

A Conversation with Robert C. Elston

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Abstract. Robert C. Elston was born on February 4, 1932 in London, England. He went to Cambridge University to study natural science from 1952-1956 and obtained B.A., M.A. and Diploma in Agriculture (Dip Ag). He came to the U.S. at age 24 to study animal breeding at Cornell University and received his Ph.D. in 1959. From 1959-1960, he was a post-doctoral fellow in biostatistics at University of North Carolina (UNC), Chapel Hill, where he studied mathematical statistics. He then rose through the academic ranks in the department of biostatistics at UNC, becoming a full professor in 1969. From 1979-1995, he was a professor and head of the Department of Biometry and Genetics at Louisiana State University Medical Center in New Orleans. In 1995, he moved to Case Western Reserve University where he is a professor of epidemiology and biostatistics and served as chairman from 2008 to 2014. Between 1966 and 2013, he directed 42 Ph.D. students and mentored over 40 post-doctoral fellows. If one regards him as a founder of a pedigree in research in genetic epidemiology, it was estimated in 2007 that there were more than 500 progeny. Among his many honors are an NIH Research Career Development Award (1966-1976), the Leadership Award from International Society of Human Genetics (1995), William Allan Award from American Society of Human Genetics (1996), NIH MERIT Award (1998), and the Marvin Zelen Leadership Award, Harvard University (2004). He is a Fellow of the American Statistical Association and the Institute of Mathematical Statistics as well as a Fellow of the Ohio Academy of Science. A leader in research in genetic epidemiology for over 40 years, he has published over 600 research articles in biostatistics, genetic epidemiology, and applications. He has also coauthored and edited 9 books in biostatistics, population genetics and methods for the analysis of genetic data.

The original conversation took place on August 4, 2009 during the Joint Statistical Meetings (JSM) in Washington, DC by GZ and ZL. NLG had dinner with RCE during the 2013 JSM in Montreal, Canada and added supplementary material and edited the conversation. RCE updated and clarified certain points.

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1. EARLY EDUCATION

Gang and Zhaohai: Robert, it is a great pleasure to have this opportunity to talk with you about your life, research, career, mentorship, and some of your views of genetic epidemiology.

Can you begin by telling us about your early years?

Robert: I was born in London, and I was 7 years old when World War II broke out (1939). My brothers and I were evacuated to a little village, Lea Green in Hertfordshire, about 30 miles from London. That's where I first loved farming and thought I'd be a farmer when I grew up. In 1941 my father arranged for us to live in Hertford, where Battersea Grammar school had been evacuated from London. I don't know how he got me into that grammar school since I was really too young. They put me in the lowest form (grade). I eventually took what was called the school certificate at 14 while most took it when they were at 16.

Zhaohai: What did you study in high school?

Robert: In addition to the usual subjects, we studied French and a year later got to choose Latin or German. I did Latin mainly because my elder brothers had done Latin, and because I knew I needed Latin to go to Oxford or Cambridge. The following year, the class master who taught Latin chose the two or three best students and said: Okay, you will do Greek. My brothers had done Greek but they had to give up physics to do Greek and I was not going to give up physics! I said: if you want me to do Greek, I'll need to eliminate history or geography or both. So they agreed!

When World War II ended, Battersea Grammar school moved back to London, so I had one year at Hertford Grammar school. In 1946 we returned to London as a family. Then I went to University College School, which was "a public school", meaning it was open to anyone who was willing to pay (laughs). Although I studied Latin and Greek and the classics for two years, I also wanted to do science. As I was young, I could stay there in the sixth form for four years,

mixing 2 years of classics (Latin, Greek, a little French, and ancient history) with 2 years of biology, physics, and chemistry. I never studied calculus, highly unusual in the U.S., but not so unusual at that time for a science student in England. When I got to the states, I estimated that what we did in England in the sixth form was equivalent to one or two years of undergraduate work in the states.

2. CAMBRIDGE UNIVERSITY

Gang: How did you get to Cambridge University?

Robert: In those days, the way you got to a university was either you were rich or royalty, or you sat for a scholarship examination. I applied to both Reading and Cambridge Universities and had to take a scholarship examination at each. The scholarship wasn't much in terms of the money, but if you passed the scholarship exam, the local government would pay for your education.

Zhaohai: So you got the scholarship?

