and our embargo — and the exceptions to these policies discussed below — are meant to address this tension between quality and speed. The Ingelfinger Rule is essentially an agreement between the *Journal* and authors. It stipulates that the *Journal* will consider a manuscript for publication only if its substance has not been submitted or published elsewhere. The embargo is an agreement between the *Journal* and the media. The media agree to wait until Wednesday at 6 p.m. (for the electronic media) or Thursday morning (for the print media) before reporting stories based on that week's *Journal*. In return, we send the *Journal* by first-class mail to members of the media who agree to honor the embargo, to give them time to prepare their stories. (We do not send out press releases.) The effects of these two policies are that the public

and our subscribers — who are mainly practicing physicians — get the information at about the same time and that both the media and our subscribers get the information in final form, after the process of peer review and revision has been completed.

We intend to continue to apply the Ingelfinger Rule and the embargo, because we believe that on balance they serve the best interests of medical research, our subscribers, and the public. Over the years four exceptions to these policies have evolved as the editors have responded to the occasional need for rapid dissemination of research findings. To avoid ambiguity for potential authors, we will state them explicitly here.

First, we exempt from the Ingelfinger Rule all presentations at scientific meetings and all published abstracts, as well as any media coverage based on them. But we discourage authors from giving out more information, particularly figures and tables, than was presented at the meeting to their scientific peers.

Second, we defer to the judgment of public health authorities, such as the National Institutes of Health or Centers for Disease Control, about whether prepublication release of research conclusions is warranted because of immediate implications for the public health. If these agencies make such a decision, presumably after appropriate review, we will consider a manuscript even though the results have already been released — say, in a press conference, a special alert, or the *Morbidity and Mortality Weekly Report* (MMWR). For example, we published the first full clinical descriptions of AIDS,<sup>9-11</sup> even though some of the cases had been reported six months earlier in the MMWR.<sup>12,13</sup> We also published reports on the prophylactic chemotherapy of early breast cancer,<sup>14-16</sup> despite the earlier release of the conclusions in a special alert by the National Cancer Institute. And we published the first report of the efficacy of zidovudine in the treatment of AIDS,<sup>17</sup> although the FDA had already publicly announced the results.

Third, we will consider manuscripts even when researchers have had to release their data

in the course of governmental deliberations — for example, during Congressional hearings or in the course of deliberations by regulatory bodies such as the FDA.

And fourth, we are quite willing to discuss the possibility of special arrangements with authors or institutions when they believe that their findings are of such urgent concern that they should be released before publication in the *Journal* or reviewed faster than normally. (Because of the intense public interest in AIDS research, we consider all clinically relevant AIDS studies in this category.) If we concur, the peer-review process can be short-circuited (that is, an announcement can be made before peer review) or expedited. In general, we prefer expediting the peer-review process to short-circuiting it. When necessary we can complete a review within a week and handle any required revisions by phone or fax. At that point, if we agree that the paper has immediate clinical implications or if that is the judgment of a public health authority, we may accept it and permit the authors to make their conclusions public without waiting the necessary eight weeks until actual publication.

It is difficult to balance the competing attributes of quality and speed in conveying news of medical research to the public. On the one hand, if researchers and editors compromise the usual process of peer review and revision, they risk misinforming physicians and the public. The greater the implications of the research, the worse the potential damage. On the other hand, if important studies are delayed in the review process, the public may be denied life-saving information. We hope that our policies achieve a reasonable balance. We intend them to be flexible and open to appeal if the interests of the public are at stake. Although we are editors, we will not lose sight of the fact that, first and foremost, we are doctors.

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## Violations of the Embargo and a New Policy on Early Publicity



Given the public's interest in the possibility of preventing illness or forestalling death by taking vitamins, it probably was inevitable that the paper entitled "The Effect of Vitamin E and Beta Carotene on the Incidence of Lung Cancer and Other Cancers in Male Smokers" in the April 14 issue of the *Journal*<sup>1</sup> would receive wide attention. The study failed to demonstrate a protective effect of those antioxidant vitamins on the risk of lung cancer and even suggested that beta carotene might increase the risk. Our subscribers, most of whom do not receive the *Journal* until Thursday, the day of publication, must have been surprised when they heard the study reported on ABC's *World News Tonight* Tuesday evening, April 12. Ordinarily, papers from the *Journal* are not reported by the news media until Wednesday evening (for the electronic media) or Thursday morning (for the print media), because of an embargo.

As we have explained,<sup>2</sup> we send members of the news media copies of the *Journal* by first-class mail if they agree to honor the embargo. Most of them receive it by Tuesday, two days before the publication date, and this extra time allows them to learn about the subject, interview authors and other experts, and prepare their stories. In return, they agree to abide by the embargo, which ensures that our subscribers have access to the complete paper at about the same time their patients learn of it from the news media. Doctors can then answer their patients' questions with the evidence before them.

Since this "equal opportunity" policy puts all journalists on an equal footing and gives them time to prepare their stories, it has received widespread support from journalists as well as

from our subscribers. Thus, when ABC broke the embargo on April 12, other reporters who had held back from reporting the story were especially dismayed, as evidenced by the many calls we received from ABC's angry competitors. Because of the media's consternation, we are taking space here to explain the sequence of events. But before we do so, it is necessary to differentiate the embargo from a second policy governing the early release of information from studies published in the *Journal* — a policy known as the Ingelfinger Rule, named for the former editor who established it.

Unlike the embargo, which is an agreement between reporters and the *Journal*, the Ingelfinger Rule is an agreement between authors and the *Journal*, whereby we consider a paper for publication only on condition that its substance is not submitted or reported elsewhere. The Ingelfinger Rule prohibits publicity about an unpublished report from the time of submission, whereas the embargo applies only to the time between the printing of the *Journal* and its date of publication. The policies in tandem are designed to ensure that our readers have the full article when the media report on it.

We occasionally waive the Ingelfinger Rule, for reasons explained earlier.<sup>2</sup> These reasons include a judgment by public health authorities, such as the National Institutes of Health, the Centers for Disease Control and Prevention, or the Food and Drug Administration, that a study's results are of such immediate importance to the public health that they must be communicated at once. Rarely, we may ourselves make this judgment and tell authors that they need not follow the Ingelfinger Rule because in our view their paper has immediate clinical implications. When the Ingelfinger Rule is waived, the paper is usually publicized immediately after it is accepted, approximately two months before publication. The embargo is then irrelevant, because reporters do not want to report old news.

But in the case of the vitamin E and beta carotene study, neither the Ingelfinger Rule nor the embargo was waived. The findings, however

interesting, were not considered to be of urgent public health concern. We thought it preferable, then, not to short-circuit the usual process of ensuring that the full article is available to our readers when the media report on it. Although the Ingelfinger Rule was honored, the embargo was violated just one day before the study would normally have been in the news. This peculiar timing followed a decision by the National Cancer Institute (NCI) to hold a press briefing on Tuesday rather than Wednesday, when the embargo normally is lifted. In our view, there was no compelling reason to hold the briefing one day early. If the NCI considered the results of the study to be of immediate clinical importance, it should have released the results in January, when the paper was accepted for publication. To its credit, however, the NCI made it clear at the press briefing that the information was embargoed until Thursday.

