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A Conversation with Tavia Gordon

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Abstract. Tavia Gordon was born on December 14, 1917, in Chicago, Illinois. He received a B.A. degree in anthropology from the University of California in 1938. He did graduate work in anthropology at the University of Chicago in 1938–1939, in mathematics at the University of Southern California in 1947–1948, and in mathematical statistics at the University of California, Berkeley, in 1948–1950. He is a Fellow of the American Statistical Association and the Council on Epidemiology, American Heart Association. His tenure at NIH included the years 1954–1960 and 1966–1977, beginning as an Analytical Statistician with the Biometrics Research Section of the National Heart Institute. He spent the next two years at the Biometry Branch at the National Cancer Institute. His last 10 years at NIH were spent at the National Heart, Lung and Blood Institute. During this period he was heavily involved in the development of the design and analysis of the first long-term, large-scale community-based follow-up study in the United States, the Framingham Study. He was awarded the NIH Director's Award in 1977. Since leaving the National Institutes of Health, he has been a consulting statistician, a senior scientist for General Electric Corporation and, since 1981, a Research Professor at George Washington University Biostatistics Center.

Geller: Where were you before coming to NIH?

Gordon: After graduate work in mathematical statistics at Berkeley in 1950, I went to work at the California State Department of Mental Hygiene. That was at a time that the Department of Mental Hygiene ran a large number of inpatient facilities throughout the state with one of the largest mental health populations in the country. But I wanted to get to Washington, D.C., and if possible to NIH, where they were doing really good statistics. In those days, getting hired for a government position anywhere was extremely difficult. I began work for the federal government in the United States Public Health Service as a "temporary indefinite" employee on a household polio survey in Phoenix. From there I had a short tenure with the National Office of Vital Statistics in the Mortality Analysis Branch until Eisenhower became president and cut a number of federal jobs (times never change). I found a temporary haven in the Medical Statistics Division of the Office of the Surgeon General of the Army until 1954, when a permanent position finally opened at the Heart Institute, NIH.

Geller: You left the Heart Institute for the Cancer Institute, but then you returned. How did that come about?

Gordon: I left the Heart Institute in 1958 for the Cancer Institute, where I stayed until 1960, working with Bill Haenszel and Mike Shimkin. By 1960, there were two competing epidemiology/biometry units and one was going to be disbanded. Since I had an offer from the National Center for Health Statistics to work on the National Health Examination Survey, I left NIH. Then in 1966, Jerry Cornfield recruited me to take over the Field Epidemiology Studies Section at the then National Heart, Lung and Blood Institute (NHLBI).

Geller: Can you describe some of the projects and the structure of the staff and collaborative efforts when you first came to the Heart Institute?

Gordon: The Biometrics Research Branch in the NHLBI was set up by Felix Moore. When I arrived, Felix had a small staff which included Max Halperin as a consulting statistician. Max was located at the NIH Clinical Center, consulting across all of the Institutes.

