

A Conversation with Ross Prentice

Li Hsu and Charles Kooperberg

Abstract. Ross L. Prentice received his B.Sc. from the University of Waterloo and his Ph.D. from the University of Toronto. He joined the University of Washington (UW) and the Fred Hutchinson Cancer Research Center (the Hutch) in 1974, and is currently Professor of Biostatistics at these institutions. He was Senior Vice President at the Hutch, and Director of its Public Health Sciences Division, for more than 25 years.

Dr. Prentice's expertise and research interests are in the fields of biostatistics, epidemiology, and disease prevention. He played a central role in the conception, design, and implementation of the Women's Health Initiative. In statistical and medical literature he has over 500 scientific papers, including more than 40 with 500 or more citations. His substantial contributions to the theory of population and clinical research include the use of surrogate endpoints and case-cohort designs and other areas such as survival analysis, nutritional epidemiology, genetic epidemiology, biomarkers, and measurement error. Dr. Prentice is recognized for his mentoring of students and junior colleagues, and for his generous collaborations.

Dr. Prentice has received numerous awards for his work, including an honorary doctorate in mathematics from the University of Waterloo, the Mantel Award for Lifetime Contributions to Statistics in Epidemiology from the American Statistical Association, the Mortimer Spiegelman Award from the American Public Health Association, the Committee of Presidents of Statistical Societies Presidents' Award and RA Fisher Award, the Marvin Zelen Leadership Award for Outstanding Achievement in Statistical Science from Harvard University, the American Association of Cancer Research/American Cancer Society Award for Research Excellence in Cancer Epidemiology and Prevention, and the American Association for Cancer Research Team Science Award. He was elected to the Institute of Medicine/National Academy of Medicine in 1990. The Ross L. Prentice Endowed Professorship of Biostatistical Collaboration was created at the UW in 2005 and has been awarded every year since its inception. The interior space of the Public Health Sciences building at the Hutch has been named the Ross L. Prentice Atrium. In his spare time, Ross enjoys sports including water skiing, golf, running, and spending time with his wife, Didi, and with his daughters, sons-in-law, and grandchildren. He ran daily from when he was in his 20s until his knees objected about 10 years ago.

This interview took place with Li Hsu and Charles Kooperberg via Zoom in December 2020.

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EARLY YEARS

Li: It's really an honor, Ross, to have this conversation with you and get to know you beyond being your student or colleague. I was wondering about where you grew up?

Ross: I grew up in Southern Ontario on a farm near a little village called Epsom, near a little town called Uxbridge, near a big city called Toronto. That was a good place to grow up. As a rural area, it was somewhat resource poor, but still a good environment. I went to a one-room school from first to eighth grades. A one-room school was good if you had a good teacher, which I did: Mrs. Wilbur, for all the years that I was there. One of the advantages was you could listen in on the other grades when they were being taught. Another advantage was that because it was a handful for a teacher with that many grades, the older kids shared in the teaching of the younger kids, and that was relevant experience!

The most exciting time during those years was when the school burned down. My mother would regularly shout to my brother Murray and me to "Get out of bed! It's time for school!" And then one day she said, "The school is burning!" and we said, "Sure Mom. We believe you." But, in fact, it was. It didn't completely burn down, but it was gutted, and the only other building in the village that was big enough for a school of 40 kids was the church. So we had school in the church for some months while repairs took place.

I had two great older brothers: Murray and Don. Murray was about three and a half years older than me and was a natural teacher. When he started school, he'd come home and teach me what he had learned that day. So when I got to first grade I had quite the exposure to first through third grade material, which was probably the key factor in the teacher bumping me quickly through these grades. So I found myself in 5th grade at 7 years old. That acceleration had some salient effect on me, and kindled a desire toward doing things at an early age.

Li: It seems at young age you were already very interested in mathematics.

Ross: It's somewhat embarrassing to think back, but as my brother was teaching me what he learned, I remember at about 4 years getting hands on a blank notebook. I thought I'd like to write down all the numbers until I found the largest one. I went page after page after page non-stop. I was very pleased some years later to discover that there's a very simple argument to show that there isn't a largest integer.

Charles: Besides schooling, since you grew up on a farm, were you involved with the farm work? As a Canadian boy, did you play hockey or any other sports?

Ross: Living on a farm is quite conducive to having meaningful responsibility. My father decided he didn't like farming all that much, and he spent much of his time building houses, often with my older brother Don. My



FIG. 1. Ross as a school boy

middle brother Murray and I would be left to bring in the crops during the summer. As time went on Murray and I also joined in the house building. These were good practical training experiences. I did play pretty much every sport that came along. Certainly ice hockey was dominant, but the activity that I had the greatest success at was track and field, mostly running, but also things like discus throwing. As I saw high school coming I would run the fields. If I was a mile away from a work site, I would usually run that, sometimes while pushing a lawnmower. I put a high priority on competition and enjoyed it. I believed that sports competition and academic achievement were highly linked, and that one needed to keep up both if one wanted to do well at either. You asked me about motivation. I knew from a very early age that even though our little corner of Southern Ontario was a nice place to live, I liked the people there, and I had a good family life, it wasn't where I was likely to spend my life. I thought of education as the ticket out of town, so to speak. That thinking spurred some of my later choices.

Charles: Was moving from a rural community to University of Waterloo a culture shock?

Ross: Well getting to the University of Waterloo physically was a little bit stressful. I was 16, and the day before I was to leave for University, I said to my dad, "I could use a little money from my work over the summer." He said, "Well, I'm a little bit short right now." And I said, "Well, I need some money to pay for residence living." He didn't have it, so I had to go without knowing whether I would be able to live in the planned residence. The other question I asked him was, "Can I take this old car over here?" And he said, "Yes, you can take it, but first you have to change the oil." I had never changed the oil in a car before, but we had a pit in our garage, and I got underneath and pulled out a plug, and some oily substance came out. I put the plug back in, and it didn't seem to take much additional oil when I refilled it. I start driving to Waterloo, and soon I heard a grinding sound. I pulled into a service station. It

turned out, you guessed it, I had drained the transmission fluid. So we replaced the transmission fluid and no harm done. I was able to drive that old car for many subsequent years.

I got to Waterloo and it was not a culture shock. In fact, somewhat the opposite. Waterloo was not a very big city at the time. Some of my classmates had similar interests to my own, including goofy behavior, leading to an enjoyable and stimulating experience from the outset.

Charles: Was a Ph.D. something you even knew about when you were growing up?

Ross: I was barely aware. However, it became apparent early in my years at Waterloo that I needed to have education beyond undergraduate or Masters if I wanted to have independence, especially if I were to stay in academia. While I would say that academia was my mindset, I also was interested in an entrepreneurial component to a career, but I didn't know much at that time about what options or opportunities would be possible. Then Canada came out with a very nice '1967 Science Scholarship' awarded to 50 people across the country who were graduating in some aspect of science. Those generous scholarships even included some research support for the candidate's dissertation advisor, and it facilitated an easy transition to the University of Toronto for graduate work. My advisor there was Don Fraser, unfortunately recently deceased. He was very youthful and impressive in 1967, and he continued to be for many subsequent decades! When I first went to Toronto to meet him, I walked up and down the hall about three times, passing this person in the hall who I thought might be another student. But, in fact, it was Don, and he was already a very well-known researcher who published multiple books and lots of papers, and probably would be regarded as the outstanding Canadian statistician at that time.