Reporters at ABC were well aware of the embargo, and one of them informed us that ABC might violate it. Although this reporter is a longtime supporter of the embargo, he believed that the NCI's decision to hold the press conference early virtually invited violations. He told his producer that he thought the embargo would be broken by someone, and the producer in turn decided to run the story early to prevent being "scooped." In our opinion, this was no excuse for the violation, and we expressed our dismay to ABC. The NCI went further and informed ABC News that it will no longer be provided with advance information from the NCI. Although we might have canceled ABC's first-class subscription, we did not do so because we were assured by those involved at ABC that they regretted their decision and would not violate the embargo again.

We continue to believe that the embargo policy is reasonable, appropriate, and fair, and many other journals have followed our lead in implementing such a policy. The distinction between the Ingelfinger Rule and the embargo, however, can create a difficult problem. Consider a situation in which the *Journal* informs authors that because their study has immediate clinical im-

plications, the Ingelfinger Rule will be waived and they are therefore free to publicize it. This should be a matter for the authors' judgment. What if they choose not to do so? Two months later, when the *Journal* is printed and mailed, is that story embargoed?

This is exactly the scenario we faced in March when we published a study from Paris showing that riluzole was modestly effective in the treatment of amyotrophic lateral sclerosis.<sup>3</sup> We waived the Ingelfinger Rule on December 15, but the authors did not publicize the results until the embargo was broken by the French newspaper *Le Monde*, just two days before the March 3 publication date. It hardly made sense to object to early publicity when we had suggested exactly that more than two months before. Yet, reporters were annoyed that others had broken the embargo while they honored it.

We have therefore decided to institute the following policy: In those rare instances when we waive the Ingelfinger Rule, we will no longer permit authors to release the information at any time they choose between the waiver and the publication date two months later. Instead, we will ask them whether they intend to publicize the information. If they wish to do so, we will ask that they do it with all deliberate speed — within a week or so. We will also supply such authors with information about how the information should be released, so that the members of the media are treated in an evenhanded fashion. The information will then be in the public domain, and by the time the *Journal* issue is mailed the embargo will be irrelevant. But if the authors decide against early publicity, we will expect them to abide by that decision. Later, when the *Journal* is mailed, we will also expect the embargo to be honored.

We plan to maintain both the Ingelfinger Rule and the embargo and to follow up on any apparent violations vigorously.

**Jerome P. Kassirer, M.D.**  
**Marcia Angell, M.D.**

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## Prepublication Release of *Journal* Articles



On July 8, investigators from the Mayo Clinic and Meritcare held a press conference to announce a study of two dozen patients that linked valvular heart disease to a combination of widely used diet pills, fenfluramine and phentermine (fen-phen). The press conference was covered widely by the media. It was not until August 28, more than seven weeks later, that the full report was published in the *Journal*.<sup>1</sup> A press conference to announce the results of a study that had been accepted by the *Journal* but not yet published was highly unusual. Within several days, we heard from physicians who criticized us for agreeing to release information that they believed was not conclusive. Some suggested angrily that we allowed premature release of the study simply to attract publicity.

When is evidence from a series of similar cases strong enough to justify going directly to the public, possibly engendering grave concern among those using a drug or device? Are small, uncontrolled studies such as this one valid in our era of large and rigorously controlled case-control and cohort studies? The history of our involvement with the study by the Mayo Clinic and Meritcare illustrates our approach to this issue.

At the end of February 1997, we received a first manuscript by Connolly and her colleagues in which they described five cases of valvular heart disease in patients taking fen-phen. Information from pathological examination of the affected valves was available for only two patients. However, the authors indicated that they were aware of 11 other possible cases that were not as well documented. They believed that their few cases might be only the tip of a large iceberg. Given that the use of these drugs and valvular disease are both prevalent, the association in so few cases could have been a chance

occurrence. After review, we thought there was still substantial uncertainty about the causal connection between fen-phen and valvular disease, but we offered to publish a description of their preliminary findings in our Correspondence section. While the manuscript was under review, however, the authors were accruing more cases.

In May, we received a revised manuscript from the two institutions. By then they had accumulated 24 cases of valvular disease in patients who had been taking fen-phen. Echocardiographic studies were available for all the patients, and severe, highly unusual valvular abnormalities were confirmed in the five patients who required valve replacement or repair. We believed that the possibility of a cause-and-effect relation between fen-phen and the cardiac lesions was strengthened by the new data, and outside reviewers agreed. After the authors responded to suggestions for revising the manuscript, we accepted the paper for publication on June 25. We then waived the Ingelfinger Rule, which prohibits a prepublication press conference, and gave the authors permission to report the findings publicly and release the manuscript. Members of the press were informed that a news conference would be held on July 8.

Why make such a fuss? Why didn't we wait the seven weeks until the final paper, with all the relevant detail, was published? In an editorial accompanying the published paper, Dr. Gregory Curfman, a deputy editor, explained that we waived the Ingelfinger Rule and allowed the investigators to release their data early because we believed that the findings might have immediate implications for the health of people using the drug combination.<sup>2</sup> This decision was in accord with our long-standing policies.<sup>3</sup> Subsequent observations, some of them detailed in the Correspondence section of the December 11, 1997, issue of the *Journal*, add to the strength of the hypothesis that the link between fen-phen and valvular heart disease is causal. Nonetheless, more definitive data from case-control studies are required to confirm

(or disprove) the apparent association. In the meantime, fenfluramine has been removed from the market at the request of the Food and Drug Administration, after further data suggested an incidence of valvular disease as high as 30 percent among users of the drug. Dexfenfluramine, which has been associated with pulmonary hypertension and valvular heart disease, has also been removed, but phentermine is still on the market.

Some of the physicians who criticized us for permitting the Mayo Clinic press conference had been caught off guard by the news reports. When their patients called them to ask whether they should continue taking fen-phen, the physicians were unable to answer, because they could not assess the evidence for themselves. The existence of an electronic medium (the World Wide Web) that allows us to transmit medical news instantly to physicians all over the world suggested a solution to this problem. In this case, Connolly and her coauthors offered to put the preliminary, unedited manuscript on their web site. We agreed, and it was installed on the Mayo Clinic web site at the time of the press conference, but not all interested physicians found it.

In the future, when we waive the Ingelfinger Rule for a study that we and the authors agree has critical public health implications, we will coordinate the press release with installation of the partially edited manuscript in full text on the *Journal's* web site ([www.nejm.org](http://www.nejm.org)). We will mark it clearly as incomplete, and when the final manuscript is available we will replace the incomplete version with it. Not all physicians have access to the *Journal's* web site, but the numbers of those who do are increasing rapidly, and we expect that most will soon be able to obtain information by this method.

