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Breast cancer researcher gave false data for decade

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PITTSBURGH -- Federal investigators have documented more than a decade of fraud in some of the most important breast

cancer research ever conducted, including a landmark 1985 study that established the relative safety of the operation known as lumpectomy and made it a common surgical procedure.

The organizers of the study privately assured investigators nearly two years ago that the fraud had not affected the "direction" of their findings about lumpectomy or any of the other major conclusions that have since been drawn from a complex of related breast cancer studies.

But Dr. Bernard Fisher, the Pittsburgh surgeon who heads the giant research consortium that changed the course of breast cancer treatment in this country, has yet to publish a promised reanalysis of his data or to make any other public acknowledgment of the fraud.

Asked how soon, and in which journal, the reanalysis would be published, Dr. Fisher replied last week, "We don't know yet."

Responsibility for the fraud has been assumed by one of Dr. Fisher's principal collaborators, Dr. Roger Poisson, a professor of surgery at the University of Montreal. He served for more than a decade as a major contributor to the U.S.-Canadian research group known as the National Surgical Adjuvant Breast and Bowel Project (NSABP).

Beginning in 1977, astonished investigators found, Dr. Poisson enrolled at least 100 of his cancer patients at the university's St. Luc Hospital in breast cancer studies conducted by Dr. Fisher even though they were ineligible on medical, technical or consensual grounds.

Dr. Poisson and his assistants then falsified or fabricated the medical records they forwarded to NSABP headquarters at the University of Pittsburgh to make the patients appear to have been eligible.

Investigators said Dr. Poisson apparently was not trying to influence the outcome of the studies but simply to enroll as many patients as possible. One investigator described Dr. Poisson's motive as an "ego trip" that gained him co-authorship on several of Dr. Fisher's most prominent scientific articles and more than \$1 million in research funding from the U.S. National Cancer Institute (NCI).

The federal Office of Research Integrity (ORI), which investigates science fraud, subsequently barred Dr. Poisson from performing any U.S.-funded research for eight years. Officials said it was the stiffest sanction ever imposed in a scientific misconduct case.

In all, investigators documented 111 separate instances of data falsification or outright fabrication involving 99 patients enrolled in 14 NSABP breast cancer studies between 1977 and 1990. There were cases in which women who previously had cancer were reported as cancer-free, cases of breast cancer that were deliberately downgraded or misclassified, dates of treatment that were falsified, and cases in which proper informed consent was never obtained.

Last month, asserting that the data compiled by Dr. Poisson from more than 1,500 patients over 12 years no longer could be deemed reliable, the NCI began efforts to recover the money it has paid Dr. Poisson and St. Luc's since 1980, both directly and through the NSABP. Sources said the total involved was well over \$1 million.

St. Luc's executive director, Jean Leblanc, said in a written statement that the hospital did not accept the conclusion "that 12 years of research had been invalidated" by the fraud. Mr. Leblanc said the hospital continued, at its own expense, to treat more than 1,000 of Dr. Poisson's patients and report data on them to the NSABP, which was still supplying the hospital with cancer drugs.

In addition to the validity of the research data, the Poisson case has raised questions about the administration of the 35-year-old NSABP, which many physicians regard as the nation's premier breast cancer research effort.

Officials at ORI and NCI particularly have questioned how systematic fraud of the sort that occurred in Montreal could have gone undetected by the NSABP for more than a dozen years. They also asked why, once Dr. Fisher and his staff learned of data discrepancies, they failed to inform the cancer institute for more than eight months.

"They should have reported this immediately to the National Cancer Institute," said the ORI's Dr. Dorothy Macfarlane, the government's chief investigator in the case.

Conspiracy of fraud

In addition to its sheer scope and potential significance, investigators said the Montreal case may well be the only instance of fraud in which several members of the same research unit are known to have conspired.