Charles: What was your dissertation topic? Was it biostatistics or more theoretical statistics?

Ross: It was somewhat biostatistical. Don Fraser had developed an inference approach he called structural inference. It was related to Fisher's fiducial inference, but had a little more 'structure' to it, with an underlying error variable generating a corresponding response variable via a group transformation. It was an application of that methodology to dilution series and bioassay studies that I wrote about in my dissertation. It may have been useful for me to have had more demands placed on me as a graduate student—I wrote this document in one year, and Don Fraser was in Hawaii on sabbatical that year. I recall 'sweating it' when I defended my dissertation in Don's absence. My doctoral experience was somewhat like the British system, where one finds an interest area, researches it fairly independently, and then writes a dissertation. There was a two-year residency requirement for doctoral students at the University of Toronto at that time,



FIG. 2. *Wedding of Didi and Ross, 1966*

allowing me to do a number of things during my second year, including taking a course from renowned geometer H.S.M. Coxeter, and consulting for a life insurance company.

FAMILY

Li: Before we go further with your professional life, I would like to ask you a few questions about your personal life and family. We know your wife Didi very well, and we know she is on the opposite end of the artistic spectrum from you. How did you meet?

Ross: Even though we were, as I said, a little resource-limited, my parents did have a cottage on a lake, 75 miles north of our farm. One of the cottage neighbors had a daughter about my age, and she had a girlfriend who would come to spend time at the cottage. That person was Didi. We were pretty young, probably 14 or 15, at the time. For a couple of years we'd dated rather infrequently, usually going dancing or ice skating. By the time I had been at Waterloo for a couple of years, Didi and her friend came to visit for a weekend, and our relationship took off pretty soon thereafter. We were married pretty early: I was 19; Didi was 20. We first lived in Waterloo, where Didi worked in the university library while I completed my final year of undergraduate work.

Charles: You've got four grandchildren. Any particular proud moments you like to share?

Ross: Proud moments related to my grandchildren are easy to find: pretty much everything they do! Arranged by age, the oldest is 24 and the youngest is 15. So we have ages 24, 21, 18, and 15, in arithmetic progression, randomized according to gender: female, male, male, female. They're each great kids. We spend a lot of time together as a family. They grew up in quite a different environment from that for either Didi or me, but they are each applying themselves effectively and doing well in school or workplace. When they were younger they loved it when I



FIG. 3. Ross and Didi with children and grandchildren, 2019

would chase them around our cabin grounds, snorting like a deranged moose.

Li: What do they think about you? Do your children and grandchildren think you are a geek?

Ross: I think so, maybe. However, one of my strategies when our two daughters were growing up was to act a little unpredictably so they would think they pretty much needed to look after themselves and their own choices. Sometimes when they would come to me for advice, I would say, “Well, you’re more responsible in that area than me, why don’t you decide?” By and large, they decided well. The grandchildren know that they can ask me for math help, but they trust their own answers more.

Li: I am curious about how you handled such a very full plate for a long time. As the Director of Public Health Sciences (PHS) at the Fred Hutchinson Cancer Research Center (Hutch) and as PI for the Women’s Health Initiative (WHI) Clinical Coordinating Center, you also maintained very productive methodology research work. It must have been hard to juggle all these things between work and family. Those must have been demanding years.

Ross: Yes, those were fairly demanding years, especially after, and even before WHI, because we worked for about nine years to contribute to the underlying motivation for WHI through the National Cancer Institute (NCI)–sponsored Women’s Health Trial (WHT). To organize my time work-wise, I had a mindset of being a researcher first, who happens to be trusted enough by my colleagues to hold an administrative role. I saw it as an honor to be involved in the lives of colleagues and staff, and in their decision making. I deliberately divided my time into about a third for statistical methodology re-



FIG. 4. Ross the athlete

search, a third for collaborative research, and a third for administration. There was quite a lot of collaborative administration after WHI geared up. But I had excellent colleagues, and some administrative issues tend to pretty much resolve themselves over time, without intervention. When I was Division Director and heading the WHI Clinical Coordinating Center, students played a very valuable role, especially in methodology work. I found that I could rely on students to retain momentum in ongoing funded projects, and I very much appreciated their contributions.

At times I had to do my methodology research in the evenings and on the weekends more than I liked, and that sometimes competed with family time. Still, we had a lot of family activities throughout, some through the church which is quite central to our lives, some through sporting events and cabin activities. We bought our cabin in 1986 when our kids were teenagers, and that was a great place to restore life balance. However, I do remember one time, on a Labor Day weekend, we were finalizing what turned out to be a thousand-page R01 grant proposal (this was before we had a lot of constraints on how much one could apply for, and on how many pages you could use to make your case) for a full-scale low-fat diet intervention trial, and I worked all the days of that long weekend on that effort. Didi, at the end of that weekend, said, “Something has to change.” I listened to her very carefully! Overall, I think these time demands fit together reasonably well, though there is some natural tension. I don’t look back with any major regrets. I enjoy close relationships with my daughters and sons-in-law, and my grandchildren, and my wife of nearly 55 years too, at least when she decides to tolerate me.

FACULTY IN WATERLOO

Charles: Your first academic appointment was at the University of Waterloo, where you had been an undergraduate student. Returning as a faculty member was probably quite different. It seems like one of your main

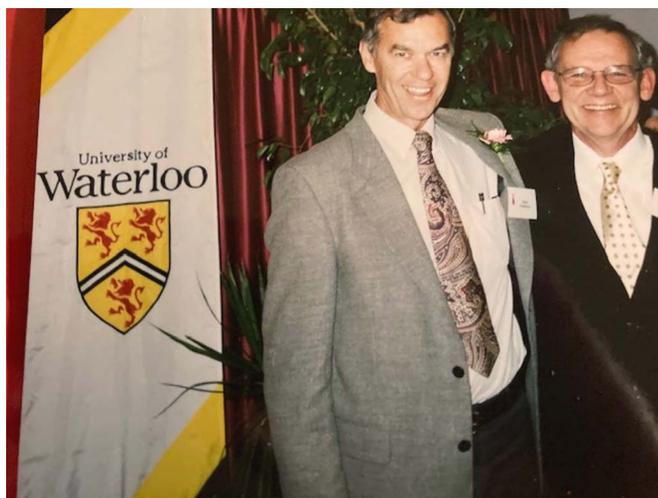


FIG. 5. With Jack Kalbfleisch, Ross received honorary doctor of mathematics degree at Waterloo, 2002

collaborations was with Jack (Kalbfleisch). How did you end up working together with him and on your book (Kalbfleisch and Prentice, 1980, 2002)?

Ross: Looking over my career, I think collaboration with Jack was an important key, and probably the most valuable collaboration I've had in the statistical methods area. Jack was not on the Waterloo faculty when I started my academic career on January 1, 1970 as assistant professor. Jack had been a student at Waterloo, a year ahead of me. I taught 3 or 4 courses per year for my first 4 semesters at Waterloo, allowing me to have a year off during 1971–2, which I spent at State University of New York Buffalo. I knew Jack was there. Also, Marvin Zelen, who headed the group in Buffalo, came to Waterloo annually to give a series of lectures. I got to know Marvin a little, and decided I would like to spend some time there. While at Buffalo, I worked mainly on clinical trials with the Eastern Cooperative Oncology Group, and the VA Lung Cancer Study Group. My year in Buffalo provided an introduction to some aspects of biomedical research, and to survival analysis. That's where I wrote my first papers on these topics, and where Jack and I began our collaboration.