Most of the studies that we and other journals publish have only an indirect and cumulative effect on medical practice. Physicians rarely change their prescribing practices on the basis of a single study, nor should they. But in the few instances in which a study suggests an immediate and important change in practice, we

will continue to try to convey information to doctors and patients as quickly as possible, having made reasonable efforts to ensure scientific validity. The line between jumping the gun and waiting too long is a difficult one to tread, and we are aware that we may be criticized for premature release of alarming findings, just as we have been criticized in the past for withholding important information. In the case of fen-phen, reducing patients' exposure to these drugs by seven weeks may have reduced morbidity and even saved some lives. We undoubtedly will permit the early release of unpublished studies again.

**Jerome P. Kassirer, M.D.**  
**Marcia Angell, M.D.**

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## On Authorship and Acknowledgments



Large clinical trials from multiple institutions now involve dozens and sometimes hundreds of people in their conception, design, implementation, analysis, and preparation of reports for publication. Increasingly, we have become concerned about two inter-related aspects of many reports of multicenter studies: ambiguous authorship and lengthy acknowledgments.

Clear specification of authors is essential so that any substantive questions about a submitted or published study can be resolved. Authorship has been defined in many ways, but most of the definitions have in common a requirement that authors have sufficient intellectual involvement with the overall study to be able to take responsibility for it.<sup>1-3</sup> Obviously, a clinician whose only contribution is to enter patients into a multicenter trial does not qualify for authorship, nor does a secretary in the trial office. Yet many such people may appear in a long list of members of a study group designated as the collective author of a study — as a hypothetical example, the Boston Porphyria Study Group. In such a case, the study has at once too many authors, because not all of them could take comprehensive responsibility for the study, and too few, because it is not clear who is accountable. The problem is not limited to multicenter clinical trials, of course, but it is more likely in such studies because the cooperation of so many people is required and there is a tendency to offer authorship to obtain it.

A second problem is the growing length and detail of the acknowledgments. Traditionally, authors use acknowledgments to identify those who made special intellectual or technical contributions to a study that were not sufficient to qualify them for authorship. In reports of multicenter clinical trials, however, acknowledgments are often made to everyone who had any-

thing to do with the study, including those who were merely carrying out their jobs, such as technicians. Sometimes principal investigators from each participating institution are acknowledged, even though they are also identified as authors. Many acknowledgments list committees, and the same person may be acknowledged several times on different committees.

We recently accepted a manuscript with an acknowledgment section that listed 63 institutions and 155 physicians, the number of patients each institution had contributed (some as few as one), the 51 members of seven different committees, their institutions and their specialties, and the secretaries in the trial office. Many persons were named on more than one committee. The paper was 12 pages long; the acknowledgments took up 5 pages. We do not consider an extensive and repetitious list of participants in a clinical trial, complete with committee assignments and other details of the trial's internal organization, a good use of *Journal* space; it cannot be of much interest to our readers. Furthermore, it tends to blur the distinction between authors and those who merely warrant acknowledgment. In the above example, all those who were acknowledged were also considered authors, because they were members of the group to which authorship was attributed.

The *Journal* subscribes to the criteria for authorship formulated by the International Committee of Medical Journal Editors and published in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals.<sup>4</sup> According to these criteria,

Each author should have participated sufficiently in the work to take public responsibility for the content. Authorship credit should be based only on substantial contributions to (a) conception and design, or analysis and interpretation of data; and to (b) drafting the article or revising it critically for important intellectual content; and on (c) final approval of the version to be published. Conditions (a), (b), and (c) must all be met.

These guidelines were developed in part as a response to episodes of research fraud in which coauthors were too remote from the work or had too limited a role to exercise the responsibility that authorship implied.<sup>5</sup> Defining the criteria

for an acknowledgment is, of course, far less important. We believe, however, that acknowledgments become less meaningful if they include people who were simply doing their jobs and who offered no unusual intellectual contribution or technical expertise to the endeavor.

In the past we dealt with concern about inappropriate authorship and acknowledgments on a case-by-case basis during the review process or after we accepted a manuscript for publication. But given the magnitude and frequency of the problems we are encountering and our concern that ad hoc decisions may appear arbitrary, we think it is appropriate to set out specific guidelines about authorship and acknowledgments. It is difficult to arrive at such guidelines because we do not wish to discourage cooperative research enterprises and we are aware that there are pressures on principal investigators to offer authorship as an incentive for enthusiastic cooperation. Yet it is not in our readers' interests to permit unlimited lists of authors and acknowledgments, and it undermines the meaning of authorship and the value of an acknowledgment.

Accordingly, we shall institute the following, fairly liberal guidelines for authorship and acknowledgments:

1. Authorship attributed only to a group (the Boston Porphyria Study Group) will not be acceptable. At least one person's name must accompany the group name. The group name should appear after the authors' names, as follows: "Thelma J. Smith, Louise J. Jones, and Duane J. Brown, for the Boston Porphyria Study Group."
2. If more than 12 authors are listed for a multicenter trial, or more than 8 for a study from a single institution, we shall require that each author sign a statement attesting that he or she fulfills the criteria for authorship of the Uniform Requirements. The reason for selecting these maximums, which are admittedly arbitrary, is that it is difficult to imagine that more than 12 people can have the comprehensive intellectual involvement necessary to fulfill the criteria for authorship.

3. We shall leave to the authors the choice of those acknowledged, but limit the space devoted to acknowledgments. To conserve space, those acknowledged will be listed only once, along with their institutions (one each). Committee names, numbers of patients contributed, and other details about the process of the trial will not be included.

4. If acknowledgments fill more than a column of *Journal* space (about 600 words of small type), we shall deposit them with the National Auxiliary Publications Service. At the authors' request we shall consider publishing fuller acknowledgments, including committee assignments, in reprints of the paper.

To remind authors of these guidelines, they are included in our Information for Authors section, which appears on page 51. We are aware that there may be individual circumstances in which these policies need to be modified. In particular, modifications may be required for reports of trials already in progress in which commitments have been made about the way participants are to be designated. Even in these cases, however, we would expect those named as authors to have fulfilled the criteria for authorship. We welcome your comments about these policies.

**Jerome P. Kassirer, M.D.**  
**Marcia Angell, M.D.**

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## Redundant Publication: A Reminder



Nobody is well served by the practice of reporting the same study in two journals, publishing a review of the same subject nearly simultaneously in two journals, or splitting a study into two or more parts and submitting each to separate journals. A recent mini-epidemic of attempts to publish redundantly in the *Journal* has alerted us to the need to remind authors and investigators of policies that seem to be breached increasingly often now. We have not called attention to this issue for several years, and a new generation of authors may have overlooked previous commentaries.<sup>1,2</sup>

Our guidelines regarding redundant publication are published each week on the Information for Authors page. In a practice followed by many journals, we ask authors to send us copies of any manuscripts closely related to the manuscript they want us to consider for publication. This allows us to decide whether there is excessive overlap between two manuscripts or whether the results of a single study are inappropriately divided into two or more papers. In the trade, the latter practice is sometimes referred to as "salami slicing."

