

BREAST CANCER

How Not to Publicize a Misconduct Finding

It was a shocking revelation: Last week *The Chicago Tribune* disclosed that some of the data underlying an influential clinical trial of surgical procedures for breast cancer were fraudulent. The trial had found that simple removal of an early tumor, or "lumpectomy," is generally just as effective as a mastectomy in preventing recurrence of cancer—a result that has influenced the treatment of tens of thousands of breast cancer patients since it was published in 1985. The revelation, picked up by newspapers across the country, touched off a wave of anxiety as women fretted over whether they had made the correct choice of treatment.

But perhaps the most shocking aspect of this news was the fact that it came as a revelation at all. In fact, problems with some data in the huge, multi-site trial were uncovered more than 3 years ago, and the federal Office of Research Integrity (ORI) reported early last year that one Canadian physician had enrolled ineligible patients and falsified their records to hide the fact. Yet these findings were never communicated directly to some of the investigators in the study or to the *New England Journal of Medicine* (NEJM), which published the original papers. And no reanalysis of the study's results excluding the fraudulent data has yet been published. As a result, when the news broke last week, physicians and their patients had to rely on verbal assurances from the study's principal investigator, University of Pittsburgh cancer researcher Bernard Fisher, and the National Cancer Institute (NCI), which sponsored the trial, that the fraudulent data did not change the study's conclusions.

In the past week, federal officials have been examining what went wrong. And they've concluded that their procedures for notifying the scientific community and the public were part of the problem: Both NCI and ORI are adopting new procedures to ensure that in the future, when cases of research misconduct have public health implications, findings and reanalyses of data are communicated to the scientific and medical community promptly—and through the scientific literature rather than newspapers. "I think that all of us are reconsidering how proactive we should be," says ORI investigator Dorothy Macfarlane.

The events that precipitated this change in policy stem from June 1990, when a data specialist in the breast cancer study—known as the National Surgical Adjuvant Breast and Bowel Project (NSABP)—found discrepancies in data from a group headed by Roger Poisson at the St. Luc Hospital in Montreal. Poisson's team was among the largest of 484 groups that supplied data to NSABP; his patients made up 16% of the study's total population. The report of discrepancies led to a formal investigation by ORI, which issued a report in March 1993 concluding that Poisson had ordered members of his team to falsify records for at least 100 patients.

In spite of the fact that the *Tribune* story came as a shock to most people, ORI didn't hide its findings. It sent its report to NCI Director Samuel Broder and published details of the case in its April 1993 newsletter, which is widely distributed to major U.S. research institutions. The agency also published a one-paragraph notice of the misconduct finding in the 21 June 1993 *Federal Register* and mentioned the case in a press release announcing the conclusion of more than a dozen misconduct cases. These notices did not mention the clinical significance of the original study, however, and they were not picked up by the press at the time.

ORI director Lyle Bivens says ORI had been assured that Poisson's data did not change the conclusions of the study; if that were not the case, "it would have been a much bigger deal and had much bigger implications for ORI's actions." ORI did, however, recommend some steps that would have brought the fraud to the attention of the medical community in a way that would have avoided raising doubts about the integrity of the study's results: In its letter to Broder, ORI recommended that the NSABP publish corrections to the 1985 papers, including a reanalysis excluding all Poisson's data. Bivens says ORI had no authority to compel Fisher to publish such a correction, but ORI counted on NCI to see it was done.

Indeed, at the time ORI issued its report, it had reason to believe a correction was in the works. In December 1992, ORI staff met with NCI officials to outline the findings and discuss what should happen next. Macfarlane says the NCI officials assured ORI that NSABP was preparing a reanalysis

and correction. "I thought we were all in agreement that [NSABP] would have something prepared for publication at the time we released our report" in April 1993, Macfarlane says.

Richard Ungerleider, head of the Clinical Evaluations Branch, says NCI wrote to Fisher in June 1992 and again in January 1993 asking him to publish the correction and reanalysis as soon as possible, "But we did nothing more than that." Fisher, he says, agreed to publish the items, but "wanted to do more than just a recalculation of the analysis. He wanted to talk about the [statistical] issues involved in such a reanalysis, and we didn't insist that he just publish [the correction]. We didn't push him hard enough."

Fisher did not respond to a request for an interview. But NSABP, in a written statement, said it has now finished its reanalysis and distributed a report to three independent reviewers for comment. Fisher sent the reanalysis to NCI last month and the NSABP statement says a manuscript will be submitted to *NEJM* and the *Journal of the National Cancer Institute* for publication.

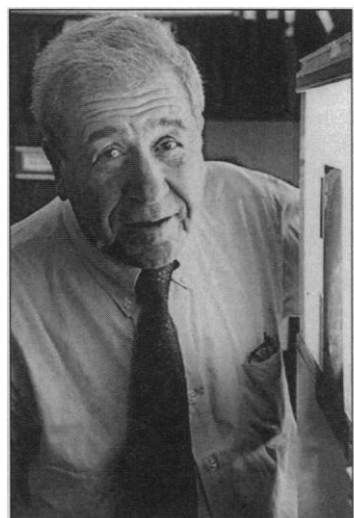
While these machinations over a correction were in motion, the editors

of the journal where the study had been published were in the dark. Jerome Kassirer, the *NEJM* editor, says he first learned about the case when he was contacted by John Crewdson, the *Chicago Tribune* reporter. ORI didn't notify the journal, says Macfarlane, because Poisson's data did not change the conclusions of the paper. Kassirer disagrees with that approach: "The fact is that the scientific record should be corrected. You want the facts available before the hullabaloo."

Bivens says that in the future, ORI will ensure that a copy of the *Federal Register* notice or newsletter account of research misconduct goes to the editor of the journal in which the research was published. ORI will also follow up if it has not had a response within 45 days to any recommendation it makes to a funding agency. And, when there are public health implications, ORI will distribute notices of misconduct findings to a broader range of interested parties.

At NCI, Ungerleider says the agency is working with its legal staff to institute a new policy under which it could publish a correction itself, or compel a grantee to publish one. "We will be aggressive and we want to make it very clear that we will step in," he says.

—Christopher Anderson



No change. Bernard Fisher says the study's conclusions hold firm.

TERRY CLARK/NYT PICTURES