Marvin was a very effective statistical scientist, leader, and communicator. He often contributed greatly to the career development of younger scientists. He had a big influence on my career, including after I had resumed my appointment in Waterloo. Soon after my return Jack moved from Buffalo to Waterloo, and we began to work closely. I hated to leave Waterloo in 1974, due to this and other valuable collaborations, but Waterloo did not have a medical school or much of a biomedical research enterprise. I let Marvin know that I was interested in a new opportunity, and he told me about this new cancer research center getting started in Seattle, where I already knew Norm Breslow and a few others. I applied for a lead statistical position at this free-standing cancer center, along with a

dual position in Biostatistics at the UW. My experience at Waterloo was quite positive, and I have enjoyed continuing interactions with Jack, Jerry Lawless, and several other excellent statistical scientists at Waterloo.

Charles: Junior people often are told now that they need to get papers out; books take a lot of time, and they're not going to get you tenure. Was advice different at that time?

Ross: First, I didn't seek or receive much career advice—my bad. Jack and I regarded our book as a research monograph. As we were writing chapters, we were also writing related papers. So it stimulated our publication output to be working on the book. A book can force one to summarize a research area with some degree of completeness. In our case, we gave short courses, in various countries and parts of the world. Some of them with Norm Breslow and Nick Day, who published their first book, on case-control studies, that same year (Breslow and Day, 1980). I organized the first of those courses in Seattle. We were all at a junior to intermediate career stage, but the turnout was amazing. It included Tom Fleming, an outstanding statistical leader who subsequently joined us in Seattle and was Biostatistics Department Chair for many years, and a number of other notables in the statistical community. It introduced us to other young researchers, who proved to be effective contacts over subsequent years.

Now, however, statistical researchers don't seem to rely on books the same way they did at that time. There are so many other ways of getting access to research communications. I couldn't recommend the writing of a book with much enthusiasm at this juncture. I think you'll get more response to your work, more interesting questions and potential collaborations, through publishing in good quality statistical journals. Of course participating in national/international meetings and committees sometimes may also help.

EARLY YEARS IN SEATTLE

Li: Besides Marvin, are there other mentors who had a major influence on your career?

Ross: Definitely. One is Donovan Thompson, who was the Chair of Biostatistics when we arrived in Seattle in 1974. Donovan was an excellent role model and mentor. He had good statistical sense and enviable generosity, and he set a tone for our faculty groups that still continues today, many years after his death in 1992. During my first year in Seattle Donovan introduced me to a gynecologist named Don Smith from Seattle's Virginia Mason hospital. Don had collected some data on menopausal estrogen therapy and needed help analyzing and interpreting it. It was an endometrial cancer case-control study, and that got me started on logistic regression for case-control studies, as well as on the study of health risks and benefits of menopausal hormone therapy. We published a paper in



FIG. 6. Opening of Fred Hutch first building, Bob Nowinski, E. Donnell Thomas, Joe DiMaggio, David Thomas, Ross Prentice, 1975

NEJM in 1975 (Smith et al., 1975). We used logistic regression, but it was logistic regression where the response variable was the exposure, either taking estrogens or not. The results are very similar to what became a common mode a few years later to analyze case-control status as the binary response variable.

Physician epidemiologist Noel Weiss was one of the first persons I met in Seattle. We even shared an office in 1974. I learned a lot from Noel. I was familiar with a Canadian system, where statisticians typically apply for small amounts of money and typically receive, say, \$10,000 for research over the summer. Noel was applying for grants of \$500,000 per year. I thought this is heaven! Another person was Rainer Storb. He was the first person I met in the Clinical Division (at the Hutch). He came to me in 1974 with great long sheets of paper with numbers on them and wanted to know what we can learn about graft rejection in aplastic anemia patients undergoing bone marrow transplantation. It was quite a small data set, but we did some survival analysis and published our results in *NEJM* (Storb, Prentice and Thomas, 1977). That led indirectly to another paper a few years later on leukemia transplant patients and graft versus host disease, which has been credited for opening the way to modern day immunotherapy (Weiden et al., 1979). Rainer was marvelous to work with, and is a terrific scientist. He's still a leading researcher at the Hutch in his mid-eighties.

Importantly, another mentor I should mention is Bob Day, Director of the Hutch from 1981–97. It was an interesting time to come to this nascent cancer research center and a very favorable time for research program development, with many federal opportunities: the NCI started its Division of Cancer Prevention and Control under Peter Greenwald's leadership, and had substantial resources to fund grants. We were fortunate to get access to some of those funds under my colleague Maureen Hen-

derson's leadership. Our Cancer Prevention Research Program started in 1983. The SWOG coordinating center, under John Crowley's leadership, started about the same time. So with public health scientist Bob Day as Director it was a most opportune time for our group's development.

Li: When was the Public Health Sciences Division actually formalized?

Ross: 1982. Bob succeeded Bill Hutchinson as director of the Hutch in 1981. He was an exceptional fit for the job. He set up the basic institutional structure with departments, and meaningful annual budget processes. We became a Division a year later with the awkward name of Epidemiology, Biostatistics, and Cancer Control Research. We soon renamed it Public Health Sciences. Donovan Thompson was the initial Division Director. In 1983 I became the Division Director. I did so for nearly 20 years, was off for about five years, and then back for another five and a half years from 2007–12, by which time our Division had about 100 faculty/staff scientists, and a total staffing of 800–900.

Charles: Was there a scientific agenda for how you wanted to grow it?

Ross: Well, less so than one might expect, at least in the early days. At that time on the biostatistical side we had a statistical methods research agenda early on with a few R01s, and Norm Breslow ran his National Wilms Tumor Study coordination activity through our group. We recruited Vern Farewell, then Art Peterson, and John Crowley soon thereafter. Suresh Moolgavkar, also a very fine recruit, brought additional biological perspective with his medical training to our statistical work. The epidemiology component of our Division similarly flourished, with Noel Weiss, David Thomas, and Janet Daling, among others, as key contributors. The aforementioned engagement with the Clinical Research Division was also an important component, and several notable projects in the disease prevention area were initiated in 1983, when we were awarded the first Cancer Prevention Research Unit in the nation, with Maureen Henderson as PI, and with Gil Omenn, who succeeded Bob Day as Dean of the School of Public Health at the UW, also offering substantial leadership through his Carotene and Retinol Efficacy Trial for lung cancer prevention, among other research projects. For myself a turning point in my collaborative research came in 1983. Bob Day, who was then a member of the National Cancer Advisory Board, stopped by my office and said that NCI was going to fund a study of low-fat diet for breast cancer prevention, and asked 'can we apply for the coordinating center?' I thought this can't be very difficult, and I decided to give it a try myself. We put in a successful proposal to form a statistical center for the initial phases of what was called the Women's Health Trial. Though many aspects of this project proceeded well, with my statistical colleague Steve Self playing a major role, it had a rather torturous history, too detailed to go into here,

and was still doing feasibility studies in 1992 when the Women's Health Initiative began.