Robert: No, I actually failed. For Reading University, the three subjects I chose for the exam were Greek, French and chemistry. They thought that combination quite useless. At Cambridge, there were six of us competing for one scholarship. At that time, the School of Agriculture at Cambridge had a three year Bachelor's degree in agriculture. I had already decided to do something in agriculture. But I had taken a special scholarship exam at Magdalene College for people who would spend four years. The first two years would be Part I of the natural science tripos. [A tripos is the course system at the University of Cambridge.] Then at the end of the second year, I would have a choice, either a two year diploma in agriculture or continue with Part II of the natural science tripos followed by a one year diploma in agricultural science. Although I didn't get that scholarship I did well in the exam, and they said they would accept me into Magdalene College for the four-year program in two years' time, with the

government giving me some support. Why two years? Because they “knew” I would have to serve two years in the military. So I had those two years to spend. Since I was going to study agriculture, I was able to get a deferment to work on a farm so I didn't have to go into the military. So I worked on a farm for a year and then spent my next year in France where I perfected my French (my mother's mother tongue).

Gang: What happened after those two years?

Robert: I returned to England and went to Cambridge. For the natural science tripos, I spent two years doing work for Part I. I had to have three science subjects. My original idea was to do botany, zoology and chemistry (organic and biochemistry). After one year, I really didn't like botany and decided I wanted to do mathematics. So I changed from full subject botany to half subject botany and half subject mathematics. I had to teach myself calculus, which I did with a little book called "Calculus Made Easy" by Silvanus P. Thompson (1946). Clearly, I needed private tutoring for mathematics. Wally Smith (Walter Laws Smith), whom I knew from my extracurricular activity on the stage (we were both members of the Pentacle club, which was a magic club), became my mathematics supervisor. He told me I wasn't very good at mathematics, but I stuck it out! I know mathematics lowered my exam result at Cambridge!

Zhaohai: What did you do next? Did you get to do genetics at Cambridge?

Robert: My first choice for a Part 2 tripos was biochemistry, which I really enjoyed, but between the lectures and the labs, the hours were too long, so I went to my tutor for advice. I said I was thinking about Part 2 genetics. I remembered his words so well, "You know this program in genetics here is new. And this man [R.A.] Fisher is considered eccentric by some, and it may not stand you in good stead in later life for it to be known you worked with him." That is why I did not do a year with Fisher! So I ended up doing the two year diploma in agriculture.

Gang: Who taught you statistics at Cambridge?

Robert: I had lectures from four people. Dennis Lindley gave us three weeks on statistics as part of the half-subject mathematics. He taught me significance testing. He did not believe in it but he taught it! In the same year, I did have lectures from Fisher because those who did zoology could do an optional series of lectures with Fisher on genetics. So I did do genetics with Fisher. I'll tell you a joke he told (translated into American). I did not know what he was doing with adding, subtracting and dividing for a 2 by 2 table. He came up with this number. He said: "Now, I am going to call this number chi-squared. Don't be alarmed. I know you are all biologists. It is no worse than calling a dog Lassie!" He said, "If this number is greater than 4, perhaps there is something going on." This was in a lecture hall which could hold 200 people. At the first lecture, there might have been 150 people; second lecture, 50; third, about 15! He made us all sit in the front row. He could sense his audience. I don't remember exactly what he said, but it was something like: if I say something is always transmitted from mother to daughter, then clearly it is never transmitted from mother to son. Then he said, "I do hope I'm not making a mistake in logic. Do stop me if I make a mistake in logic, won't you?" He could sense that we were all thinking about the truth of what he had said!

While I was spending a year in France, I had read Fisher's book for research workers (1950) and his book on experimental design (1951). So one day after lecture I said to Fisher: I read your book. What is the difference between a standard deviation and a standard error? He looked me up and down and said: "Your height is a deviation from the mean. It is not an error."

Then I also had lectures with Anscombe and RC Campbell, because they were teaching agriculture students. There we learned about experimental and split-plot design, and basic statistics. We also knew how to calculate F-statistics using a hand calculator. And I had lectures from Wishart. Wishart used a little book he had written with Sanders called "Principles and Practice of Field Experimentation" (1955). He taught us how to lay out plots in the field and for agricultural experimental designs. We were just agriculture people! He was in the School of

Agriculture.

