

In Memoriam: Joseph F. Fraumeni, Jr, MD (1933–2026)

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The world of cancer research lost one of its brightest and most gracious leaders, Joseph F. Fraumeni, Jr, MD, founding director of the National Cancer Institute's Division of Cancer Epidemiology and Genetics (DCEG) within the Intramural Research Program of the US National Institutes of Health. He died in June at the age of 93 years. For more than five decades, beginning in the 1960s, Dr Fraumeni built and led the world's premier program in cancer epidemiology, fundamentally transforming our understanding of the causes of cancer while mentoring generations of scientists who now lead major research programs across the globe.

Dr Fraumeni possessed a rare combination of intellectual brilliance, humility, generosity, and curiosity. He had an uncanny ability to recognize meaningful patterns in cancer occurrence and an instinct for identifying what he called "the interesting questions of the time." Rather than pursuing incremental advances, he envisioned entirely new directions for the field, creating the resources, collaborations, and methods needed to answer questions that others thought impossible. His advice was simple but profound: "Read more and think hard about the long game."

Dr Fraumeni was a proud New Englander, born in Massachusetts and educated at Harvard College and Duke University School of Medicine. Following residency training at Johns Hopkins Hospital and Memorial Sloan Kettering Cancer Center, he joined the National Cancer Institute in 1962. He later became founding chief of the Environmental Epidemiology Branch before establishing DCEG, an institution that remains at the forefront of cancer epidemiology. He was unwavering in his commitment to public service. As a commissioned officer in the US Public Health Service, he rose to the rank of rear admiral and assistant US surgeon general before retiring in 1999. The American flag and Public Health Service flag standing prominently behind his desk reflected his lifelong belief that scientific excellence and public service were inseparable.

One of his earliest scientific contributions, which combined clinical insight and epidemiological approaches, continues to have major importance today: his work on inherited cancer susceptibility. In 1969, together with his close colleague, the late Dr Frederick P. Li, he described an unusual pattern of cancers affecting several families, ultimately defining the condition now known as Li-Fraumeni syndrome. Their discovery led directly to identification of inherited mutations in the *TP53* tumor suppressor gene and established the field of cancer susceptibility genetics. Today, more than 120 cancer predisposition genes have been identified, fundamentally changing cancer prevention, surveillance, and patient care worldwide. The ongoing National Cancer Institute Li-Fraumeni Syndrome Study continues to expand this legacy through improved understanding and follow-up of affected families.



Dr Fraumeni's influence permeates nearly every corner of modern cancer epidemiology. Investigators confronting difficult scientific questions inevitably encounter foundational papers bearing his name or written by 1 of his many trainees. Along with Dr Robert Hoover and Thomas Mason, he developed the first US Atlas of Cancer Mortality in 1975, a pioneering series of county-level maps revealing striking geographic patterns of cancer. These observations launched investigations that linked excess cancer risk to environmental exposures such as arsenic emissions from copper smelters; occupational hazards, including asbestos; and lifestyle practices such as smokeless tobacco use in the American South. These discoveries informed public health policy, strengthened workplace protections, and undoubtedly prevented countless cancers. Many countries have since duplicated the process of developing cancer maps and following the leads they generate.

Dr Fraumeni also recognized long before others that epidemiology would be transformed by biology. He championed the systematic collection of biospecimens from carefully characterized study populations, anticipating that future technologies would unlock information not yet imaginable. He fostered collaborations across disciplines and continents and integrated emerging molecular techniques into population-based and family-based studies. In doing so, he helped establish the field of molecular epidemiology, enabling researchers to examine the interplay of inherited susceptibility, environmental exposures, and lifestyle factors in cancer development.

Dr Fraumeni also anticipated the genomic revolution. Long before genome-wide association studies became commonplace, he recognized that deciphering common genetic susceptibility would require the integration of epidemiology, human genetics,

and rigorous biostatistics. He positioned DCEG to lead this transformation, creating an environment that attracted investigators eager to explore the genetic architecture of cancer. Cancer, he suggested, is “100% genetic and 100% environmental.” The task for future generations would be to understand how those forces interact to produce individual cancers. That elegant observation continues to resonate today.

As founding director of DCEG in 1995, Dr Fraumeni created an enduring research enterprise capable of addressing scientific questions over decades. Under his leadership, DCEG established landmark prospective cohort studies that continue to illuminate the roles of lifestyle, environmental, and genetic factors in cancer risk. Other investigations focused on unique populations, including three generations of women exposed to diethylstilbestrol, demonstrating the profound influence of early-life exposures on cancer risk later in life. He also guided long-term studies of survivors of the atomic bombings in Japan and the Chernobyl nuclear accident, providing invaluable insights into the carcinogenic effects of ionizing radiation.

Perhaps his greatest gift was recognizing potential in others. He could identify exceptional talent regardless of age, degree, nationality, or gender, and then provide opportunities long before conventional credentials caught up. He promoted women into leadership positions when few institutions did so and supported flexible career paths that allowed talented scientists to remain productive during different stages of life. He trusted young investigators with substantial responsibilities while encouraging them to pursue additional training that would strengthen their futures. His confidence inspired extraordinary loyalty because it was always accompanied by steadfast support.

In truth, those fortunate enough to work with him always remained trainees, regardless of rank or accomplishment. His command of the scientific literature was legendary. During discussions, he would often cite an obscure paper from decades earlier, summarize its essential findings from memory, and thoughtfully explain both its insights and its limitations. These lessons were delivered with characteristic gentleness and genuine interest in what others thought.

His mentorship extended well beyond scientific ideas. His editing transformed manuscripts into clearer, stronger papers. His handwritten comments, neatly inscribed in tiny pencil script, became legendary among trainees, who often gathered to

decipher them together. Each marked-up manuscript was a master class in scientific writing. He consistently encouraged collaboration over competition, reminding investigators to “work doggedly together and be sure to listen to each other.”

Although widely recognized with virtually every major honor in epidemiology, medicine, and cancer research—including election to the National Academy of Sciences, the National Academy of Medicine, and the American Academy of Arts and Sciences—he never displayed his awards. His office reflected curiosity rather than prestige. His scientific legacy is documented in more than 900 publications and several influential books, including *Cancer Epidemiology and Prevention*, universally regarded as the definitive textbook in the field, with its fifth edition in formation.

His office contained two objects that perfectly captured his philosophy. One was a *New Yorker* cover showing a row of birds perched along a rooftop, all facing forward except 1. “That’s the epidemiologist,” he would explain. “We must look back to understand how we arrived here.” The second was a framed *kanji* calligraphy reading, “When you drink the water, don’t forget who dug the well.” It reminded everyone to honor those whose work laid the foundation for future discovery. Conversations in his office often concluded with lighter topics. After discussing science, he delighted in conversations about New England, Harvard traditions, the Boston Red Sox, or lobster rolls. Often, he would conclude a meeting with his signature questions about obscure university mascots.

Dr Fraumeni is survived by his brother, Arthur Fraumeni, and many nieces and nephews. Earlier this year he was predeceased by his beloved wife of nearly 49 years, Patricia (D’Arcy) Fraumeni.

It is difficult to imagine the field of cancer research without the quiet presence of this gentle giant. Joseph Fraumeni transformed epidemiology, established entirely new scientific disciplines, and mentored generations of investigators whose work continues to improve human health around the world. His enduring legacy lies not only in discoveries that changed medicine but also in the countless scientists he inspired to ask bold questions, think deeply, collaborate generously, and always remember those who dug the well before them. In every sense, he embodied Ralph Waldo Emerson’s enduring words: “Do not go where the path may lead; go instead where there is no path and leave a trail.”