I do think there are some lessons here for statisticians and other population scientists about persistence in pursuing funding for large-scale research activities that may be needed to address certain important public health questions, while simultaneously leading to valuable research infrastructure building. However, another message concerns the need to retain one's other ongoing research at the same time, because there's a lot of risk involved in seeking large project funding, and one can expect to fail more often than succeed. As a population science community we need to come together to formulate a research agenda that can be justified, and to sell current needs and opportunities to NIH leaders and perhaps even directly to Congress if necessary, if we are to make a difference in chronic disease prevention in our society, with its former smoking-related epidemic, and current obesity-related epidemic. At present we are not well organized for shaping and communicating such a research agenda.

Another lesson is that statistical training is actually pretty good in the public health research arena. This training provides an entree into a lot of areas, without being too threatening. We're trained to look for biases and barriers in research projects. Even though we may lack detailed subject matter knowledge, this training may be quite important for identifying research questions that need to be answered. We need to strive to provide this crucial input to the research communities that we are a part of, including taking our turn at overall program leadership roles, as appropriate and needed.

Charles: Can you describe the state of biostatistics in Seattle? It seems that when you arrived it was not only an era of growth at the Hutch, but was also an era of growth for biostatistics in Seattle in general. How did you split your time between the University and the Hutch?

Ross: The Hutch had just gotten its first Institutional Support (core) grant in 1974 when I arrived, and Lincoln (Nayak) Polissar and I were the two Hutch-based statisticians. Biostatisticians at the UW were my principal peer group. The School of Public Health formed in 1970 with Biostatistics as one of its departments. Dick Kronmal, Norm, Polly Feigl, Paula Diehr, Pat Wahl, Lloyd Fisher, and Don Martin were in the Department, with Donovan Thompson as Chair in 1974. Gerald van Belle also moved to Seattle at about the same time I did. It was a very nice department, and I spent a fair amount of time there, teaching a regular survival methods course and occasionally other courses during the first few years. I had already advised a couple of Ph.D. students back in Waterloo, but right away I had some fine students here in Jim Anderson and Jay Lubin. Steve Self followed a short time later, followed by many other excellent students.

I liked the fact that the Hutch didn't have too much administrative structure, nor imposed too many constraints

on faculty at the time, while offering a considerable opportunity. We had substantial control over our own destiny by the nature of the institution, and by a congenial affiliation with the UW School of Public Health. I can't tell you how rare it is to have a large academic institution and a free-standing research institution that cooperate the way the Hutch and the UW have, especially in the public health area. The fact that this cooperation continues to this day is extremely valuable and mutually beneficial. We do a lot of student advising at the Hutch and provide research opportunities for a number of students that extends what the university may be able to offer on its own. We at the Hutch have the benefits of being in a place where we can substantially charter our own destiny, and still have academic affiliations and access to students. Together, we have a strength beyond the sum of the parts.

METHODS RESEARCH

Li: Nine years ago at the Prentice Symposium, Danyu Lin (UNC Bostatistics) made a top 10 list of your methods publications from his perspective (Lin, 2013). I wonder whether there are any other publications that you would consider in the "Top 10" list?

Ross: We may all like to think that whatever we have been working on recently is highly meritorious. Being no exception, I would like to point to a statistical publication that's taken a very long time to come out in *JASA*, with former student Shanshan Zhao. We called it "Regression models and multivariate failure time data" (Prentice and Zhao, 2020). There's also a related, more applied *American Journal of Epidemiology* publication on dual outcome analysis in the WHI hormone therapy trials (Prentice et al., 2020). Our recent book (Prentice and Zhao, 2019) also provides an account of this work, which pairs marginal hazard rate modeling for single outcomes with marginal hazard rate modeling for dual outcomes also, with the latter possibly dependent on a bivariate covariate history that evolves over time. In many of the studies that we engage in, whether cohort studies or intervention trials, the participants experience an array of clinical outcomes. Often they are time-to-response outcomes, and we haven't had a suitable regression approach for summarizing such data, in my view. We've had some semiparametric models for bivariate survivor functions that allow one to ask association strength questions, but this dual outcome hazard ratio modeling asks a somewhat different question: 'How does the rate of a pair of clinical outcomes that occurs at specific points in the upper right quadrant of the plane depend on treatments or other covariates?'

Charles: Some of the publications in Danyu's top 10 list were precursors for this work?

Ross: Yes, there was some modest thinking breakthrough that led to this series of papers: several possible analytic approaches were considered. For example, I tried,

with Shanshan's help, to do some other types of modeling, such as cross-ratio regression modeling, but we just couldn't get stable calculations. In retrospect, I think the single and dual outcome (and higher dimensional) hazard ratio modeling is the better approach anyway, especially when it comes to regression parameter interpretation.

Secondly, in terms of recent research emphases, we have conducted considerable research, mostly over the last maybe 10 years on measurement error modeling, stimulated by nutritional epidemiology studies. These methods aren't nearly as pretty, and our measurement methods are still somewhat crude. In public health research we often need to rely on observational studies for addressing important questions. These measurement issues are quite central in such areas diet and physical activity epidemiology. The need to address these issues represents a big challenge for our population science research community. We've seen what can happen in the genetic epidemiology area when good quality measurements come on the scene. We're probably not going to obtain measurements of that same accuracy and precision in the other areas just mentioned, in part because the exposures under study may be highly variable over a person's life span, and more importantly, because of systematic biases in self-reported exposure data. For the past 15 years a multidisciplinary group of us at the Hutch have been working on objective biomarker development for dietary intakes using urine and blood measures, and on the application of such measures in cohort sub-studies to strengthen nutritional epidemiology association studies.

Li: Ross, you have worked on multivariate survival analysis for over 30 years. With the work you just mentioned on multivariate hazard ratio modeling, do you feel some closure or still have any further plans?

Ross: It is a bit of a relief to have something to offer recently, after all of this time. I wouldn't say closure though, because our work is just a start in this new direction and there are many needed further developments. As these methods become known and used in applications, I expect to see related methodologic work spring up. For example, these methods may stimulate research methods for using electronic health records, which typically have a lot of complexities related to measurement error and measurement intermittency. I am sometimes teased for being a Cox model "afficionado," but I think hazard rate modeling has many advantages for these types of purposes, separating baseline outcome rates from comparisons among individuals. These comparisons often have useful, even causal, interpretations, even though they don't always have the simple counterfactual average difference interpretation that some would require for causality.

Charles: Are there any other older papers you feel have interesting angles?

Ross: The most highly ranked on Danyu's list was that with Ron Pyke (Prentice and Pyke, 1979). Ron was a wonderful person and a fine collaborator, also from Southern Ontario with RP as initials. We referred to our contribution as RP². Ron was based in the math department at UW. He asked if he could spend that summer with us here at the Hutch. At that time, I had just finished a couple of papers on the use of logistic models for case-control studies, and he was happy to join this effort. He recognized right away that the estimator under consideration could be viewed as deriving from a two-sample problem for asymptotics development purposes. I did the gut work of working through the asymptotics to show that one had valid asymptotic distribution theory by acting as though one had a prospective study, except for the location parameter. Ron told me that he had a more elite way of developing this result, and he planned to write a paper on it, but it unfortunately never transpired. But we recognized that our contribution had a breakthrough quality related to choosing a parameterization that could meet constraints using an orthogonality feature, which turned out to be related to some core efficiency properties in semiparametric modeling theory.