Zhaohai: And you still wanted to be a farmer after you got your diploma in agriculture?

Robert: What else was I going to do? I learned how to run a farm in England and knew quite a lot of animal physiology, plant physiology, soil science, how to work out the feeding and animal nutrition, but I had no capital. To be a farmer, you needed capital for the land and the machinery. I couldn't afford a farm.

3. COMING TO THE U.S. FOR A Ph.D.

Zhaohai: How did you end up coming to U.S. for your Ph.D. in animal breeding?

Robert: I got the B.A. in 1955. The way it worked was that two years after you got your B.A., you could pay 10 guineas and you got an M.A. So I had an M.A. My mother wanted me to take an academic job. I saw a notice: Fellowships to America. All right, I thought, I'll just go to America for just one year. These were King George VI memorial fellowships from the English Speaking Union of the U.S. and they were giving about 25 scholarships a year. You could have up to three choices of where you wanted to go, but you had to sign that you would go wherever they sent you. My choices were UC Davis where Michael Pease was doing chicken breeding or Ames, Iowa which was known for dairy cow breeding. I left the third choice blank. They sent me to Cornell, where there was a department of animal husbandry. There I was sent to Chuck (Charles Roy) Henderson, who said all his students minored in biometry, and suggested that I go to see Professor Federer. So I went to see Walter Federer, who asked me why I did not stay for a Ph.D. I said I had only money for a year. He told me that they would find me money.

I had to return to England at the end of the year because I was called for military service; and if

I passed my 26th birthday outside of England, I could have been called up to age 36. Again I avoided military service, this time by working on a pig farm. I was able to leave England before my 26th birthday because the farm owner was willing to say I was still there. I actually spent my 26th birthday on the high seas en route back to Cornell. I did this so I could get to Cornell when the semester began.

So I returned to study animal breeding for a Ph.D. with Chuck Henderson with minors in biometry and mathematics. My thesis was in mixed model non-orthogonal ANOVA. We had one of the first computers, an IBM 650. I spent three months with punch cards to invert a 79x79 matrix!

Zhaohai: Who were your contemporaries in graduate school at that time?

Robert: I was exactly contemporaneous with a student of Chuck Henderson's, Shayle Searle. He had a degree in mathematics and a diploma in statistics. Chuck Henderson had just spent a year at the New Zealand Dairy Board with Shayle Searle and recruited him to be a graduate student at Cornell. I learned a lot of from both of them. Chuck Henderson told me he was an animal scientist, not a statistician. The reason he was doing BLUP (Best Linear Unbiased Prediction) was because statisticians wouldn't do it for him. He never considered himself as a statistician at all.

4. FROM CORNELL TO UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL (UNC)

Gang: How did you choose a post-doctoral fellowship in statistics after finishing up your PhD in animal breeding?

Robert: I was going to finish my Ph.D. in the summer of 1959. I didn't know what to do next. Walter Federer advised me to do a post-doctoral fellowship in statistics. He said I should apply to Princeton, where there were fellowships in statistics for biologists. They paid \$5,000 a year, tax free. So I applied. Before I heard from Princeton, I drove to Miami for an international student conference. On my way back, I stopped at Chapel Hill to see my old friend Wally Smith who had moved to the Department of Statistics there. He told me they could offer me \$4,800 a year as a tax-free fellowship in the Department of Biostatistics, as Bernard Greenberg, the chairman, had some money. So I went to UNC at Chapel Hill. I wrote to Princeton that I was no longer interested, and received the nicest letter back from Sam Wilks. From that experience, I learned that when you are trying to recruit students or post-docs, write a nice letter.

Zhaohai: How long was your post-doc at Chapel Hill?

Robert: Just one year. Bernie Greenberg insisted that teaching was part of the training for all students, pre- and post-docs, so I became a teaching assistant for Statistics 101 for public health. My affiliation was with biostatistics, but I had my office in the statistics department. In addition, I took 5 theoretical statistics courses in each of the two semesters, although I did not do all the homework. I took courses in multivariate analysis from S.N. Roy and Norman Johnson, response surface designs from R.C. Bose, experimental design from Indra Chakravarti and David Duncan, non-parametric statistics from Wassily Hoeffding (U-statistics) and mathematics for statistics from Wally Smith. During that time, James Durbin, Maurice Kendall and E.J. Hannan (time series) were visitors. I also published work from my dissertation, my first paper in *Biometrics* (1961). **(Figure 1 near here.)**

Gang: You spent most of 1959 to 1979 at UNC Chapel Hill. Since you came as a post-doctoral fellow, how did you manage to stay?