The reasons for preventing redundant publication are not arbitrary. As earlier editorials have pointed out, multiple reports of the same observations can overemphasize the importance of the findings, overburden busy reviewers, fill the medical literature with inconsequential material, and distort the academic reward system.<sup>1,2</sup>

The results of huge clinical trials or epidemiologic studies with multiple and unrelated end points, such as the GUSTO (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) trial of thrombolytic therapy after acute myocardial infarction, the Framingham Heart Study, or the Physicians' Health Study, could not be reported

as a single study. It often takes years to collect and analyze such data, and it is legitimate to describe important outcomes of such studies separately. On the other hand, reports of studies involving several dozen patients should not be split into overlapping manuscripts. Because the line between appropriate and inappropriate practice is not always clear, it might be helpful to provide several concrete examples.

First, some examples of overlapping publications: Two years ago we accepted a paper on bone lesions in patients with chronic renal failure. We asked a distinguished nephrologist to write an editorial to accompany the paper. While preparing the editorial, the nephrologist came across a study published in a specialty journal several months earlier. It was written by the same authors, described the same patients, and reported virtually the same end points. The authors had not told us they had published similar data elsewhere. Although we were well along in the production process, we pulled the paper. This example of fragmenting the results of a single study and reporting them in several papers is not unique. Several months ago, for example, we received a manuscript describing a controlled intervention in a birthing center. The authors sent the results on the mothers to us, and the results on the infants to another journal. The two outcomes would have more appropriately been reported together. We also received a manuscript on a molecular marker as a prognostic tool for a type of cancer; another journal was sent the results of a second marker from the same pathological specimens. Combining the two sets of data clearly would have added meaning to the findings.

After we published a recent study describing diagnostic tests on 101 consecutive patients with suspected traumatic rupture of the thoracic aorta,<sup>3</sup> we learned that the report was remarkably similar to two papers that had been published in the surgical literature.<sup>4,5</sup> One, published only two months earlier, described 160 patients.<sup>5</sup> The other, published two years earlier, described 69 patients.<sup>4</sup> All three papers were from the same institution; three persons were

listed as authors on all three papers, and two others were listed as authors on two of the papers. Before we accepted the paper for publication, we were not informed about the report on 160 patients, although it had already been accepted for publication elsewhere. The paper published two years earlier was also not brought to our attention by the authors, although we were aware of it because it was listed in the bibliography. No information was given in any of the papers about which patients were being reported on two or more times. In fact, as the letter from Drs. Smith and Kearney in the Correspondence section of the August 17, 1995, issue of the *Journal* indicates,<sup>6</sup> some patients in fact were reported on in all three papers, providing a misleading impression of the number of patients studied and the value of the tests.

It is surprising that these practices still occur, despite growing attention and nearly universal disapproval. Most of the time the redundant publication is quickly exposed by readers. In addition, an investigator's peers often recognize a succession of "least publishable units." The motivation for publishing two or more papers when one would do is not always clear. In some instances authors have argued that they were interested in getting the information to different audiences. In others, they have claimed that they perceived the overlap to be far less substantial than did the editors. Finally, there is reason to suspect that the academic incentive system fosters a desire by authors to lengthen their bibliographies. Ways of counteracting this distorted incentive have been proposed<sup>7</sup> but have not been universally implemented.

We are not eager to act as prior-publication police, and we do not regularly search the literature to determine whether an author has committed one of the several forms of redundant publication. But we have rewritten the relevant portion of our Information for Authors as follows: "Authors should submit to the Editor copies of any published papers or other manuscripts in preparation or submitted elsewhere that are related to the manuscript to be considered by the *Journal*" (we formerly asked for

“copies of any related manuscripts”). We will continue to rely on the honesty and judgment of authors in informing us of any work of theirs that is related to a manuscript they are submitting to the *Journal*.

When preparing a manuscript, authors might heed the advice offered previously.<sup>2</sup> In deciding whether reports are redundant, authors should ask themselves whether a single paper would be more cohesive and more informative than two. When there is any doubt, authors should submit with their manuscripts any other papers possibly representing duplication or fragmentation of results, whether published, submitted for publication, or already accepted for publication.

**Jerome P. Kassirer, M.D.**

**Marcia Angell, M.D.**

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## The Internet and the *Journal*



The word “publishing” has taken on new meaning. For centuries, publishing required an intermediary, someone who had an editorial staff and a press — in short, a publisher. Today, anyone equipped with a computer, a modem, and a connection to the Internet can be a publisher. The consequences of this technical transformation should give pause to all of us in medicine. Direct electronic publishing of scientific studies threatens to undermine time-tested traditions that help to ensure the quality of the medical literature.

The first hint that electronic publishing by medical researchers might become a reality came from the field of physics. Research physicists have been communicating with one another electronically for approximately 15 years, sharing preliminary results (“preprints”) before sending their data for publication. Approximately four years ago, a physicist, Paul Ginsparg, began collecting these preprints of research papers in a host computer at the Los Alamos National Laboratory. That computer has since become a vast repository of physics preprints. Every day, thousands of physicists in 60 countries receive e-mail messages from the Los Alamos computer, and any of them can download the files from the host computer.<sup>1</sup> The physicists submit and replace their research “papers” and make changes whenever they see fit. The system functions much like an electronic journal, yet because the individual communications can be constantly revised by the investigators, they are not fixed in time as are papers in print journals.

Some have suggested that this method of publication might be desirable for medical studies. One group of devotees of electronic publishing recently proposed that, as in physics, medical-research communications might be stored electronically and titles and abstracts dis-

tributed by the Internet daily.<sup>2</sup> Papers would be considered works in progress that could be changed as the author wished. In this system an open process in which anyone could comment on any paper would replace the peer-review system. The quality of a paper would be assessed by the number of times it was cited and retrieved.

What are the flaws in this proposal? In our opinion, a study represented by an abstract or a presentation at a medical meeting is incomplete until it undergoes peer review, is revised accordingly, and is published. A study found to be badly flawed during peer review may be completely revised or never published. Publishing preprints electronically sidesteps peer review and increases the risk that the data and interpretations of a study will be biased or even wrong. Investigators cannot be expected to judge their own work dispassionately. They are usually enthusiastic about their hypotheses and may be unaware of flaws in the design of their experiments or of the insufficiency of their data to support their conclusions. They need independent experts to evaluate their data. Most journal editors rely on carefully selected reviewers whose opinions about the originality, validity, and timeliness of a manuscript count heavily in the decision for or against publication. The reviewers are an investigator's peers; they cannot be replaced by multiple unspecified users of the Internet. When a scientific study is assessed by majority rule, the result is likely to be highly unreliable. Such a process could also invite manipulation and even fraud.

