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Paul Meier, Statistician Who Revolutionized Medical Trials, Dies at 87

By DENNIS HEVESI

Paul Meier, a leading medical statistician who had a major influence on how the federal government assesses and makes decisions about new treatments that can affect the lives of millions, died on Sunday at his home in Manhattan. He was 87.

The cause was complications of a stroke, his daughter Diane Meier said.

As early as the mid-1950s, Dr. Meier was one of the first and most vocal proponents of what is called “randomization.”

Under the protocol, researchers randomly assign one group of patients to receive an experimental treatment and another to receive the standard treatment. In that way, the researchers try to avoid unintentionally skewing the results by choosing, for example, the healthier or younger patients to receive the new treatment.

If the number of subjects is large enough, the two groups will be the same in every respect except the treatment they receive. Such randomized controlled trials are considered the most rigorous way to conduct a study and the best way to gather convincing evidence of a treatment’s effects.

Before randomization, the science of clinical trials was imprecise. Researchers, for example, would give a new treatment to patients who they thought might benefit and compare the outcomes to those of previous patients who were not treated, a method that could introduce serious bias.

The Food and Drug Administration requires randomized trials before approving new drugs, and the National Institutes of Health spend large parts of their budget conducting randomized clinical trials.

Among the other leading advocates of randomization was Sir Richard Peto, a renowned researcher at Oxford University. In an e-mail, Mr. Peto said that Dr. Meier, “perhaps more than any other U.S. statistician, was the one who influenced U.S. drug regulatory agencies, and hence clinical researchers throughout the U.S. and other countries, to insist on the central importance of randomized evidence.”

“That strategic decision half a century ago has already saved millions of lives,” Mr. Peto

continued, “and those millions should be attributed to Paul.”

Perhaps as significant to the field of medical statistics was Dr. Meier’s cooperation with Edward L. Kaplan, a researcher at the University of California Radiation Laboratory, in formulating a now widely accepted standard for estimating patient survival. (Dr. Kaplan died in 2006.)

In a paper published in the Journal of the American Statistical Association in June 1958, the collaborators put forth a new, efficient method for estimating patient survival rates, taking into account the fact that some patients die during research trials while others survive beyond the trials. The method, called the Kaplan-Meier estimator, is based on a complex mathematical formula using information from those who died and those who survived to estimate (depicted in a curve) the proportion of patients alive at any point during the trial.

“If you have a patient with breast cancer receiving a particular treatment or drug, you can estimate her 5-, 10- or 15-year survival rate,” Theodore Karrison, a researcher at the University of Chicago, said Thursday. “It has become the standard tool used by medical researchers for determining the duration of survival in thousands of studies, ranging from cancer to AIDS to cardiovascular disease to diabetes, to name just a few.”

Today, almost every medical study includes Kaplan-Meier curves. And the original paper is one of the most widely quoted in medical literature, having been cited more than 35,000 times, according to the Thomson Reuters Web of Knowledge, a Web site that maintains citation databases.

Born in Newark on July 24, 1924, Paul Meier was one of two sons of Frank and Clara Meier. His father was a chemist; his mother, a school principal.

Besides his daughter Diane, Dr. Meier is survived by his wife of 63 years, the former Louise Goldstone; two other daughters, Karen Meier and Joan Meier; and five grandchildren.

Dr. Meier received his bachelor’s degree in physics and mathematics from Oberlin in 1945, then earned his master’s in mathematical logic in 1947 and his doctorate in statistics in 1951, both at Princeton. He taught at Lehigh from 1948 to 1952, at Johns Hopkins until 1957 and then joined the faculty at the University of Chicago, where he became chairman of the statistics department. He later taught at Columbia.

Researchers were not always attuned to Dr. Meier’s advocacy. “When I said ‘randomize’ in breast cancer trials,” he recalled in a 2004 interview for Clinical Trials, the publication of the Society for Clinical Trials, “I was looked at with amazement by my medical colleagues: ‘Randomize? We know that this treatment is better than that one.’ I said, ‘Not really!’ ”

On Thursday, Robert T. O’Neill, director of the Office of Biostatistics at the Federal Drug Administration’s Center for Drug Evaluation and Research, said that as a member of the agency’s advisory committee, Dr. Meier “forcefully expressed the statistical principles that we follow today, particularly randomization and the follow-up of patients.”

"When Paul spoke, people listened, and few could spar with him."