The last paper on the Danyu's list was a discussion of Cox's 1972 paper (Cox, 1972, Kalbfleisch and Prentice, 1972). This one had an interesting development. Marvin Zelen had organized a ski trip to Utah the year that Snowbird opened, 1972, before a cooperative group statistician meeting in Seattle. Included were Marvin, Jack Kalbfleisch, David Byar, and myself. Marvin had been sent a draft of Cox's paper before it appeared, and he pulled it out during our trip. We studied it together. The first reaction from Jack and myself was that Cox had to be wrong! He's calling his proposed estimator a maximum conditional likelihood estimator but what's the conditioning event? Well, it turned out not to be conditional likelihood inference, but the main results were correct in terms of both the regression estimator and its variance estimator. This work triggered so many follow-up studies in the area of semiparametric inference, often trying to explain and extend the Cox model. And for Jack and myself it led to many collaborations—including entries on Danyu's list.

Li: One fun fact: do you know which of your statistical papers has the most citations?

Ross: It's *Statistics in Medicine* 1989, right (Prentice, 1989)? Li, I think you know the history of that one because of what Jay Herson wrote in the *Lifetime Data Analysis* volume that you coordinated with Jianwen Cai (Cai and Hsu, 2013). Jay Herson triggered my interest in this topic when preparing the program for an ENAR (Eastern North American Region, International Biometric Society) meeting. Jay asked if I would be a discussant on this sur-



FIG. 7. *Speakers and organizers at the Symposium in honor of Ross Prentice, 2011*

rogate outcome topic and I was sent three papers to comment on. I read these on the airplane en route to the meeting and formulated an initial set of thoughts on what kind of formal criteria might be in line with what we expect of a surrogate outcome as a replacement for a hard clinical outcome in a clinical trial setting. I did some work on it after the meeting to try to add specificity. Interestingly, this contribution still impacts this important research area many years later. However, I think some statistical investigators steeped in counterfactual modeling would like to see the criteria I proposed replaced by other criteria, but it seems their formulation may be very narrow for this purpose.

NUTRITIONAL EPIDEMIOLOGY

Charles: A lot of your recent applied and methods research is on diet, environment, and cancer. Can you tell us something about that?

Ross: My interest in nutrition and chronic disease developed soon after I became Division Director in 1983. The NCI wanted to do a clinical trial of 6000 women on a low-fat dietary pattern for breast cancer prevention. We were awarded the statistical center for this project, but things became controversial a couple of years down the

road, because of concern that dietary adherence design assumptions may not be realized.

I remember one meeting in 1985 or 86, where prominent nutritional epidemiologist Walter Willett came to talk about results from their Nurses Health Study, with a semi-quantitative food frequency questionnaire (FFQ) used for dietary assessment. Walt's analyses estimated breast cancer rates across categories of FFQ percent energy from fat intake that went up somewhat and then went down a little toward the upper end. Why was that happening? Did it mean that the hypothesis was flawed? The main trial motivations came from animal experiments, which were quite supportive, and also from ecologic and time trend studies, though these had some pretty serious weaknesses. I spent a lot of time studying the epidemiology literature on this topic, and slowly became convinced that observational nutritional epidemiology as practiced at that time, using self-reported dietary data, was not likely to yield reliable information on topics of great public health importance. I came to believe that the central issue was dietary measurement in conjunction with diets that are a complex mixture of foods, food groups, and nutrients. I still think that we do not yet have reliable information on many nutrition and chronic disease topics. Largely for this rea-



FIG. 8. Vern Farewell, Ross Prentice, Art Peterson, 2002

son a group of us at the Hutch, including nutritional researchers Marian Neuhouser and Lesley Tinker, and biochemist Johanna Lampe, started working on biomarkers of dietary intake. We measured the few established dietary biomarkers, and found that there was a very limited correspondence between total energy intake as assessed from doubly-labeled water, a short-term but very accurate biomarker and total energy intake as measured by any of the available self-report tools (frequencies, records, or recalls). Furthermore, overweight and obese participants were found to underestimate energy intake on self-report by 30–40%, while normal weight women did not. These types of systematic biases, if uncorrected, can play havoc with energy and disease association analyses. Over the last few years our efforts have turned to the development of novel nutritional biomarkers. We have had some success, for example in developing suitable biomarkers for certain micronutrients (Lampe et al., 2017). We have applied those new biomarkers to chronic disease incidence in WHI cohorts. We found inverse associations of the intake of specific carotenoids with breast cancer, coronary heart disease, and diabetes (Prentice et al., 2019a). We are currently exploring the use of blood and urine metabolomic profiles as a source of biomarkers, in a nice collaboration with Dr. Dan Raftery and his colleagues in the UW medical school. We are finding that diets having a higher percent of energy from carbohydrates as measured by our novel metabolomics biomarkers are associated with lower chronic disease risk for vascular diseases and breast cancer, and even diabetes (Prentice et al., 2021). This is truly an exciting research area, with much need for the involvement of additional quantitatively-oriented investigators.

Li: You're talking really like an epidemiologist here, understanding the issues—not just the statistical issues.

Ross: Looking back at my career, some observations I would like to pass on to the biostatistical community are the following: early in one's career, one needs to demonstrate technical tools and skills that can contribute to your collaborations. At the same time it is important to develop

your own ideas concerning the substantive issues focused on in these collaborations. Also, don't assume that someone else's ideas on these issues are more valuable or insightful than your own. When we thoroughly work with the data, and commit to certain applications, we may well be in a position to identify needs and opportunities, as well as blind spots in earlier research.

One of the features that attracted me to public health and nutrition was that statistical input, and statistical thinking, are key research components in a multidisciplinary setting. Statisticians have a lot to contribute. I made a conscious choice early in my time that I had to tell my good colleague Rainer Storb that I had to leave collaboration with him to my other statistical colleagues. That was a sacrifice for me. But moving into this public health arena you likely will have an opportunity to contribute to the substance of important ongoing research related to the health of the nation.

STUDENTS

Li: I was one of your many students. I remember you gave me a lot of freedom: basically we met every other week and I explained what I had done, we discussed it, and two weeks later I would come again. You rarely told me directly that I should do this or that. Did you have a philosophy when you advised students, and has that changed over the years?

Ross: Thank you. I really enjoyed working with students such as yourself, Li. My mindset was that it was a collaboration. We were working together on some research topic, and neither of us knew how it was going to evolve. The dissertation stage is a key juncture for many students, because they may not have had much experience in trying to address problems where you don't know what will work well, or even know what is possible. That context requires persistence, and someone with related experience in statistical methods research may be able to help avoid wasted time. But for me student advising was a collaborative enterprise, where we both benefited if progress was made. That mindset came naturally because the students I worked with had all the skills needed for independent research, and appreciated having a major role in determining how the project would develop. This mode of operation was also efficient for me, especially if the research topic aligned with goals on our funded grants.

Students are sometimes on a different time-frame than might be required for getting the next grant funded. But many students I worked with were good at getting papers submitted from their dissertation and contributing to the funded research effort. I think my contributions, especially in methodology, would have been much reduced if I didn't have access to a cadre of good students through the UW. I learned quite a lot from some of them, actually. Many methods that we rely on now didn't exist when I received my own training. Working with students

sometimes provided an efficient way for me to receive a methodology booster.