Another source of concern is the fact that much information about health issues on the Internet, such as the risks of medications and the effects of various foods on health, is of uncertain parentage. (Surely, anonymity has no place in reporting medical research.) At present the Internet seems to promote medical rumors more than dispassionate scholarship. Papers in medical journals are technical communications intended for physicians, not for direct consumption by the public. Physicians should act on new studies only after carefully considering the

strength of the research and how the new data relate to previous studies, and after assessing whether the population studied is relevant to the patient at hand. Public access to Internet preprints of medical studies might lead some people to use the wrong medications or to stop taking needed ones on the basis of inadequate information, as has happened from time to time when news reports failed to interpret adequately a presentation at a medical meeting.

According to our current policies,<sup>3</sup> we do not consider a manuscript for publication if its substance has already been reported elsewhere. An explicit policy is needed for the Internet because of its enormous capacity to transmit information to a large number of people simultaneously. We have decided that electronic publication should not be regarded differently. Thus, posting a manuscript, including its figures and tables, on a host computer to which anyone on the Internet can gain access will constitute prior publication. On the other hand, sending manuscripts by e-mail to a limited number of colleagues — a dozen or two, let us say — will not. Such a practice is analogous to faxing manuscripts to a group of research collaborators.

For studies submitted to us that have immediate health implications, we will continue our efforts to see that dissemination of urgent medical information is not delayed by either peer review or the publication process. Accordingly, we will discuss with authors the need for expedited review and rapid disclosure of studies, as we have described elsewhere.<sup>3</sup> We believe that these policies are the best way to minimize dissemination of uninterpretable information while permitting the free exchange of ideas and data among colleagues and collaborators.

Physicians have not been at the forefront of electronic communication, but many are beginning to use e-mail and to explore the Internet. Electronic communication is likely to become critically important in medicine,<sup>4</sup> and it behooves physicians to become competent in using it. In the future, when the Internet is widely used by physicians, information about advances that may have an immediate effect on

the health of individuals or populations may best be communicated through this medium. But medicine is not physics: the wide circulation of unedited preprints in physics is unlikely to have an immediate effect on the public's well-being even if the material is biased or false. In medicine, such a practice could have unintended consequences that we all would regret.

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**Marcia Angell, M.D.**

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## Financial Conflicts of Interest in Biomedical Research



Financial conflicts of interest in medicine — what they are and how to deal with them — constitute one of the most contentious issues in our profession. Organized medicine and its critics have debated whether clinicians should gain financially from their practice in any way other than through their direct fees or salaries for service. And the academic community and its critics have debated whether medical researchers should gain financially from companies whose products they are evaluating. Opinions vary greatly — from those advocating that all conflicts of interest be proscribed to those arguing for disclosure and caveat emptor to those maintaining that there is no problem. There are even disagreements about the definition of a conflict of interest. Many attach qualifiers, such as “potential” or “apparent,” in an attempt, it often seems, to be delicate or nonjudgmental.

In the August 19, 1993, issue of the *Journal*, Thompson<sup>1</sup> provides a thoughtful and compelling analysis of the controversy. He defines a financial conflict of interest as a condition, not behavior; clinicians or researchers who might benefit financially by distorting their work have a conflict of interest regardless of whether they actually distort their work. We agree with this definition. The circumstances determine whether there is a conflict of interest, not the outcome.

Because of the increasing prevalence of commercial interests in biomedical research, the *Journal* in 1984 became the first of the major biomedical journals to announce a policy for dealing with financial conflicts of interest among researchers submitting manuscripts.<sup>2</sup> Arnold S. Relman, then editor-in-chief, requested that all authors disclose to us any associations they had with businesses that could be affected by their

work — including direct employment and consultancy, stock ownership, and patent-licensing arrangements. He made it clear that this information would play no part in the assessment of the report; indeed, reviewers would not even have access to it. Only at the time of publication would a decision be made about whether to disclose the information to readers. The policy also stipulated that the editors themselves could have no financial interests in any business relevant to clinical medicine; given the collegial nature of a small editorial office, it was thought insufficient for editors merely to excuse themselves from considering a particular manuscript that presented a conflict of interest. The *Journal* continues to differ from other journals in the breadth of its conflict-of-interest policy for editors.

In 1990 we modified the conflict-of-interest policies to apply a more stringent standard for review articles and editorials.<sup>3</sup> Unlike reports of original research, these articles represent the judgment of their authors, based on their evaluation of the literature. What studies they select to discuss and their analysis of them are necessarily subjective. Bias may be extremely difficult to detect because these articles contain no primary data to speak for themselves. For this reason, we decided not to publish review articles or editorials by authors with financial holdings in a company (or its competitor) whose product figured prominently in the article.

We have retained these policies on financial conflicts of interest. In our view, they acknowledge that conflicts of interest are now widespread and widely accepted, but they also recognize their problematic nature. As editors, we cannot simply ignore them, as Koshland recently emphasized.<sup>4</sup>

Many arguments have been raised against our policies. The most frequent are that disclosing conflicts of interest impugns the integrity of honest researchers, that prohibiting conflicts of interest in authors of review articles and editorials is a form of censorship, and that our policies unfairly ignore intellectual biases in favor of financial ones. Let's look at these arguments.

Disclosing a conflict of interest does not impugn the honesty of authors (despite the rhetoric of a recent article referring to disclosure as “McCarthyism”<sup>5</sup>). On the contrary, if problems were apparent during the peer-review process and not corrected in revision, the paper would not be published. Furthermore, the issue is not primarily one of honesty but of unconscious bias, which may be quite subtle and difficult to detect. This is one reason for disclosure; bias not appreciated in the peer-review process may still be detected by readers.

It is difficult to take the charge of censorship seriously. Freedom of the press does not imply that anyone can publish anything anywhere; it means only that government cannot prohibit the publication of certain ideas. Obviously, editors of journals set many criteria for publication; for example, we rarely publish reports of studies in animals or of research without clinical implications, regardless of their scientific validity. We nearly always solicit review articles and editorials from senior, rather than junior, investigators. Our decision to exclude authors with financial conflicts of interest is simply another criterion, designed to ensure that the articles are of maximal credibility and interest to our readers.

Our conflict-of-interest policy is directed toward financial arrangements because, as Thompson points out, they are both widespread and optional, as well as seductive. Many intellectual conflicts of interest — for example, the desire for positive or important results in a research study — are not optional. They are inherent to the endeavor. Fortunately, these conflicts are not hidden and they are well appreciated, since nearly all researchers share them; there is therefore no need for disclosure. Other conflicts are unusual or idiosyncratic (for example, a Seventh-Day Adventist doing research on the health effects of the sect's lifestyle), and there is no practical way of anticipating all of them or dealing with them with a blanket policy. Like Thompson, we believe that the fact that a policy cannot cover all contingencies is hardly a reason not to have one.