Robert: In order for me to stay at Chapel Hill Bernie Greenberg suggested a job as a

Research Assistant Professor of Pathology to work on a project for the blood bank, which he thought must be related to genetics, my interest. I worked on a project to estimate the amount of blood that the blood bank should keep on hand (Elston, 1962, Elston and Pickrel, 1963). I simulated blood units being purchased by the blood bank and being sent out for use (Elston and Pickrel, 1963). Computers and statistics had not been used before in blood banking. I noticed from the data that O negative blood was not coming in at random. I ended up writing several other papers on the blood bank project (Elston and Pickrel, 1965; Elston, 1966; Elston, 1968; Elston, 1970).

Towards the end of that second year, Bernie Greenberg said he needed someone to teach bioassay the next year, and did I know anything about it? I said I knew a little, and yes, I could teach that, but in truth, I was one chapter ahead of the students most of the time.

Gang: But then there was this two year gap, 1962-64 when you went to Aberdeen. Why was that?

Robert: My third year at Chapel Hill was the sixth year I had been in the U.S. I had a J-1 visa and U.S. law required that you had to return to your home country for at least two years. Exceptions to stay in the U.S. were only by an act of Congress. David Finney contacted me for a permanent position as a Senior Biometric Fellow in Aberdeen Scotland and, since I couldn't stay in the U.S., I accepted. My wife and I didn't like the idea of going to Aberdeen very much, but this was a permanent position. (I had just got married in Chapel Hill and my wife came from Gloucestershire, 100 miles west of London, so we were both from southern England.) After being in Aberdeen for about six months, I put down a deposit on a house, and the next day I got a letter from Bernie Greenberg asking me to come back to Biostatistics as an Associate Professor after the required two years outside the U.S. He asked me what salary I would want and when I named the largest salary I dared, he offered me 25% more. I was trapped! This time I came to the U.S. with a green card. We returned to Chapel Hill with a nine-month old daughter, and for her to get her visa, I had to sign on her behalf that she wasn't coming into the U.S. for the

purpose of becoming a prostitute; she remarked recently that she kept her half of the bargain!

Gang: Describe the Biostatistics Department on your return

Robert: I was the 6th or 7th faculty member of the department. The department grew with the help of federal grant support. In the mid-sixties we were tremendously successful. In 1966 I managed to get a five-year Career Development Award and then a five year renewal. There was an interdepartmental training grant in genetics and biostatistics had its own training grant, but there was no Ph.D. in biostatistics. At that time the Ph.D. students funded by the departmental training grant took either a Ph.D. in Experimental Statistics at Raleigh or a Ph.D. in Statistics at Chapel Hill, with a minor in Public Health. I wanted a Ph.D. program in biostatistics with a minor in genetics to have students funded by the interdepartmental training grant, so I wrote the Ph.D. proposal. Greenberg was told it wasn't broad enough, so I rewrote it allowing for minors in genetics, demography and other fields as well. The Ph.D. program in Biostatistics officially began in 1968 with Rose Gaines-Das being the first to get a Ph.D. in biostatistics, with a thesis in statistical genetics.

Initially it was difficult for my students to get positions. That's why Joe Haseman went to the National Institute of Environmental Health Sciences; there were no academic positions in statistical genetics. Haseman could not get a job in statistical genetics despite the fact that Haseman and Elston (*Behavior Genetics*, 1972, from Haseman's dissertation) became the most cited paper ever published in *Behavior Genetics*.

By now, many of my Ph.D. students funded on that training genetics grant are retired. I can't imagine why!

Gang: While you were at UNC, you did a lot of traveling. How did you manage that?

