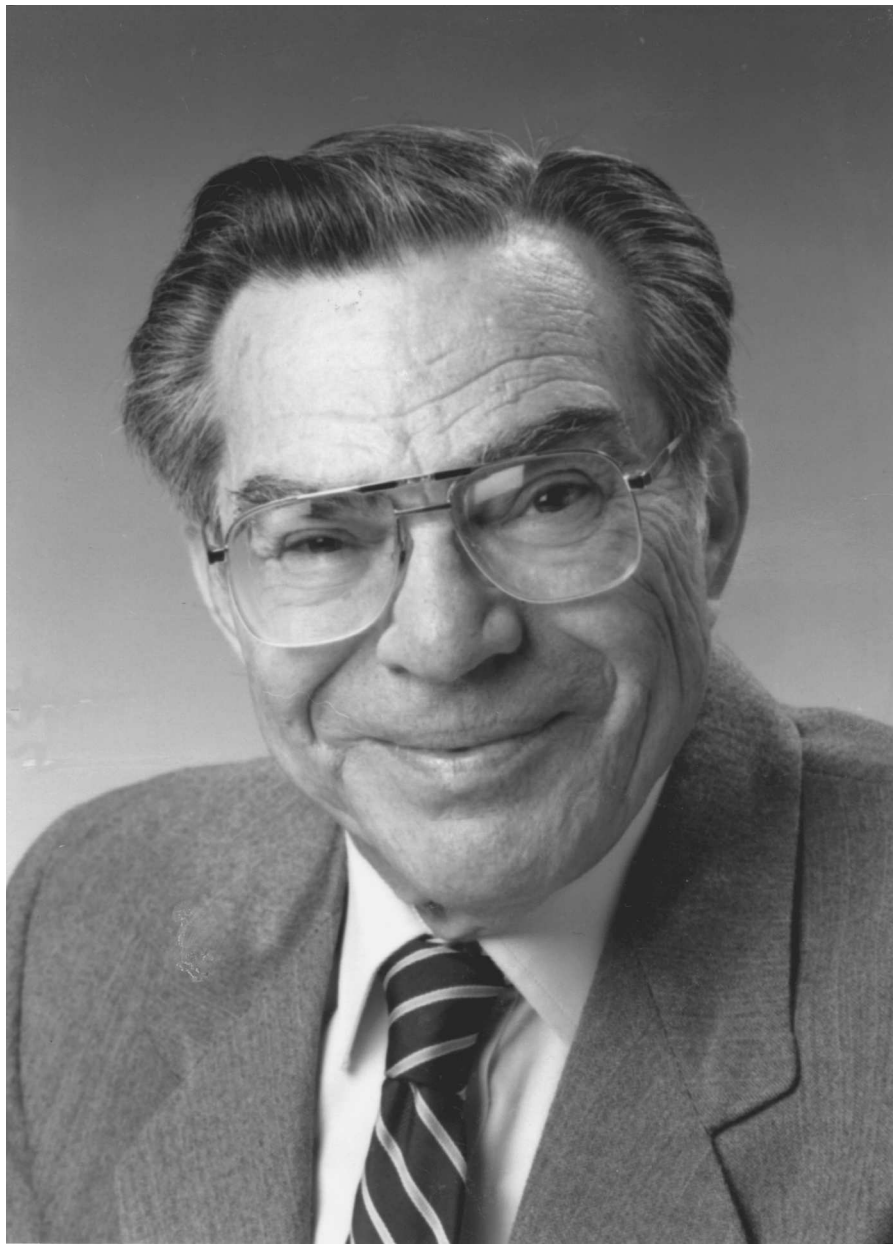

FIG. 1. *Samuel W. Greenhouse.*

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Some Reflections on the Beginnings and Development of Statistics in "Your Father's NIH"

