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## PROFESSIONAL REMINISCENCE

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(For additional information, visit [my CV](#))

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### 1 Introduction

I report on selected features of my employment, sabbaticals, service activities, closing with a few vignettes and pronouncements. Having been somewhat professionally nomadic, I've been employed by a .com (before there was such a label), several .edu organizations, a .org and two .gov institutions. My professional journey produced a broad perspective and, most certainly, an interesting and fulfilling career.

### 2 Graduate School & Principal Employment

**1966–1967:** Actuarial Trainee, Chubb and Son Insurance, New York

I learned BASIC programming at Dartmouth and put it to good use at Chubb, which has just acquired a GE time-sharing computer. I programmed what was a pretty naive merit rating plan for automobile insurance (it was in the spirit of empirical Bayes before I knew such a thing existed) and many other routines. Computer memory wasn't available, the programs were saved via tape punched by a Teletype machine. Warren Cooper was my boss (looked a bit like Auric Goldfinger!); he was an accomplished medical photographer. Hendon Chubb was high-up in the company, which is unsurprising. He was brilliant and eccentric. My most notable, non-actuarial accomplishment was "the catch" I made in an insurance company league softball game. I was playing third base, dove for and snagged a line drive along the line, got up and nailed the runner who had not made it back to first base for a double play that ended the inning. I didn't pay for beer after that game.

**1967–1972: PhD Student & Lecturer, Department of Mathematical Statistics, Columbia U**

(Lecturer 1971–1972) It was a traditional math. stat. department with very little contact with data, but lots of contact with cutting-edge methods, many developed by department faculty; Herb Robbins, David Siegmund, Y. S. Chow, the list goes on and on of statistics notables. It was an exciting graduate program.

For a few years, Math. Stat. had winning and maybe dominant inter-departmental basketball seasons. We had some good shooters, some good defenders, AND David Siegmund who, I believe at one point, had been recruited by an NBA team. Therefore, if in doubt, feed the ball to David!

**My first consult**

Around 1970, there was a controversy regarding the New York versus the New Jersey lotteries. Tickets came in books, and if you bought 5, 5 were torn from the top of the book. In NY, the tickets were sequentially numbered, in NJ they were numbered “at random,” thereby the controversy in that lottery players claimed that due to the randomness, there was a better chance of winning in NJ. A reporter for the *NY Daily News* called the Math. Stat. department to get an opinion, and the department secretary dished it off to me. I stated that if the same number of tickets were sold, and if the payoff formulas were the same, and if drawing the winner was truly at random, then it didn’t matter which lottery you played, the chance of winning was the same for both lotteries. The article appeared in the newspaper and I got a few, heated letters from readers (email didn’t exist). One stated something like, “Dear Mr. Statistics, you can stay in your ivory tower, we’ll play New Jersey.

**My lecturer role**

I taught, “Statistics in the Social Sciences” and also had the opportunity to sublet David Siegmund’s glorious apartment at 460 Riverside Drive with a doorman, marble columns in the lobby, an apartment with many rooms. Not bad digs for a graduate student!.

**1969–1971: IBM Thomas J. Watson Research Lab., Yorktown Heights, NY**

I got to know Betty Flehinger, who worked at Watson Lab, and through her spent two summers at the lab, also as a “consultant” my last two years in graduate school. The lab was/is in a beautiful setting with an expansive glass wall overlooking valley. No office had such a view, only the library. The explanation, either true or a rural myth, was that when architects viewed previous IBM research locations, they noted that most offices didn’t have outside windows (most of the research at those offices dealt with optics!). The lack of view didn’t negatively affect the research, and my thesis on data-dependent allocation in clinical trials was hatched there. Other joys were rock climbing the rock-constructed outside walls, playing around with APL (A Programming Language) and running things on the IBM model 91, a water-cooled beast of a computer with parallel processing (rue the imprecise interrupt!). APL was fun, elegant and inefficient, but you could program lots of complicated routines in one or two lines by taking advantage of matrix algebra. Frequent discussions with Benoit Mandelbrot (father of fractal geometry) was a great opportunity, and though I spend a fair amount of time with him, I regret I didn’t spend more.

**1972–1973: NIH Postdoctoral Fellow, Mathematics, Imperial College, London**

I was funded by an NSF post-doctoral fellowship, and what a fortunate year to be at Imperial. During my postdoc., visitors included Rupert Miller, Brad Efron and many

more, then or soon to be luminaries. Faculty included, of course, D. R. Cox and also David Hinckley; Rod Little was a very notable grad. student. I got about five years of education that year. We rotated giving talks on articles, including on the generalized jackknife; Brad outlined the initial phases of what became the bootstrap. One could spend a big fraction of the day drinking coffee or tea (11ses, after lunch, afternoon tea, ...). There was a regular seminar that rotated amongst Imperial, U College London, Birkbeck; with each location attempting to outdo the others with their tasty treats at the tea.

**1973–1979: Assistant Professor of Mathematics, Boston University**

The statistics group, all five of us (I think five) were a subset of the mathematics department, a department quite friendly to statistics. Art Albert (of pseudo-inverse fame) and Ralph D’Agostino were the leaders (Ralph is still very active, as of 2021). Art led obtaining an NIH grant to study cancer screening, my first research grant experience. I spent a fair amount of time in the medical school, which solidified my interest in biostatistics. I taught a variety of graduate-level courses and the big, introductory course, Stat. 101 or something like that, with several hundred students. My midterm exam was open book and notes, True/False along with a brief justification for the choice. A week or so before the exam, I announced that one question would either be “Disjoint events are independent” or “Disjoint event are dependent” and I gave the correct T or F and the reason. I recommended that students mark that page in their notes. Well, over the years, the prevalence of correct T or F was very close to 50%(!).