Li: I had a really good experience as a student. After I graduated, I didn't feel lost, because I had gone through that research process of adjusting, working, and adjusting again. Nowadays students often have many publications upon graduation! Given the current competitiveness and the time that it takes to generate good publications, it seems there's a little conflict there. Do you have any advice for how students and junior faculty should perceive that?

Ross: Many biostatistics graduates have a technical area that they've contributed to in their dissertation, and it's often pretty essential that they continue and publish vigorously in that or a related methodology area, for some initial period of time. If they're fortunate to also be engaged in meaningful applied research, they're bound to come up against methodology topics to resolve and publish on, preferably in high quality statistical journals. Over time the young statistical scientist will gain expertise in substantial aspects of the applied research, then the nature of the individual's research contributions becomes less important. If the research makes an advance in methodology or subject matter, either is great. If it's contributing to the broader public health or biomedical research areas that we're engaged in, then all good. I don't think statisticians need to feel restricted in their research foci as their careers develop. It's true that one needs to show productivity and independence to move through the ranks in a timely fashion, but equally important is to be developing a career path that may lead to valuable contributions to the larger applied research enterprise.

Charles: I agree, but we are at the Fred Hutch, where even though we have the discipline programs, we operate broadly in the PHS Division. Would the same hold true for people in a biostat department of a university, where the review might be more disciplined-focused?

Ross: I think it largely would apply to our Biostatistics Department at the UW, because it has the same kind of traditions as we have at the Hutch. The opportunities and review processes may depend unduly on the attitudes of the school leadership. Research groups need to have a good measure of autonomy. Autonomy comes with responsibility too, but you need autonomy to recruit and reward people who are engaging in needed research, and excelling in doing so, and to procure adequate space for your research projects. We need also a meaningful measure of autonomy as individual faculty members, supporting a status of creative investigators who are largely responsible for the content of our own projects and careers.

SURVIVAL ANALYSIS

Li: There are many new fields in biostatistics, partially driven by technology developments like statistical genetics and imaging. Survival analysis was a major area 30

years ago when I entered the biostatistics program, but it seems that very few students nowadays are doing research in this area. What can we do to attract students to the survival analysis area?

Ross: We can work on survival analysis methodology pertinent to the kind of evolving areas that you allude to, like statistical genetics or high dimensional data analyses more generally. There are lots of questions being worked on in these areas that could benefit from a survival analysis formulation. In biomedical research we are often following individuals to observe the occurrence of certain types of events. You could think of survival analysis as part of the infrastructure for a broad range of biomedical studies. One way to advance a research emphasis on survival analysis is to work on the application of survival methods to the problems in emerging research areas. That's what we've been doing in the nutritional epidemiology area with measurement error and biomarkers. The methods that are available are often too simplistic and crude to yield fully satisfactory answers. We don't have models for measurement error that fit together nicely with models for the outcome data unless we reduce the outcome to some simple quantity that is fairly inflexible. Physical activity epidemiology with accelerometer data might be another priority area for survival data methods development. Furthermore, available methods for the joint analysis of longitudinal data and time-to-event data as arise in many application areas, are still quite rudimentary.

In biomedical research contexts each level of -omics data comes with its own features, starting with genotype, which is comparatively easy to analyze because it's largely a permanent set of characteristics for an individual that are very well measured. When you move to gene expression, proteomics, and metabolomics, you're getting back to the kind of exposures (e.g., nutrition and physical activity histories) that we were discussing earlier. There are constraints on the sampling that can be carried out when dealing with tens of thousands of people in cohort studies with exposures that change over the lifespan. Those types of research projects may benefit from a survival analysis framework. Within survival analysis methods, hazard rate modeling provides a pretty flexible starting point for the modeling of multi-level omics data, for example.

Li: So survival analysis has to evolve with the applications, and along the way there will be new issues and problems that need to be resolved.

Ross: Yes. I was actually rather encouraged when we initiated an ASA section on survival analysis. Mei-Ling Ting Lee did a great job of spearheading this development. The related conferences on lifetime data analysis methods were well attended and covered quite an interesting array of topics. I went away from these venues with thoughts on the many questions that still need to be addressed, or that need to be better addressed.



FIG. 9. Paul Meier, Sir David Cox, Mitch Gail, Tom Fleming, Ross Prentice at the 1st Seattle Symposium in Biostatistics, 1995

WOMEN'S HEALTH INITIATIVE

Charles: We want to talk a little bit about the WHI. Clearly it's been the biggest research project you've been involved in. Can you remind us how WHI got started?

Ross: It was a rather long and bumpy process. On the low-fat diet trial side, I remember a few of us talking for four hours with then-NCI Director, Sam Broder. He would say, "How can I allocate 60 million to this project when non-Hodgkin's lymphoma incidence is rising rapidly in this country?" I responded to him that I had just completed a study of international disease rates around the world, and that U.S. rates were tremendously high for many diseases that appear to be diet-related. When it didn't look as though NCI was likely to allow our proposed trial to be funded, we worked to have some language related to the need for a large research program among postmenopausal women to be included in that year's NCI appropriation. In response, NCI funded an additional feasibility study, which was still ongoing when Bernadine Healy, in 1991, became the first female NIH director. She observed that women had been under-studied in large-scale clinical trials. She read our proposal for a full-scale low-fat diet trial, along with some observational study and intermediate outcome trial history on the possible health benefits and risks of menopausal hormone therapy. Then she went directly to congress to obtain a \$500 million appropriation to conduct the WHI, organized as a trans-NIH research effort.

Things were getting started nicely for WHI in the early 1990s when the Institute of Medicine (IOM) was prevailed upon to conduct a review of WHI. The IOM committee assessed that the benefits of hormone therapy, especially for heart disease, were so well established from observational studies that no trial was needed, and that

the low-fat diet trial wasn't well motivated since it was already known from cohort studies that dietary fat isn't important for breast cancer risk. Five of us involved in the WHI program met with some members from the committee along with Harold Varmus, who was then in his very first days as the new NIH director, to help him decide the fate of WHI. For years, I thought Dr. Varmus had supported WHI continuation after we heard soon thereafter that we could proceed. Much later, after the intervention phase of WHI came to an end in 2005, I had lunch with Bernadine Healy and she confided that Harold Varmus had recommended *against* funding WHI. Apparently, with Bernadine's input, the HHS secretary overruled this recommendation. In summary, there was a long gestational period for WHI, and we can thank Dr. Healy that we were ultimately able to conduct a research program that has been projected to have reduced breast cancer incidence by 15,000–20,000 women per year in the U.S. ever since, and has saved many billions of dollars in health care costs, due to the sea change in the use of menopausal hormones that these trials induced.

Charles: The most publicity that WHI got was when the hormone therapy, estrogen and progestin trial was stopped early because of the increased rate of breast cancer, along with some elevation in coronary heart disease and stroke incidence, among changes in the rates of several other clinical outcomes in participants randomly assigned to take these hormones. Can you talk a little bit about it from how you felt about the trial being stopped early? How do you look back at these 18 years after the results came out?