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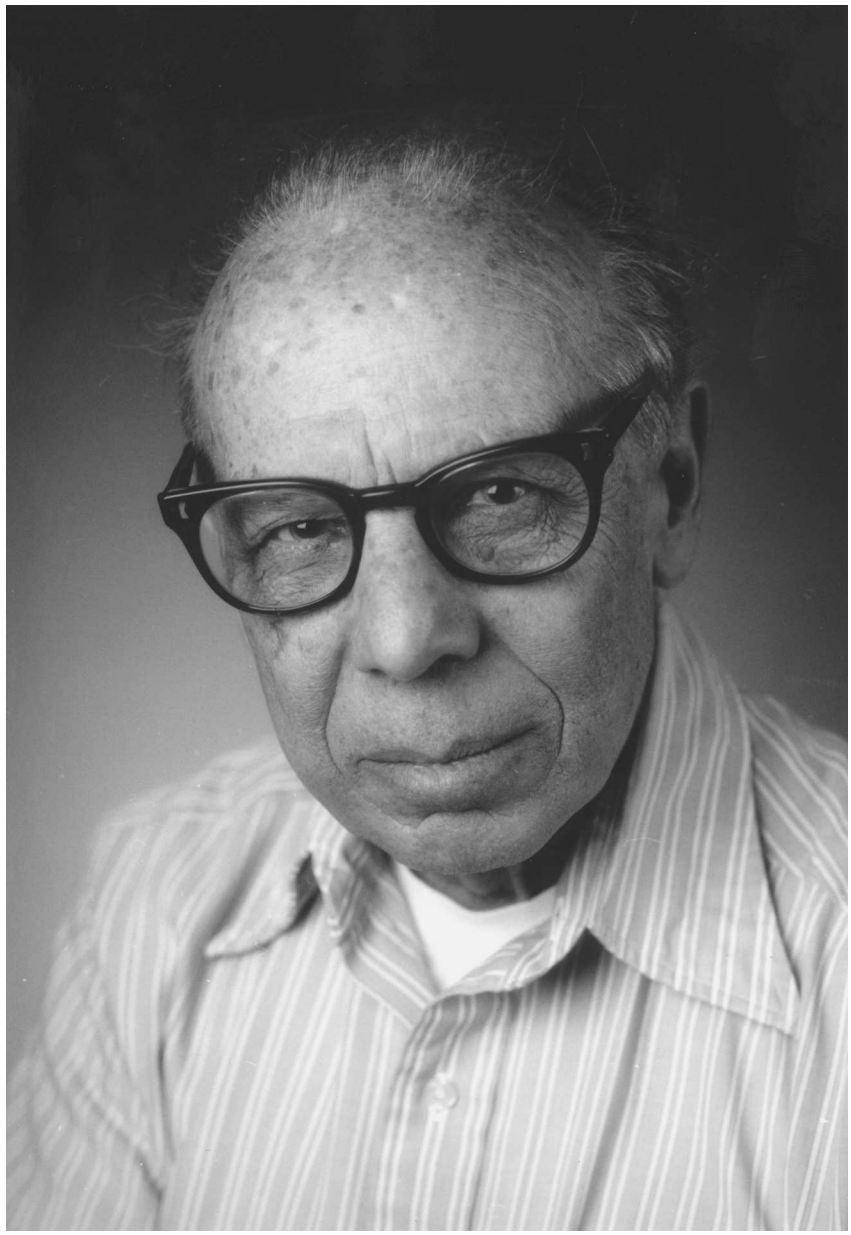

FIG. 1. *Tavia Gordon.*

FIG. 2. *Max Halperin.*

The Biometrics Research Branch was engaged in two major activities when I got there. One of them was the Framingham Heart Study and the other was the Cooperative Lipoprotein Study. First I worked on the Cooperative Lipoprotein Study, and later I worked on Framingham.

The Cooperative Lipoprotein Study [9, 12] was an investigation of a hypothesis which was postulated by John Gofman, a physicist who was interested in medical research. He postulated that lipoprotein in the range now called low-density lipoprotein (LDL) was the causative factor for coronary heart disease. A variety of centers came together, in a cooperative prospective epidemiological study, to compare low-density lipoprotein with total cholesterol in healthy populations as predictor(s) of coronary heart disease. The Gofman group did their own analysis. The Biometrics Research group analyzed the data for the others. The Gofman group concluded that the low-density lipoprotein was a better predictor and all the remaining investigators concluded that total cholesterol was at least as good. Gofman had additional follow-up data from some of the centers and used a slightly different endpoint. As it turned out, Gofman was right, and everybody else was wrong. Of course, there is a fairly high correlation between total cholesterol and LDL.

The Framingham Study originated outside of NIH. It was Felix Moore who convinced Dr. James Shannon, the then Director of Intramural Research for NHLBI, to support the Framingham study. Felix transformed Framingham from what was essentially a screening program into a population-based prospective study [6]. After I left in 1958, Harold Dorn took over the Field Epidemiology Studies Section, which supported the Framingham Study. His contribution was to set up a series of prospective studies around the world on the model of Framingham. They began with a group of middle-aged men who were characterized and then followed for as long as the funding allowed. There were studies in Yugoslavia, Puerto Rico and one in Hawaii, which eventually became the Honolulu Heart Study. There were also studies of the Japanese in California and one in Israel.

Geller: The Framingham Study still exists today. So, when you returned to the Heart Institute, did you work on that?