Samuel W. Greenhouse

Abstract. Samuel Greenhouse was born on January 13, 1918, in the Bronx (New York). He received a B.S. degree in mathematics from the City College of New York in 1938, an M.A. degree from George Washington University in 1954 and a Ph.D. in mathematical statistics from George Washington University in 1959. He is a Fellow of the American Statistical Association, the Institute of Mathematical Statistics, the American Association for the Advancement of Science (AAAS) and an elected Fellow of the Royal Statistical Society. He is also an elected member of the International Statistical Institute, a Fellow of the American College of Epidemiology and a Fellow of the Council of Epidemiology, American Heart Association. He is a past President of the Eastern North American Region of the Biometric Society and served on the Council of the International Biometric Society. He has served as President of the Washington Statistical Society, as Chairman of Section U (Statistics) of the AAAS and as a member of the AAAS Council Executive Committee. He has been an Associate Editor of the *Journal of the American Statistical Association*, and has served on the Board of Directors of the Society for Clinical Trials. His tenure at the National Institutes of Health included the years 1948–1974, where he began as a mathematical statistician at the National Cancer Institute. He served next as Chief of the Theoretical Statistics and Mathematics Section in the Biometry Branch of the National Institute of Mental Health (1954–1966), with an interlude as Visiting Professor of Statistics at Stanford University. He joined the National Institute of Child Health and Human Development (NICHD) in 1966 as the Chief of the Epidemiology and Biometry Branch. He wore two hats at NICHD, as Associate Director for Epidemiology and Biometry and as Acting Associate Director for Program Planning and Evaluation at the time of his retirement from NIH in 1974. Since leaving the NIH, he has been Professor of Statistics at George Washington University, serving as Head of the Department of Statistics 1976–1979 and 1986. During this time he was also Visiting Professor of Biostatistics at the Harvard School of Public Health. He is currently Associate Director for Research Development at the Biostatistics Center of George Washington University, and Professor Emeritus, George Washington University.

The scientific program for the National Institutes of Health Conference on Current Topics in Biostatistics [3] covered a wide range of recent biostatistical advances as well as paid tribute to the origins and the development of statistics at the National Institutes of Health (NIH). [The members of the organizing committee were Jonas H. Ellenberg, Chair, Susan S. Ellenberg, Mitchell H. Gail, Nancy L. Geller, Sylvan B. Green, William R. Har-

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lan, Joseph K. Haseman and Richard M. Simon.] I would like to provide some additional perspectives relevant to the history of biostatistics at the NIH.

Biostatistics began in earnest at NIH with the arrival of Dr. Harold Dorn on the NIH campus in 1947. His first statistical recruits were Nathan Mantel, Jerry Cornfield, Jack Leiberman and George Deal. Strictly speaking, Dorn's unit was initially in the Division of Public Health Methods of the U.S. Public Health Service, not in the NIH. Marvin Schneiderman and I arrived at Dr. Dorn's office in a temporary building known as T-6 a day after Labor Day, in 1948. I did not know Cornfield, Mantel or Deal. Jack and I, however, worked together in the Census Bureau during the 1940 Census. We both did a lot of work checking Edward Deming's book on the adjustment of data [2]. Dr. Dorn's operation dealt almost entirely with statistical collaboration within the recently established National Cancer Institute (NCI). It was not too long—a matter of two or three months—before Dr. Dorn and staff were transferred to NIH in the National Cancer Institute and became the Biometry Branch. The NCI administrators thought that they were going to do us a favor by taking Jerry, Jack, Nathan, Marvin and me and putting all five of us in one office. Aside from the obvious good or bad features of this move, there was one unusual and unexpected outcome bearing on each individual's choice of statistical activities: namely, whoever answered the phone became the consultant for the calling investigator, if he, of course, was calling about a statistical question. It was as a result of this fortuitous procedure that there arose the important collaboration between biologist Abe Goldin, Nathan and myself [4, 5] which extended conventional biossay to a probit plane. Abe's laboratory was in Baltimore and Nathan and I would travel there about once every two weeks in my car. After about two years, Nathan learned how to drive and bought a car. It is not true as some have claimed that I left the collaboration when Nathan began to use his car to drive to Abe's lab; it was rather that I moved over to head a Section in Mort Kramer's Biometry Branch of the National Institute of Mental Health (NIMH).