Robert: With the Career Development Award, my position didn't cost the university and

Bernie Greenberg said I could do whatever I wanted because it didn't cost him anything. This allowed me to visit the University of Hawaii to work with Newton Morton and D.C. Rao for one year and, during summers I had further trips to Hawaii and England (the Galton Laboratory in London and the University of Cambridge). When I visited the Galton laboratory (1967), I met John Stewart, who was a graduate student at Cambridge. We ended up writing a paper together, which appeared in *Human Heredity* (1971), a minor journal at that time. We computed the likelihood of the model for the observed phenotype data in a given pedigree. We could handle large pedigrees and relatively few markers. I didn't then know I was using Bayes' theorem recursively to compute the likelihood. Stewart's contribution was to apply the result to linkage. In the discussion, Stewart wrote that this paper answered a fundamental question in human genetics, that is, is some phenotype polygenic or is there a major gene? It was Ken Lange who named this "the Elston-Stewart algorithm." It was overall a most productive time.

5. FROM UNC TO LOUISIANA STATE UNIVERSITY MEDICAL CENTER (LSUMC)

Gang: Why did you leave UNC for LSU in 1979?

Robert: I moved to LSU for two major reasons. I went to New Orleans for the ENAR meeting and they wanted me to come there to be chair of the Department of Biometry in the LSU Medical Center. They offered me a hard money position. That was the first reason: all positions at UNC were soft money and by then I had four children, all within six years of age, to put through college. The second reason was that at UNC I had gotten a grant which allowed me to purchase my own computer and the university would only let me house it in the computer center. At that time, nobody in the School of Public Health was permitted to have his own computer. So those were the primary reasons that I left.

Zhaohai: Tell us about your years at LSU. (Figure 2 near here.)

Robert: Even though I had a hard money position, I kept writing grants. Because I had all of these federal grants, I was able to start a Ph.D. program in statistical genetics and expand the faculty. I wrote four proposals for Ph.Ds and masters' degrees in Biometry and Genetics. Alec Wilson, Joan Bailey Wilson and George Bonney became part of my faculty.

Gang: What kind of training did you give at LSU?

Robert: I trained several post-docs there. I especially like to train statisticians to do genetics. At LSU I had a training grant from NHLBI which was initially only to train post-docs. From 1992-1993 Dan Schaid of the Mayo Clinic was my post-doc. I remember the year because Hurricane Andrew hit Louisiana that year. It was supposed to hit New Orleans. We boarded up the windows and left for our eldest daughter's wedding in Ann Arbor. We thought we might not have a house when we got back. But the hurricane missed New Orleans. Dan Schaid completed his year with me and went back to the Mayo Clinic and was able to analyze the genetic data that they had been collecting. He is now a leader in the field of genetic epidemiology.

Zhaohai: Why did you leave LSU?

Robert: My faculty was good and I wanted to raise their salaries. The administration said there were no faculty raises and "no exceptions". Of course there were exceptions! That's why I'm a lousy administrator: I refuse to lie! In one of the following years, the Chancellor wrote a letter to the department heads saying that again there would be no faculty raises and noted that good people would leave and "this should be taken as an opportunity." I was fed up with being a department head anyway and had \$1,000,000 in grant money. That and the climate were the reasons I decided to leave!

6. FROM LSU TO CASE WESTERN RESERVE UNIVERSITY (CWRU)

Zhaohai: You have been at CWRU since 1995. Why did you choose CWRU?

Robert: My wife hates the heat, so staying in the south was out of the question. She wanted to go to Maine or Vermont, so Cleveland was a compromise. I accepted a full professorship at CWRU without administrative responsibilities so I could get some work done!

Gang: Tell us about the department when you arrived.

Robert: I was hired by an epidemiologist, Alfred Rimm. He wanted me to have my own division, so we called it Genetic and Molecular Epidemiology. (Figure 3 near here.) The Department is really a mini-school of Public Health. Aside from my division, it had divisions of Epidemiology, Biostatistics, Health Services Research and Public Health. The names have changed over the years, but with the exception that there are no longer formal divisions, the structure is the same.

When I moved, only two people from LSU came with me, Xiuqing Guo, a graduate student, and Hemant Tiwari, a post-doc. I was also able to take my training grant in biometric genetic analysis because nobody remained at LSU who could do the work. Joan Bailey-Wilson and Alec Wilson moved to the National Human Genome Research Institute (NHGRI) of NIH because they had family in the Washington, DC area. I was also able to take my computers.