Financial conflicts of interest are a matter of choice. Researchers do not have to have them, nor do restrictions based on them constitute a violation of rights. In many areas of life, such restrictions are the norm. For example, judges are expected to excuse themselves from cases involving companies in which they have an interest. And no one with such an interest would be selected for a jury, no matter how much he protested his objectivity. Why should those in the biomedical research community consider it an affront to have to submit to similar restrictions? Furthermore, when researchers choose to invest in health-related companies rather than in other types of business, it raises the question of whether they are attempting to profit from the specialized knowledge they gain in the course of performing research. In other settings, this would constitute insider trading. Can this be the face we want to present to the public?

Given the current climate of clinical investigation, financial conflicts of interest will probably continue to be a fact of academic life, but they must be responsibly regulated, with disclosure being a minimal requirement. Most academic institutions and journals have not gone far enough in dealing with this problem.

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## Editorials and Conflicts of Interest



In the August 29 issue of the *Journal*, we published an Original Article by Abenhaim et al., entitled "Appetite-Suppressant Drugs and the Risk of Primary Pulmonary Hypertension."<sup>1</sup> It dealt with the increased risk of primary pulmonary hypertension in subjects taking antiobesity drugs. In the same issue was a solicited editorial by Dr. JoAnn Manson and Dr. Gerald Faich, entitled "Pharmacotherapy for Obesity — Do the Benefits Outweigh the Risks?"<sup>2</sup> As is the usual practice of the *Journal*, the editors asked the editorialists to put the study results into perspective for our readers.

What we did not appreciate until it was too late was that Dr. Manson and Dr. Faich had both been paid consultants for companies that stood to gain from the sale of one of the antiobesity agents studied. In 1995, Dr. Manson consulted for Interneuron Pharmaceuticals and for Servier Amérique, the manufacturer and a distributor of dexfenfluramine (Redux), one of the most common of the appetite suppressants studied by Abenhaim et al. Her coauthor, Dr. Faich, had also consulted for Servier Amérique, beginning in 1994, and for Wyeth-Ayerst, the North American distributor of Redux, beginning in April 1996 and continuing until as recently as the month of publication. We did not become aware of the essential features of these associations until three days before the publication date, when the first of many reporters phoned to ask us about the conflict of interest. The ensuing publicity was as intense as any we have experienced at the *Journal*, but despite the generally accurate media coverage, we owe it to our readers to set the record straight ourselves.

Since 1990 the *Journal* has had a policy that prohibits editorialists and authors of review articles from having any financial connection with a company that benefits from a drug or device discussed in the editorial or review article.<sup>3</sup> This

policy was an extension of our earlier policy, announced in 1984, that required authors merely to disclose their financial connections with industry.<sup>4</sup> In the case of scientific reports, disclosure seemed adequate. Scientific reports are self-contained. They present original data, and readers can judge for themselves whether the authors' interpretations are supported by the data. Editorials and review articles are different. They are not self-contained, and there are no primary data. Instead, editorialists and authors of review articles evaluate an issue on the basis of what they select from the literature as relevant. In the case of editorialists, their task is to use the study they have been asked to editorialize about as a springboard for an open-ended consideration of an important issue. It is expected that they will provide an unbiased and authoritative opinion about the matter. That is why we insist that editorialists have no financial ties to products that figure prominently in their work.

There is no better demonstration of the reason for our policy than the Manson and Faich editorial. Although Abenhaim et al. found a significantly increased risk of primary pulmonary hypertension in subjects who had taken anti-obesity drugs (the adjusted odds ratio for those who had taken appetite suppressants for more than three months was 23.1, with a 95 percent confidence interval of 6.9 to 77.7), Manson and Faich calculated the offsetting risk of obesity itself and found it to be greater. They concluded their editorial with the sentence, "Although physicians and patients need to be informed, the possible risk of pulmonary hypertension associated with dexfenfluramine is small and appears to be outweighed by benefits when the drug is used appropriately." When considered as the opinion of unbiased experts, this is just the sort of practical summary we want from editorialists. But when considered as the conclusion of people who were paid consultants for companies that sell dexfenfluramine, it raises troubling questions. Did the authors give sufficient attention to the possibility that the risks associated with long-term use would be even greater? Were they too quick to attribute the

risks associated with obesity to obesity itself? Were they too dismissive of other, nonpharmacologic treatments of obesity? Mere disclosure of their conflicts of interest would not have answered these questions for readers not expert in the field.

Critics of our policy might contend that it is unnecessary, because experts cannot be influenced by financial ties. That is probably true for the great majority of them, including Drs. Manson and Faich. But some no doubt can be influenced, and readers should not have to go through the exercise of assessing editorials to decide which to trust. Furthermore, even if very few experts would knowingly tailor their opinions for gain, close association with a company can engender good will that may manifest itself as unconscious bias, a condition that is probably much more frequent and even more difficult for readers to assess. Editorialists who have worked with a company are also accustomed to seeing issues from that company's perspective, and this viewpoint can affect the focus of an editorial. As we pointed out earlier, a conflict of interest is not synonymous with bias. If Drs. Manson and Faich had not consulted for companies that stood to gain from the use of Redux, they might very well have written exactly the same editorial. We have no reason to believe otherwise. But no one should have to make that judgment, least of all readers who are counting on editorialists for a balanced perspective on a sometimes highly technical issue.

On June 24, 1996, before the editorial was written, we sent Dr. Manson the standard letter to prospective editorialists. In it is a paragraph set in boldface: "Because editorials involve interpretation and opinion, we ask that authors not have ongoing financial associations (including equity interest, regular consultancies, or major research support) with a company that produces a product (or its competitor) discussed in the editorial. If there are any questions about this policy, please phone us." Because Dr. Manson's consultancy was not "ongoing" at the time she was asked to write the editorial, she evidently believed she was not precluded by this

paragraph from writing the editorial. Dr. Faich's consultancy *was* ongoing, but he did not interpret it as "regular." Accordingly, in the covering letter they sent us with their editorial was the statement: "Drs. Manson and Faich participated in the FDA review of dexfenfluramine as scientific consultants on the health risks of obesity. They have no financial interest or equity in any pharmaceutical company producing anti-obesity agents." Nothing was said in their letter about being paid as consultants by companies that manufactured or marketed Redux. Dr. Manson had disclosed a connection with Interneuron and Servier in a scientific report she coauthored in the *Journal* last year,<sup>5</sup> but we gathered from a telephone conversation that it was not relevant to the editorial.

The purpose of the words "ongoing" and "regular" in our standard paragraph quoted above was to allow for the common circumstance of editorialists writing about a product made by a company with which they have had a past, no longer relevant financial association. Dr. Manson's connection with Interneuron and Servier Am rique did not fit that description. Although her consultancy was not ongoing, it did concern the very drug she was being asked to consider in her editorial. It was in a gray area not explicitly covered by the language of our policy and therefore required further discussion. Dr. Faich's connection, however, was in no such gray area, and if we had known the facts of his consultancy we would not have permitted him to coauthor an editorial on the subject. In the Correspondence section of the October 3, 1996, issue of the *Journal* (page 1064), Drs. Manson and Faich present their view of the matter.