There were some small but important matters that have more or less affected the careers of every statistician at the NIH today. In the early 1950s, Dr. William Sebrell, the Director of NIH at that time, had evidently been informed by some very prestigious scientist outside of the NIH that he was impressed by the work of one of the statisticians at the NIH. (I believe that the statistician was Jerry Cornfield and I believe the scientist was Warren Weaver, who was then at the Rockefeller Institute). Sebrell, apparently convinced by these comments of the importance of a statistical presence at NIH, met with Harold Dorn and offered to establish a central NIH Division of Statistics and probably of Mathematics or Mathematical Biology. The Division was to be independent of the administrative control of any of the categorical Institutes but would assume the responsibility of serving all the professional staff, scientists and others, in all the Institutes. Dorn brought this proposal to the five of us for consideration. Our immediate response was to go for it, a response that was clearly motivated by the prospects of the prestige of attaining equality with biomedical investigators. We considered the advantages and disadvantages of being centralized as opposed to being decentralized. However, several days later, Harold came into our office and mentioned an extremely critical factor. He pointed out that as a central Division there would be one line of command: one GS-15 (at that time there were no supergrades), possibly a couple of GS-14's, and so on down the line. [The Federal Government pay scale had 16 pay grades called the General Schedule (GS), with grade 16 the highest. Supergrades were formerly grades 17 and 18, which were subsequently superseded by the Senior Executive Service with a five-level system.] On the other hand, if we opted for decentralization, that is, a Biometry Branch in each of the five or six separate Institutes, we would be able to recruit for five or six GS-14's, later becoming 15's, and 10 or 12 GS-l3's and so on down the line The proper choice was obvious and NIH and its biostatistical community are now enjoying the fruits of the decision to create a Biometry Branch within each categorical Institute.

In those early days, a great camaraderie developed among us. We almost always lunched together, sometimes going out to a luncheonette called the Blue Bell but most often eating in the cafeteria in the NIH Administration Building, Building 1 (subsequently named the James E. Shannon Building in honor of a long-time NIH Director). We were often joined by others, most notably by members of the Public Information Office with whom we shared common intellectual interests. Our luncheons were usually quiet and sociable, as long as we discussed subjects other than statistics. But when we raised statistical topics, almost always there were loud shouting matches without regard to the comfort of those around us. In fact, biochemists, chemists, secretaries, even the senior administrative people of the NIH would comment on "that group of

statisticians"—which now included Max Halperin, who joined the Heart Institute in 1951. We were all guilty of raising our voices: Max, Jerry, Nathan, Marvin and myself. At times, the arguments would carry over when we returned to the office and Dr. Dorn would stick his head through the doorway and innocently inquire what was going on.

Not all of our discussions at lunch or in the office involved technical statistics. Our most serious, enjoyable and fruitful discussions related to our view of statistics at the NIH, and what should be the mission of mathematical statisticians at the NIH. Before elaborating on the mission referred to, it is necessary to make some distinctions among the statisticians at the NIH and their activities. Clearly, not all their objectives were the same.

The NIH Institutes generally comprised an Intramural and an Extramural program. The Extramural program dealt primarily with awarding and supervising grants and contracts, which in some cases involved close direction and/or collaboration of the Extramural scientists with the awardees. In contrast, the Intramural program clinical and laboratory scientists established their own research agenda to be carried out on the whole within the NIH. As a rule, most of the work of the mathematical statisticians who arrived circa 1948 involved consulting with the Intramural scientists at the NIH in all the then existing Institutes. In addition, they engaged in research on statistical theory and methods, the design of experiments, applied probability and applied mathematics. At the time there was no central clinical research facility (subsequently developed as the "Clinical Center") as a source for clinical collaboration. However, now and then we were called upon to consult with clinical investigators outside of NIH. For example, I was recruited by Dr. Jack Dunn in Cancer Control at the National Cancer Institute to provide statistical guidance to a group of four pathologists in different medical schools participating in a program to develop a serodiagnostic test for the detection of cancer.

The statistical work going on under Dorn's direction at the National Cancer Institute was much broader than statistical consultation with Intramural scientists and methodological research. It involved collaboration on major studies with investigators outside of NIH such as collecting data on cancer morbidity and mortality, initiating community studies and other similar research [7, 8]. Later, Bill Haenszel as the successor to Dorn, set out on a major program of detecting differences in cancer data between populations remaining in their native lands and those who had migrated to other countries [9]. Similarly, Felix Moore as Head of the Biometry Research Branch in the Heart Institute had the foresight and initiative to bring the Framingham Heart Study [1] to his Branch from the Public Health Service and made important changes in its design and implementation. Also, in the early 1950s, Mort Kramer established a Biometry Branch in the Mental Health Institute, where he founded a program called the Model Reporting Area (MRA) that invited voluntary cooperation of State Mental Health workers to submit a variety of reports on admissions to and discharges from State Mental Health Institutions. Dr. Kramer and his yearly statistical data obtained from the MRA's became extremely important to the Director of the Mental Health Institute especially when he testified before Congress. I am sure that the Directors of the other Institutes were equally dependent upon their Biometry Branches.