For years, investigators said, Dr. Poisson's staff kept duplicate sets of reports, some actually labeled "true" and "false" in French, and forged the signatures of other physicians at St. Luc's on documents they sent to Pittsburgh.

The staff members, none of whom have been charged in the case, told investigators that Dr. Poisson had assured them the falsifications were being done "for the good of the patient" and would not affect the study's results.

Jerome Kassirer, the editor of the New England Journal of Medicine, where several of Dr. Fisher's most influential articles have appeared, said last week he never was told about the fraud or the possibility that it might affect the conclusions of research studies published by the journal. Mr. Kassirer said he would "try to find out what's going on."

The articles include some of the most frequently cited papers in the modern medical literature, among them the seminal 1985 article showing that many women with early breast cancers have essentially the same chance of disease-free survival after a partial mastectomy, or lumpectomy, as with a more disfiguring total mastectomy.

Study changed treatment

That study, to which Dr. Poisson contributed about 16 percent of the patients, is generally credited with having promoted a far greater willingness to perform lumpectomies among American breast cancer surgeons, many of whom previously had presented total mastectomy to their patients as a far safer option.

Although the NSABP has been supported mostly with U.S. government money, many of the patients in the lumpectomy study came from Canadian hospitals. The reason, a former cancer institute official said, was the greater willingness of Canadian surgeons to essentially roll the dice by assigning patients at random to undergo a then-unproven lumpectomy.

Dr. Poisson was also a major contributor to a 1989 NSABP study, which triggered a "clinical alert" from the cancer institute, showing that many women whose cancers had not spread significantly beyond the breast could benefit from postoperative treatment with various anti-cancer drugs, including the controversial drug tamoxifen.

Because Dr. Fisher and the NSABP have yet to publish a statistical reanalysis, the precise effect of the Montreal fraud on these and related studies remains unclear.

The initial clue in the case emerged more than three years ago when a member of Dr. Fisher's staff discovered that the Poisson group, apparently having fallen victim to its own double record-keeping, had submitted two reports of a breast cancer operation for the same patient.

The records were identical, with one glaring exception: One contained a date for the woman's surgery that made her eligible for the study, while the date on the other record made her ineligible.

When other patient records from Montreal were examined by Dr. Fisher's staff, more alterations were found, along with documents that appeared to show that Dr. Poisson had enrolled at least two patients in the tamoxifen study after they explicitly had refused to participate.

Rather than notifying the cancer institute or demanding an explanation from Dr. Poisson, NSABP officials decided to wait for the next scheduled audit of the Montreal program, then three months away.

It was not until February 1991, more than eight months after the first discrepancies were discovered, that Dr. Fisher finally suspended Dr. Poisson's authority to enroll patients in the NSABP studies. A few days later he notified the NCI that unspecified "irregularities" had been discovered in the data from Montreal.

Inquiry begins

The NCI quickly informed the ORI, whose fraud investigators immediately began their own inquiry. Over the next four months, teams of investigators flew to Montreal, where they compared each of the 1,511 files on patients enrolled by Dr. Poisson with the data Dr. Poisson had sent to Pittsburgh.

What they found, according to the ORI's report, was nearly 100 cases in which Dr. Poisson, or someone acting on his instructions, had altered medical data -- or simply made it up -- to render patients eligible for one of the NSABP's many protocols.

Non-government cancer experts called in to assess the evidence suggested that the investigators might have found only the "clumsy," or most obvious, falsifications in the Montreal data, and that the 99 documented cases of fraud merely represented "the tip of the iceberg."

Within days of the experts' warning, new data fabrications began to turn up, including some pointed out by a contrite Roger Poisson, who then volunteered to investigators that he had falsified data in an unknown number of other cases.

Concluding it was "likely that additional data changes in other cases were not recognized during the audit," the ORI warned the cancer institute that "little confidence" could be placed in any of the data Dr. Poisson had amassed from the 1,500 patients he had enrolled in the NSABP.

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