So where do we stand? No one can say for certain whether the views of Manson and Faich were in any way influenced by their associations with Interneuron, Servier, and Wyeth-Ayerst. Readers will have to decide for themselves, difficult though that is. But the episode should be put in perspective. To our knowledge, this was the first violation of our policy in the six years it has been in effect. That is not a bad record.

Disturbing as the episode was, we see no reason not to continue to trust prospective editorialists to honor the policy. Trust is essential in scientific research, and we believe it is rarely betrayed. Prospective authors need to remember the reason for our conflict-of-interest policy; if that is clear, then the exact wording of the statement in our letter becomes less important. Nevertheless, we intend to make the statement more inclusive by modifying it slightly to read: "Because editorials involve interpretation and opinion, we require that authors be free of financial associations (including equity interest, consultancies, or major research support) with a company that stands to gain from the use of a product (or its competitor) discussed in the editorial. If there are any questions about this policy, please phone us. Otherwise, please sign the attached form attesting that you have no such associations."

After the *Journal* instituted its 1984 policy requiring disclosure of conflicts of interest, other major medical journals adopted similar policies, but so far we stand alone in our contention that disclosure is not enough in the case of editorials and review articles. In our view, the increasing involvement of researchers in commercial activities makes this policy all the more important. Readers must be able to rely on editorialists to be disinterested. We hope that we will soon be joined in our policy by our sister journals.

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## The *Journal's* Policy on Cost-Effectiveness Analyses



Concern about cost now dominates many decisions about the use of drugs and other therapeutic interventions. Increasingly, such decisions are being influenced by published economic analyses that relate the effectiveness of treatments and their associated costs (cost-effectiveness analyses). Many of these analyses are supported by grants from the National Institutes of Health (NIH) or other neutral sources. Some, however, are funded by companies that hope these analyses will put their products in a favorable light.<sup>1</sup> Companies might then even use particularly favorable analyses to justify the prices of new drugs.

A cost-effectiveness analysis is usually performed by developing a model of the outcomes of alternative treatments, selecting published data on the probabilities of the outcomes to enter in the model, identifying the expenses associated with each therapy, and then comparing the results (often given as dollars spent per year of life saved) with those of various benchmark therapies. Such analyses vary in their complexity; the data can be derived from a single randomized, controlled clinical trial or from many sources, and the costs incorporated vary extensively from one analysis to another. Most analyses consider the costs of an intervention — be it a drug, device, procedure, or program — as well as the costs arising from the disease or condition that may be caused or averted. The costs of hospital stays, laboratory tests, and physicians' follow-up visits are usually included. Some analyses also include the costs of diseases that may ultimately affect those whose lives are prolonged, as well as the wages that may be gained or lost. The approaches to formulating the models and identifying costs vary substantially.

Because of the discretionary nature of the methods used to analyze cost effectiveness and the increasing importance of such analyses (in some countries they are now required before drugs are approved for use), it is incumbent on authors, journal editors, and the funders of these studies to minimize any source of bias. Doing so is particularly important given the tangled financial arrangements that may exist between the authors and the for-profit companies that fund them. For example, we recently saw an analysis for which an author received money directly from the company, another in which the author had a patent pending on an application described in the report, and another in which an author was a consultant to the company that markets the drug that was studied. Although we had no special reason to believe that any of these cost-effectiveness analyses was biased by these financial arrangements, we could not comfortably assume that they were not — either intentionally or unintentionally. Certainly the financial arrangements created an incentive for bias.<sup>1,2</sup>

To eliminate any ambiguity, we describe here our recently formulated policy on the publication of cost-effectiveness analyses. As background, we review our long-standing policies on authors' financial conflicts of interest in other types of articles.<sup>3-5</sup> As we explained recently,<sup>5</sup> we ask authors of scientific articles who have financial connections with a company that makes the product under study (or its competitors) to inform us of these connections when they submit their manuscripts. We do not make such financial relationships known to reviewers, but we do disclose them to our readers, when appropriate, at the time of publication.<sup>5</sup> In contrast, we do not even consider review articles or editorials by authors with any financial connections to companies whose products are featured prominently in the article (or their competitors).<sup>5</sup> The rationale for these policies is explained elsewhere.<sup>3-5</sup>

In our view, formal cost-effectiveness analyses have some of the features of both original scientific articles and review articles. They are similar

to original articles in that the methods and data are explicit and the conclusions are based on the data presented. Yet, they are like review articles in that the assumptions made in constructing the models and the data used in the analysis are usually chosen selectively from the literature, and the choices could be biased. Because of these characteristics, we will treat formal cost-effectiveness analyses partly as we do original articles and partly as we do review articles. Like original articles they will not be excluded from consideration if they are supported by a grant from industry to a nonprofit institution, but like review articles they will be excluded from consideration if any of their authors has a personal financial conflict of interest. Simply disclosing such conflicts of interest, as others have suggested authors do,<sup>1</sup> will not suffice.

We will consider for publication any high-quality cost-effectiveness analysis, whether or not the analysis is supported by industry and regardless of whether it uses primary data from a single clinical trial or secondary data from a variety of published sources. When a cost-effectiveness analysis is submitted for publication, we will expect its authors to provide information that will allow us to judge whether an incentive for bias exists. The following conditions must be met: First, any study supported by industry must be funded by a grant to a not-for-profit entity such as a hospital or a university, not to an individual or group of individuals. We will not review such studies if any of the authors is receiving a direct salary from the sponsoring company or a competing company, or if any author has an equity interest in, an ongoing consultancy with, or membership on the scientific advisory board of such a company, or a related patent pending. Second, we must receive written assurance that the agreement between the authors and the funding company ensures the authors' independence in the design of the study, the interpretation of data and writing of the report, and decisions regarding publication, regardless of the results of the analysis. The investigators must retain access to the data. Third, to ensure that the analysis can be assessed or replicated by

reviewers and readers, the manuscript must include all the data used in the analysis, all assumptions on which the data are based, and any model used in the analysis. There must be a clear explanation of the assumptions made in building the model. The model must be sufficiently straightforward and lucid so that ordinary readers can comprehend it.

Some will argue that these policies are unnecessarily restrictive. In fact, they differ little from our policies on review articles and editorials, except that they do not prohibit the publication of studies supported by industry. We recognize that bias can compromise even original scientific studies, but we believe that the opportunities for introducing bias into economic studies are far greater, given the discretionary nature of model building and data selection in these analyses. In addition, unlike the effectiveness side of the equation, which is based on biologic phenomena, the cost side is highly artificial. Drug costs, in particular, can be quite arbitrary, since they are prices (not costs) set by the company and are based on criteria known only to the company.