Al Rimm asked me to do genetics only, not biostatistics and I did that for over ten years. One project was S.A.G.E. (Statistical Analysis for Genetic Epidemiology), which I had started in New Orleans, funded by an NIH Resource Grant. I also took that with me. The Resource Grant required collaborations, providing a service for which you had to charge (the S.A.G.E. software), training and dissemination (S.A.G.E. courses). Initially there was a charge for S.A.G.E. because the grant required that. Beginning in 2005 we were able to distribute S.A.G.E. for free (See

Elston and Gray-McGuire, 2004 and <https://code.google.com/p/opensage/>.) Version 6.2 was meant to be web based so people could use other programs with it, but funding to complete this project never materialized.

Gang: How come you became department chair at CWRU?

Robert: In 2008 Al Rimm resigned as chair and they asked me to be interim department chair and I agreed. They needed a real chair to apply for stimulus money, so in 2009, they took the “interim” away. They continued to advertise for a real chair and it took several years - until now (2014) - to fill the position. Call it a second childhood! (Figure 4 near here.)

Zhaohai: How did you arrange your time as chair on administration, research, and mentoring graduate students and post-docs?

Robert: When I first became chair, we needed to reorganize our Ph.D. program. Under the previous chair, the department was acting as though each division had a separate Ph.D. program. The different divisions found it hard to agree on one Ph.D., but the graduate school did not recognize multiple Ph.D. programs in one department. So I put a lot of effort into establishing the one Ph.D. program in Epidemiology and Biostatistics, with several different concentrations. When that was done, with several faculty committees to make sure that the program ran smoothly, a lot of the administration was taken care of. And I have always considered my research and mentoring of students, both pre- and post-docs, to be all part of one and the same thing. (Figure 5 near here.)

These days I spend a lot of time writing grants. It's getting harder to get them. Renewal of my research grants and the training grant is taking more time than I wish. It's hard to know how much detail the reviewers want. Sometimes the projects described in the grant proposal get published before the grant gets funded! And of course, if we don't get funding, we won't be able to support Ph.D. students to do research.

I also spend a lot of time helping others. For junior faculty, I tell them not to put my name on their paper as an author because when they come up for tenure, people may think the paper was my idea and not theirs. If my name is on a paper, you can be sure I really contributed something. I don't notice all the authors when I am reading a paper, but I find that people notice if my name is on a paper. So I have to be sure that every sentence is accurate. My purpose is to be pedagogical as well as do research, and this makes me very fussy about proper wording and clarity. I read the galley proofs personally and I have my secretary read them too. I learned that at Aberdeen from Finney. He had a sign up in the tea room which said, "No paper leaves this department without the Professor's permission."

I still work on family studies, although that has become less fashionable than case-control GWAS. My recent work is still a mixture of theoretical and applied and I still enjoy writing and publishing with students.

Gang: Do you ever plan to retire?

Robert: I don't know when I shall retire – probably when I am no longer able to get grants to fund my research. I have four children and ten grandchildren. By the way, three of my children are university professors in mathematics/health sciences, and the one who isn't decided to be creative and studied acting. She puts on the high school play every year (and her older son is majoring in mathematics at college). I look forward to spending more time with my family when I do retire.

7. SUMMING UP

Gang: You have directed 40 Ph.D. theses and had 45 post-docs. By now they too have had trainees. What does your "research pedigree" look like?

Robert: My research pedigree has more than 500 progeny. The International Genetic Epidemiology Society had a special tribute for me on my 70th birthday and someone drew it out. At that time, half of the field of genetic epidemiology was in my pedigree. There are at least four generations.

Gang: How would you sum up your career?

Robert: Like that of many other academics, my career path was an accident. When I talk to others in academia, most of the time they had no idea what field they would end up in. In my case, I didn't even expect to go to academia. But once I decided to apply statistics to genetics, I think I made a happy choice; and I'm glad I decided early on to make all of my students collaborators. I only hope they learned as much from me as I from them.

Gang: What is your advice to a young statistical geneticist starting out today?

Robert: My advice is quite simple. First, make sure you keep learning as much statistics as you can and second, keep up to date with computing technology. Statistical genetics may go out of fashion, but there will always be a need for statisticians who can compute.

Zhaohai: Do you have any closing comments?

Robert: It is really nice to have this conversation appear in *Statistical Science*. I actually never considered myself to be a statistician. I was a geneticist among the statisticians and a statistician among the geneticists!

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