The mission we were trying to define refers only to the role of mathematical statisticians involved principally in Intramural research. One thing was not subject to any debate, namely, we were at the NIH, in accordance with Harold Dorn's directive, in order to provide the best statistical advice in response to questions posed to us by Intramural scientists in the laboratory and by investigators in nonlaboratory settings such as epidemiologists. This purpose was a sine qua non which we never questioned. (I believe much later this principle was not adhered to and may not even have been recognized, so that mathematical statisticians came to the NIH with the goal of concentrating primarily on statistical research.) A secondary objective was for the mathematical statistician to conduct research in methodology and theory. Clearly, to the extent to which this research related to our laboratory consultations, either in extending and generalizing existing techniques or in developing new ones, there was no problem. But the interesting question arose as to whether our research should be limited in that way. What if our own research or our readings led to questions not immediately related to any laboratory problems? We finally agreed among ourselves, and I believe (but am not certain) that Dorn also agreed with us, that there should be no limitations on the scope of our statistical research. So, for example, Jerry Cornfield contributed to Bayesian inference and methods, Nathan Mantel did research on the Buffon needle problem, and so on. Although most of the research

output from the statisticians at the NIH over the following four decades was primarily related to biomedical issues, it was and still is gratifying that we took this position.

There were some interesting incidents related to this unwritten policy. One occurred in the ad hoc Statistics and Biomathematics Study Sections where we advised the Executive Secretaries not to reject grant applications on the basis of health relevancy. At one such meeting of an ad hoc group, a well-known statistician became upset with an application which he considered to be outside the realm of NIH support. We could not convince him otherwise and he refused to participate in the review. A second incident involved Jerzy Neyman. He was invited to spend a few days at the NIH. When he asked us what he should talk about, we shocked him by responding that he should talk on his work on galaxies. I suspect he thought we would want to hear about his work on the genetics of the fruit fly.

During our discussions on mission, we got sidetracked to consider interesting questions on the nature of statistical consulting or on the essence of statistics itself. These discussions took place in 1948–1949; the subject would probably be considered old hat today, as it is now fashionable to refer to the field as *statistical science*. What we asked was how much, if any, of what the statistician in a research organization does is strictly science. This was not a very clear question because of the ambiguity of the word "science." But in our context we meant this in the very narrow sense of mathematics and probability. Of course, after a year of consulting with biochemists, chemists, biologists and pharmacologists, and later on when some of us consulted with social scientists and clinicians, it was easy to obtain an answer to the question. It was amazingly clear to each of us that the totality or gestalt of the investigator–statistician interaction was for the statistician as much art as it was science. The art was in the way in which one elicits the specific information from the investigator needed to find an optimum research design: the question, the nature of the measurements, the intervening factors that ought to be controlled, and so on. But even more important than the design is the art necessary in the analysis of the data. What is the information in the data relevant to the question being asked? How do you extract this information from the data in an efficient manner? What is the pool of techniques available to provide an answer to the question and how do you choose the best among these choices? And I might mention that among statisticians the world over we had probably the greatest artist of all—Nathan Mantel. No one could match him in quickly identifying the information in the data relevant to the question and the swiftness with which he was able to choose an optimum method of analysis. The statistical procedures that bear his name are really nothing compared to his ability to analyze data. The former would have eventually been derived by others, but it is doubtful whether any one else has had his intuition.

I would like to conclude with remarks related to an article written by Dr. Bernadine Healy (Director, NIH, 1991–1993) in *Science* [6]. The article is entitled "Is this your father's NIH?" In general, the article deals with Dr. Healy's strategic plan that presents five major challenges to the NIH of the future. There is much to argue with in her assumptions that underlie the five innocuous questions she poses, but that is not my concern here. I just want to quote one sentence from her article: "NIH does not exist to do science for science's sake but rather for practical and humanitarian purposes: to improve and preserve the health of the American people." One's immediate and obvious reaction is: "How does she or any one else know which pure science research will lead to the ends that she desires?" But I do not think Dr. Healy means to go as far as this sentence implies in ruling out doing DNA research, say, for molecular biology's sake. Rather, I wish to contrast her position in 1992 with our more liberal, and possibly more productive, position with regard to statistical research at the NIH in the early 1950s. In every age, I believe that ours will be judged to be the more advanced policy.

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