To reduce the likelihood of bias in these analyses, it would be highly desirable to create some distance between the investigators and industry support. If neither the insurance industry nor federal agencies (such as the Food and Drug Administration or the Agency for Health Policy and Research) are willing or able to fund such efforts, an independent entity funded by a consortium of companies in the drug-and-device industry could be created expressly to support economic analyses. Grants from such a fund could support cost-effectiveness analyses on a competitive basis and eliminate the concern that support from a single company might lead to hidden biases.

The *Journal* does not have an extensive history of publishing cost-effectiveness studies, and we certainly do not see ourselves as a repository for many of them. When evaluating such studies for publication, we will also apply our usual criteria: How valid and important are the observations? How interesting will they be to

our readers? Lest authors think that any mention of the costs of a treatment or intervention must be confined to formal cost-effectiveness analysis, we also wish to make it clear that these policies do not exclude less formal information about costs in original articles. Such information may be requested by the editors from time to time.

Conflicts of interest in clinical research grow more numerous and problematic as the links between academia and industry grow closer and more complex. The likelihood of bias in cost-effectiveness studies can be reduced if these relations are kept at arm's length.

**Jerome P. Kassirer, M.D.**  
**Marcia Angell, M.D.**

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## Controversial *Journal* Editorials



Over the years we have received numerous queries from readers and reporters about controversial editorials. Many of these inquiries suggest considerable confusion about the purpose of *Journal* editorials and Sounding Board articles (opinion pieces written by people not on the editorial staff). The confusion centers on two questions: Whose opinions do editorials represent? And why don't we regularly seek "balance" on controversial issues? In this editorial, we address these questions.

A quick look at other journals shows why it is so easy to become confused about the first question. Consider, for example, the five largest general medical journals: the *New England Journal of Medicine*, the *Lancet*, *JAMA*, *BMJ*, and *Annals of Internal Medicine*. The single-page lead editorials in the *Lancet* are signed with the name of the journal, clearly indicating that they represent a consensus of the editors. Although the other four journals publish only editorials signed by individuals, each editorial in *JAMA* is accompanied by the explanation, "Editorials represent the opinions of the authors and The Journal and not those of the American Medical Association," implying that the journal as a whole somehow endorses the content.

In the *New England Journal of Medicine* editorials are always signed by individual authors, and they represent the opinions of the authors alone, not those of the *Journal* itself (assuming journals can have opinions). Nor do they represent the official view of the *Journal's* owner, the Massachusetts Medical Society. When the editor-in-chief wrote an editorial in favor of making marijuana available to relieve symptoms in terminally ill patients,<sup>1</sup> he was presenting his own analysis and opinion; when the executive editor argued for physician-assisted suicide in certain circumstances,<sup>2</sup> she spoke for herself;

when one of our deputy editors urged restrictions on the use of appetite-suppressant drugs,<sup>3</sup> he spoke for himself, as did another deputy editor who concluded that there has been enough research on electromagnetic fields<sup>4</sup> and still another editor who suggested nationwide reporting of human immunodeficiency virus infections.<sup>5</sup> Only when editors write about editorial policies do they speak for the *Journal* itself. Thus, editorials about such matters as the Ingelfinger Rule,<sup>6</sup> authors' financial conflicts of interest,<sup>7</sup> or criteria for authorship<sup>8</sup> are not merely the opinions of the authors but explanations of policies that govern the *Journal's* practices. The distinction between editorials about general issues and those that announce or clarify editorial policies (as this one does) is readily apparent.

Most of our editorials fall into neither category. Instead, they are solicited expert commentaries on Original Articles or Special Articles appearing in the same issue of the *Journal*. Their purpose is to put into perspective for our readers research findings that are particularly important, unexpected, or difficult to understand. Although these editorials often include the authors' personal judgments about the subject, they are meant primarily to interpret, explain, and advise. Sounding Board articles, in contrast, are opinion pieces not tied to another article in the *Journal*, and almost all are unsolicited. They often deal with health policy, economics, law, or ethics.

Editorials written by the editors and Sounding Board articles sometimes take strong positions on controversial issues. What is our responsibility to seek an objective or balanced viewpoint in these articles? We believe we have no such responsibility. In the editing process we do not ask that opinion pieces hew to a middle-of-the-road view. Even if it were possible to define such a thing, a journal filled with conventional wisdom would not be useful to our readers, let alone stimulating. No one is particularly interested in reading that everything is just as they thought it was yesterday. Furthermore, a view that seems eccentric or even out-

rageous today may become commonplace tomorrow. When we select opinion pieces for publication, therefore, we consider the importance of the topic, the novelty of the argument, and the logic and persuasiveness with which the argument is made, but we do not ask whether it conforms to today's dominant view, nor do we necessarily agree with it. (Indeed, the requirement of freshness militates against publication of the currently dominant viewpoint.) An editor may choose to write an accompanying editorial when the subject is particularly interesting and the editor believes he or she can make a substantial contribution. Editorials, like Sounding Board articles, should offer fresh insights and be well reasoned, but all the editors need not agree with them.

Since we do not try to achieve balance in opinion pieces, what about doing so by publishing opposing points of view in the same issue of the *Journal*? In fact, sometimes we do solicit a piece on the other side to accompany an especially contentious paper and publish the two together as Sounding Board articles. And our new series, Clinical Debate, from time to time presents opposing perspectives about diagnostic or treatment choices. But we believe that publishing opposing articles on every controversial issue discussed in the pages of the *Journal* would not only be unwise but also tedious. First, it would suggest that all issues have two, equally persuasive sides. Although the popular media, with their adversarial style and emphasis on combat, may promote that idea, we believe it is simplistic. Sometimes there are not two but many points of view, and sometimes there is only one credible one (there is, for example, no need to waste paper on those who do not accept the microbial theory of disease). Furthermore, the debate format tends to drive out considerations of the subtleties of an argument in favor of its most extreme or provocative elements, which are usually well known.

We also believe that trying to balance one point of view with its opposite each time we feature a controversial subject would be insulting to our readers. It would imply that they cannot

evaluate an argument on its own merits or retain and modify it in the light of later arguments. Ideas, even unpopular ones, do not need antidotes. Instead, we try over time to present as many well-reasoned perspectives as possible on important controversial issues. We also try to keep our correspondence section interesting and critical. This section is the best place to air disagreements about published articles. Thus, although we do not seek balance in any given issue of the *Journal*, we often achieve it in the long run, because it serves our readers. That is not so different from what good newspapers and periodicals do. We see these policies as a way to maintain a lively and varied marketplace of ideas from which readers can choose, and we intend to continue this practice. We cannot afford to be too concerned about whether some people or groups will be offended. As Benjamin Franklin said, "If all Printers were determin'd not to print anything till they were sure it would offend nobody, there would be very little printed."<sup>9</sup>

Jerome P. Kassirer, M.D.  
Marcia Angell, M.D.

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1. Lahita R, Kluger J, Drayer DE, Koffler D, Reidenberg MM. Antibodies to nuclear antigens in patients treated with procainamide or acetylprocainamide. *N Engl J Med* 1979;301:1382-5.

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