Ross: Our 2002 *JAMA* publication (Rossouw et al., 2002) was a defining moment for WHI. The combined hormone trial of estrogen plus progesterone in 16,608 women with uterus—conjugated equine estrogen plus

medroxyprogesterone acetate—stopped early. As you say, Charles, a breast cancer incidence (the designated primary safety outcome) elevation in the active hormone randomization group was the trigger for early stoppage, in conjunction with some elevation in coronary heart disease, which was the designated primary efficacy outcome, and a noteworthy elevation in stroke. We had defined a global index as part of the monitoring plan, and that too was elevated. We and our NIH colleagues, including impressive cardiovascular epidemiologist Jacques Rossouw, were the primary people who had access to the trial data to quickly pull together the manuscript after the external data and safety monitoring committee recommended early stoppage based on harm. We rolled it out, with my exceptional coordinating center colleague, Garnet Anderson, doing much of the writing, submitted it to the *Journal of the American Medical Association* with the help of NHLBI Director Claude Lenfant, who had a deep commitment to chronic disease prevention. *JAMA* wanted it published right away, and did so. Gynecologists and cardiovascular scientists around the country had no opportunity to access the information prior to publication. We were proper clinical trialists: we didn't let anybody know, because we were concerned that the results might leak and compromise the trial. There was a lot of immediate and strong feedback, especially from the gynecologic community, whose practices were suddenly inundated with hundreds of phone calls from women taking menopausal hormones, asking what they should do. These clinicians were unprepared and very unhappy.

Some media sources featured our results as generating a state of confusion about the health consequences of hormone therapy. The cardiovascular epidemiology community was pretty upset because the driving force for the trials was an estimated 40 or 50 percent reduction in coronary heart disease from observational studies. Some speculated that there was something wrong with the trial. The cardiovascular epidemiologists and gynecologists were quite inflamed and reluctant to accept our findings. However, regulatory agencies, our own FDA and others in England and elsewhere in Europe, took the results very seriously and responded quickly. They changed package inserts to include suitable health warnings. The women who were taking these preparations made a big change: about 70% of the women taking the combined preparations stopped right away, as well as about 40% of those taking estrogens alone, which we hadn't reported on at the time, but did so a couple of years later.

Wyeth-Ayerst, the manufacturer of Prempro, which was the combined preparation tested, and Premarin, the estrogen-alone preparation tested, naturally questioned the reliability of our findings. They tried several legal maneuvers to gain access to more and more trial data, even data that we had yet to publish. A judge in Arkansas

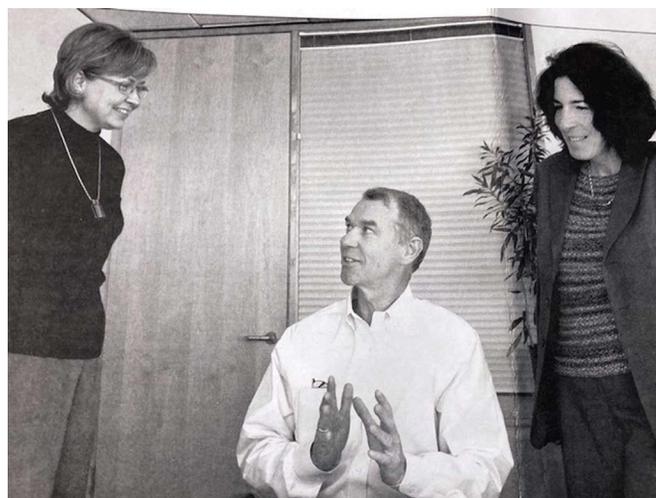


FIG. 10. WHI—Garnet Anderson, Ross Prentice, Andrea LaCroix, ~2000

forced us to provide essentially all the data they wanted in a redacted form, from our database, along with piles of email correspondence. This went on for three or four years.

Charles: I remember having to hand over my email as well.

Ross: Eventually there was a settlement, and the pharmaceutical company took responsibility for the elevated breast cancer risk. Inquiries about the details of the trial data stopped at that point. It was a learning experience and a good lesson for academics coordinating and conducting these kinds of big trials: One doesn't expect to get in the middle of that kind of exchange. We did some things slightly differently a couple of years later when the estrogen-alone trial was also stopped early, mainly because of a stroke elevation ([The Women's Health Initiative Steering Committee, 2004](#)). We took the liberty of giving some professional societies and other key organizations a confidential heads up, allowing them to be better prepared for the fallout. Also, the results were not nearly as dramatic as for the combined hormone trial.

In response to your question, Charles, I look back at this time period as difficult for the WHI research group, but also a triumph for randomized controlled trials. The attitude about the health risks and benefits, especially the safety, of menopausal hormone therapy likely would be very different now if those trials hadn't been conducted. Millions of women in the U.S. and around the world would likely still be taking high doses of the tested agents, and doing so for many years. As time has gone on we've gone back and analyzed our own observational data on menopausal hormones and disease risk, and other groups have done the same. With careful allowance for several key timing variables, these analyses have largely corroborated the clinical trial findings.

I especially appreciated the response to the clinical trial data by the regulatory agencies. By and large the scientific community, and the pertinent journal editors likewise gave high priority to the randomized trial design of the WHI trials. For example, *JAMA* published seven or eight papers on specific outcomes after the first combined hormone therapy trial report. So even though there was a large body of observational literature, the clinical trial data were recognized as giving a higher level of reliability. That's something to remember going forward in our public health research agenda. We need a strong integration between observational studies and clinical trials. We need to rely mostly on observational studies because of cost and the wide variety of important topics to be addressed. But there may come a time for topics that have sufficient public health importance and motivating data, to spend the money to do the large-scale clinical trials. We population scientists need to do what we can do to make sure that it's understood there's a special place for randomized controlled trials in the public health research agenda.

Li: In recent decades there has been substantial development on causal inference based on observational data. What's your view of observational studies vs. randomized trials? Do you think that if WHI were conducted 30 years later, do you think that it would launch?

Ross: It's really difficult to get large prevention trials funded. I think NHLBI was much more attuned to the value of incorporating large-scale clinical trials in their funded research program than some other NIH institutes. This may have happened in part because recognized intermediate outcomes tend to be somewhat stronger for cardiovascular diseases than for cancer, for example. But I think it was substantially Claude Lenfant's leadership that allowed the WHI to flourish with NHLBI as its administrative home. He ruled firmly at NHLBI, and he valued large-scale trials, which had been instrumental in reducing heart disease rates in the U.S. We've had NCI directors who clearly value trials for therapeutic interventions, but I'm not sure about a comparable commitment to trials for disease prevention.

Charles: The other major trial, the dietary modification trial, formally ended up null with some suggestions of benefit of a low-fat diet. How do you think of that now, 15 years later?

Ross: That's a good question, Charles. In fact, we need to continue to work on communicating long-term trial results. We continued to collect the outcome data from the 48,835 trial participants, and we've published quite a few recent analyses. For example, a recent paper (Chlebowski et al., 2020) showed a low-fat dietary pattern benefit for breast cancer mortality over an 18 year median follow-up period. A bit earlier I led a summary paper on this massive trial (Prentice et al., 2019b), which demonstrated benefits with long-term follow-up. We also found evidence of

benefit for coronary heart disease, the secondary trial outcome. This evidence was not apparent initially because of post-randomization confounding by statin use. Statin use increased dramatically during the trial intervention period, and did so differentially between randomization groups in this necessarily unblinded trial. We also found evidence of reduction in the risk of diabetes requiring insulin among participants assigned to the low-fat diet intervention. All together it adds up to a picture of some benefit for a low-fat dietary pattern, without observed adverse effects. This trial was not designed as a test of an overall healthful diet, but we hope it will help to set the stage for further observational studies and occasional intervention trials in this very important public health research area.