Gordon: When I came back in 1966, I was given the assignment of coordinating all of the studies based on the Framingham model. By then, Dorn had died and Jerry Cornfield was Branch Chief. The Biometrics Research Branch was split up into two groups: the Field Epidemiology Studies Section and the more mathematical statistics group. In 1969, Max Halperin (Figure 2) took over the Biometrics Research Branch from Jerry Cornfield. I continued to take care of the Field Epidemiology Studies Section, with whatever staff I needed for the purpose. Max took care of the consulting Mathematical Statistics Section, and was also Chief of the Branch.

Geller: And what were some of the other projects?

Gordon: There was a clinical trial of rheumatic fever, which I think was the first randomized placebo-controlled clinical trial sponsored by NIH. The active treatment was a steroid and the placebo was aspirin, and the end point was the development of rheumatic heart disease. This study was jointly designed by Felix Moore and a statistician from the American Heart Association. To everyone's surprise, it turned out the placebo was better than the treatment—that it wasn't a placebo—in fact, it was an active treatment [13].

A major problem occurred when the original polio vaccine was field tested. There were some cases of polio which arose from the fact that not all of the virus had been inactivated. NIH was called in to evaluate the situation. Felix Moore, Jerry Cornfield and Max Halperin set up an ad hoc statistical evaluation group to look at the data and make a judgment as to what was going on [2]. I remember that as a rather interesting experience because Max and Jerry were mathematical statisticians, Max more so than Jerry, and Felix was more of a public health statistician. I think they all came away from that experience with a heightened respect for each other. Like a lot of analytical work, there was a political dimension to it, and Felix was the one who could recognize the political concerns and directed the work to avoid or address those where necessary. Felix also had a *very* strong feeling for data, and this was invaluable in trying to sort out what was going on in this disaster. There were many ad hoc statistical evaluative groups at NHLBI, where several statisticians would work together on a problem and pool their resources.

Geller: What are some important methodological results or applications which demonstrated the contributions of statistics to the science produced at NIH?

Gordon: The Framingham Study is an excellent example. Felix Moore had done the primary analysis based on a six-year follow-up. He simply took the three risk factors in which he was interested (serum cholesterol, borderline hypertension and cigarette smoking) and dichotomized them. He then considered all the combinations of values of the three variables, looked at the incidence of heart disease for each combination of risk factors and did a chi-square test on the results. He came up with all the right answers [3].

However, it seemed to me that there was a lot of information thrown away by this dichotomization. I approached Jerry Cornfield with the question, "How would you assess the risk factors, treating the variables as continuous variables?" It turned out that the solution to another problem Jerry had been working on was applicable to our problem. Basically, his model considered two normal distributions which differed in their means but not in their variances, and he constructed a logistic function on the basis of the mixture of the two [1]. While the model was dependent on the assumption of normality, it was fairly robust. If I had been a little more knowledgeable then, I would have recognized that I could have accomplished the same thing with a discriminant function, except, of course, I could not provide an estimate of the probability of developing heart disease.

Another methodological approach was developed in trying to estimate a logistic function using a sample of all the data available. Use of all the data would have been very time consuming with the computers of the day. The idea was to use all the cases and then a sample of the noncases. Max Halperin struggled with that concept, but he could not come up with a solution which he thought was satisfactory. We finally asked Nathan Mantel and he came up with a very simple, straightforward, elegant solution [10].

There were occasions when the straightforward use of the Mantel–Haenszel test wasn't applicable. For example, we were interested in a test of the homogeneity of the odds ratios across strata. Nathan whipped out a solution for that [11]. All of these techniques are standard now, but then they were new.

We also participated in the development of the Multiple Risk Factor Intervention Trial (MRFIT) [8]. For that purpose, Max and I devised a sampling procedure for identifying high-risk people using Framingham information to set up a risk identification.

Geller: I'd like you to comment on some of what Sam Greenhouse says about the research mission of NIH statisticians in his paper introducing these conversations [7]. Did the scope of research under-

taken by the NHLBI statisticians in the early days reflect the other activities of the Institute or was research for the sake of research, "external to health," as Greenhouse says?