Charles: WHI has been enormously fruitful as a catalyst for many research careers, including mine, and there have been hundreds of publications about these trials and cohort studies. What are some of the other research highlights coming from WHI, from you or others, that are worth mentioning?

Ross: There are so many research topics that our rich database and specimen repository can be used for. I can't do justice here to many of these areas. As a few examples, there's biomarker research for diet and nutrition, as well as objective measure research for physical activity. Another area that's certainly been a major focus is genomics: all the things that you and Li and others, including our mutual colleague Ulrike Peters, are pursuing. There are studies of many other treatments and pharmaceutical products using our periodic medications inventories in the overall 161,808 person WHI cohorts. I think there's a lot to be learned in the pharmacoepidemiology area, and we probably have better data than most for this purpose in WHI cohorts. It's excellent to see these and many other initiatives facilitated by the substantial WHI resource.

For me one of the biggest pluses of my long-term WHI participation is the ability to develop friendships and collaborative relationships with colleagues around the country, most of whom I wouldn't have gotten to know otherwise. I now regard these persons as my key collaborators. The fact that the expertise of this research group spans many disciplines and disease outcomes is particularly conducive to broad-based learning as a member of a research group.

I view the population science research agenda as very important. We don't have a suitable organization for articulating timely opportunities, and we may need some form of a standing group to do so. We need to be able to communicate such opportunities to NIH leaders, and congressional representatives if appropriate and needed. Many of the diseases are potentially preventable in a much larger way than has taken place so far. Reduction in coronary heart disease by 20 or 25% starting in the 80s and

90s is just one example of what can be done with a risk factor approach to identifying opportunities for interventions. Those developments mostly involved pill-taking interventions, but behavior change interventions are likely to be the more effective approach in the long-term, and on this path we have a long way to go, and need the best efforts of many more statistically trained researchers.

REFLECTION

Li: The Prentice Professorship for Biostatistics Collaboration between the UW and Hutch is a prestigious award given annually in your honor. Over time, what do you hope this professorship could achieve?

Ross: As with a number of other developments in our biostatistical community, this was a Tom Fleming initiative. The stated purpose—I have to paraphrase a little bit—was to encourage continuance of the strong collaboration between statisticians at the UW and Hutch. As leadership changes over time, it's good to have initiatives that bring the groups together so we can maximize our overall contribution. I'm delighted that the Dean of the School of Public Health at UW (Hilary Godwin), and the Director of Public Health Sciences at the Hutch (Garnet Anderson) are committed to continuing these collaborative traditions. The Prentice Professorship supports a Hutch-based biostatistics faculty member to teach a course and spend time at UW, or supports a UW-based biostatistics faculty member to spend time at the Hutch and engage in some aspect of the research based here. This involvement is culminated in an annual lecture by the recipient, which is always enjoyable. In summary, this professorship is but one of several initiatives to maintain and enhance the excellent working relationships between UW and Hutch biostatistics faculty, and I hope it continues for many years.

Charles: You have accomplished so much and positively influenced so many in your lifetime. If you have to pick just one or two things, what would you consider to be your biggest accomplishments?

Ross: I would put family and faith involvement at the top. These are not my accomplishments, but they are the fundamentals that drive my life and career choices. There's a certain amount of satisfaction that comes from whatever life balance I've been able to achieve, and from the use of whatever talents I have been given. I think the Hutch has been a terrific place for me to develop my career path, because of strong research standards and its entrepreneurial side. Also the opportunity to be involved in the development of a new institution has been rewarding. Looking at our own biostatistics faculty, just about everyone has their own research grants, and that's impressive. Of course I'm pleased with the impact and conduct of the WHI. These add up to a pretty fulfilling life and career.

I'm very pleased to have been a part of the development of the Hutch, and especially of its Public Health Sciences Division.

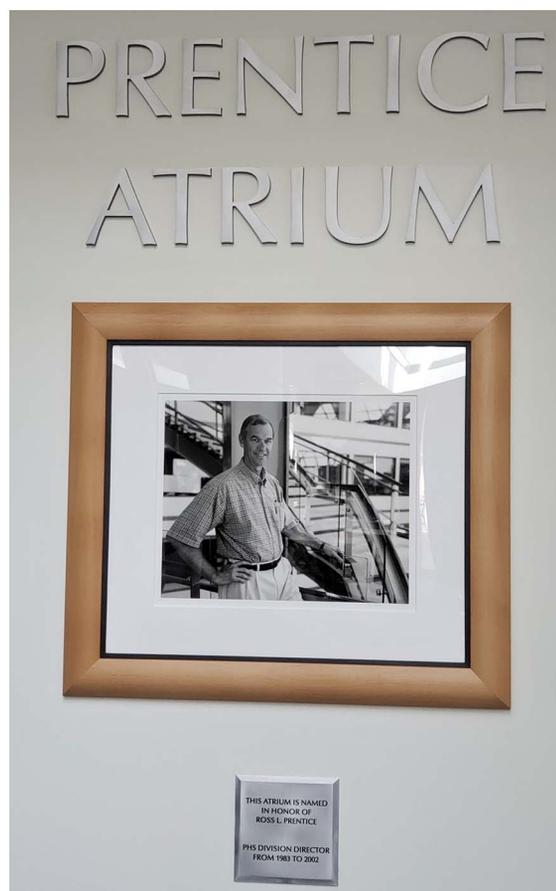


FIG. 11. *Prentice Atrium on the Fred Hutch Campus*

Li: Looking back on your demanding career, many responsibilities, and accomplishments, we are wondering where your motivation and energy come from to do all this work?

Ross: I wish that more energy was still in place! I grew up in a home where hard work was highly valued, and this attitude carried into my career. Being physically active is also quite energizing, and conducive to being productive. Having capable and congenial colleagues and students also helps a lot with one's productivity. More generally, having the freedoms to live our lives according to our own values in North America, in conjunction with plenty of meaningful opportunities, allows one to apply oneself energetically, and with a clear mind.

Charles: You said earlier that competition was a major motivating factor early on in your career. How has competition been a motivating factor during your career?

Ross: Even early in my time in Seattle, I broke competition down two ways: try to avoid undue competition at home, and that includes with our colleagues at the UW. But be more aggressive in relation to competitors at other institutions. We want to outshine other institutions when it comes to recruiting faculty and getting grants. I think it has occasionally shocked some of my local colleagues when they see my behavior, which occasionally has been somewhat extreme, when I'm standing in front of some

committee at NIH for example. We're in a competitive environment by virtue of needing to receive grant funds. We want to have enough productivity and novelty to show in grant proposals early in one's career, but also at later career stages. This is a healthy competition that keeps us all active and that prevents undue resources going to investigators who are no longer successfully competing.

Li: What were the major decision points in your career? Were there choices that could have been taken in retrospect?

Ross: Two roads diverged in a yellow wood Leaving the University of Waterloo in favor of an upstart cancer research setting; leaving therapeutic-type collaborations and moving into population science and prevention research. Those were some branch points that I don't regret. However, I remember being quite relieved when we finally had assurance of being able to conduct the Women's Health Initiative. I had a wonderful group of collaborators to work with in the WHI, in PHS, at UW, and elsewhere. It's been a very satisfying career, but I think you have heard more than enough about it already.

Charles: Thank you very much, Ross, for taking the time to talk to us. I have enjoyed it very much.

Li: Thank you, Ross!

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