Gordon: Some of the mathematical statisticians were interested in problems generated by data and others were not. There was less emphasis on publishing new methodology than there is today. I know of several examples where Max Halperin worked out some particular methodologic problem, did not bother to pursue its publication and then later somebody else derived the same solution and published it. I never felt under any pressure to publish. We would publish because we felt that what we had was interesting and useful. Now, that is no longer the case, especially in the Intramural program. I could never have made it in the Intramural program as presently constituted.

Geller: What were the training backgrounds of statisticians at NIH in the early days?

Gordon: Neither Jerry Cornfield nor Nathan Mantel nor I had Ph.D's. Today an advanced degree is a requirement. We came out of an entirely different generation growing up during the Depression, and schooling was not something that you dawdled over. I went back to school under the GI Bill, because I had never had any statistics prior to going into the Army. My undergraduate major was anthropology. When I came out of the Army, I decided I wasn't going to be able to make a living as an anthropologist. I took a bunch of tests, and they were really very helpful because they helped me focus my own interests. World War II really produced a generation of people with superb skills as a result of the GI Bill.

Geller: Sam Greenhouse comments on the far-reaching positive effects of decentralization of biostatistics at NIH in 1951, about three years before you arrived. It seems that the downside of decentralization is the less frequent interaction of statisticians in different Institutes [7]. Were inter-Institute collaborations still commonplace when you arrived?

Gordon: When I first got to NIH it was a rather small organization with just a relatively few buildings. We were first housed in a wooden building which was a temporary facility called T-6. There weren't a lot of other buildings on the NIH campus and there was a lot of nice, open space. This was all conducive to a great deal of interaction. It was a lot easier for people to communicate, because there were a lot fewer people, and also everybody was somewhat new at what was going on. There really was not a lot of attention paid to Institute lines by the consulting statisticians. In addition, the senior statisticians knew each other personally. It was a personal relationship which arose from what you might call a single cell, namely, the original group of statisticians recruited by Dorn. The senior statisticians were eventually distributed among the Institutes for administrative reasons, but consultation was still not Institute restricted. I did not have much problem getting assistance from statisticians who were not in the Heart Institute. I made ample use of Nathan Mantel and Jerry Cornfield.

Geller: Could you give us your perspective on how statisticians became involved with particular problems?

Gordon: Some of the problems we worked on would arise just from following up an idea which was an offshoot of previous work. Most of the statisticians really had to go out and persuade researchers that their skills really could be useful. Max Halperin was always looking for his stimulus from actual real-life problems. He would walk around and ask "What have you got that I might be interested in?", and he would proceed to get involved, mainly with statistical issues.

For example, a lot of our concern was with the problem of bias, selection bias, or bias arising from other sources. Max and I had a long-term running dialogue on this issue. It was always a source of amazement to us how easily bias would arise and how hard it was to spot it in either a design or analysis. In the Framingham Study, Felix Moore devised a sampling scheme to evaluate the relationship of diet and serum cholesterol. The sample was devised as follows: a sample was drawn of persons with high cholesterol, another sample of persons with low cholesterol, then a random sample of the remainder, which altogether gave a sample of the whole group. The question of analyzing that costly data set ultimately came to me. Nobody seemed to want to touch it. I asked Max, "What am I going to do with this? This is a peculiar type of sample. If you simply take the data as given, you can get a regression, but is it a reasonable regression?" Max said, "No! You have selection bias if you just take the data as given." So, Max sat down and devised a procedure for using the data to get an unbiased estimate [5], which was substantially different from the unadjusted estimate. Max recognized this problem from previous work. He devised a method for estimation from a similar sampling scheme, one in which the dependent variable is sampled. Unbiased estimates can be produced which are a good deal more efficient than if a random sample of the entire group had been drawn. This led to a paper which Max and Dave DeMets produced [4] which has proved to be of considerable interest to people interested in sampling

theory, not necessarily at the Heart Institute or in epidemiology or medicine.

Geller: Is there anything you'd like to say in closing?

Gordon: Biostatistics is a great profession. You learn things all the time. You go from one subject matter to another. It's hard for me to think of a subject area that I haven't touched at one time or another. And most of them I came on absolutely cold; I didn't know a thing about them, except what I read in the newspaper. It is a continual learning experience, and it is always stimulating.

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