I had a near miss that the BU medical school. I was working with a “rising star” clinician/researcher, but got the feeling that there were worrisome inconsistencies between data and messaging. Eventually, I decided to end that relationship. A few months later the clinician was accused of research fraud (not by me), an investigation supported the accusations, and the clinician left the university.

**Preamble to Harvard**

In the Fall of 1977, I started to attend the monthly Harvard Faculty Seminar in Health and Medicine, led by Fred Mosteller, Howard Frasier and Buckman McPeck. It met on a Thursday evening with dinner and wine, followed by the working meeting in the Kresge Building of the HSPH. Working groups formed and discussed various health policy issues, all in a post-wine, post-food, ventilation turned off environment. I did learn a lot, including a hint at how Mosteller was so productive. One evening, I proposed a way to analyze an issue, and Fred said something like, “A good idea; you might want to take a look at [he mentioned two articles].” I just happened to take a look the next morning and also happened to attend the regular Friday afternoon Harvard Biostatistics seminar that day. At the tea, Fred asked, “So, what did you think of the articles?” Nothing in his tone suggested that I wouldn’t have read them!

The continuing connection with that faculty seminar and other connections at the HSPH, generated my move to it in 1979.

**1979–1987: Associate Professor of Biostatistics, Harvard School of Public Health**

In a never-ending quest to avoid security, having just achieved tenure at BU, in July of 1979 I left for an associate professorship at the HSPH (untenured, as are all assoc. prof. positions). Within a month, I discovered the apparent intelligence conferred by the new letterhead. I had participated as an NIH program project site visitor in late

May and one in late July. The respect I was afforded in July was notably greater than that in May, even though I had had only two months to smarten up!

Mosteller was chair, Nan Laird a faculty member, Jim Ware and I arrived at about the same time, Marvin Zelen's team had recently arrived from Buffalo (Gelber, Gelman, Lagakos, Pagano, Schoenfeld, . . .). Soon thereafter, Butch Tsiatis arrived. It was quite a collection of accomplished and accomplishing academics with expertise ranging from mathematical statistics to clinical trial design, implementation and analysis; quite a collection of personalities. We implemented a few working groups with regular meetings, an important activity for me that started at Harvard, that I ported to Minnesota and operates robustly at Hopkins.

A broad array of distinguished visitors was one of the benefits of being at Harvard (there were also drawbacks). The two most notable for me were Seymour Geisser and Manny Parzen. Great friendships resulted, paving the way for collegueship with Seymour at Minnesota.

Bob Reed, one of the long-time department members gave me a great deal of excellent advice, with the following being the most valuable. I asked advice on how to deal with investigators with whom I had successfully worked that wanted me involved in another project. I had absolutely no time to give, but they stressed that it was logical for me to participate. Because I also thought it was logical, I had a hard time making my case. Bob advised that I state, "I agree that it is logical, but it's not desirable." I've used that statement on many similar occasions.

Research activities at Harvard included:

- *The New England Journal of Medicine project*, through which we got to look at submitted articles (even those that didn't get published in the *NEJM*), evaluate their statistical approach and reporting; extract examples and lessons. These ended up in several *NEJM* articles and the book, *Medical Uses of Statistics*.
- *The Carcinogen Bioassay in Small Rodents*, a  $6 = 2 \times 3$ -year grant funded by the NIEHS to study design and analysis of the assay. I was PI, Steve Lagakos, co-PI, Louise Ryan a post-doc having earned her degree at Harvard Stat with Art Dempster, Greg Dinse a graduate student and others. We made good progress, and in 1985 the pharmaceutical company Boehringer Ingelheim asked that we deliver a short course. Steve, Louise and I created a three-day course offered in three separate weeks at the the company's offices outside Danbury CT. So, three road trips ensued, each with a college road trip feel, with less alcohol, but lots of merriment. The offices were in a building with Union Carbide as principal tenant (likely the owner). The disastrous release of methyl isocyanate at its plant in Bhopal, India had recently occurred, and Union Carbide had "big brother" monitors throughout the building reporting "good news" that was in stark contrast to that from the free press.
- *The Woburn Project* emerged from the identified cancer clusters in Woburn MA. Marvin Zelen and Steve Lagakos led in designing and conducting a study that convincingly showed contaminated water supply was the cause. Several of us provided some input to the completely volunteer effort. The findings supported a successful lawsuit against the W. R. Grace chemical company, and provided the basis for the book and subsequent movie, *A Civil Action*.

Collaterally, the project induced termination of the School's "Associates Program," a program through which companies (including chemical companies) could by a membership and have special access to the school's faculty. Many of us protested the whole concept at its inception, but it was the Woburn Project that brought it down.

#### The full professor search

In about 1984, the department initiated a search for three full professorships. It was an international search, with current faculty allowed to apply, but with no special status. Nan, Jim, Steve and I all applied and, bizarrely, the four of us were the principal hosts of the external candidates. We'd take them to dinner, debrief on the department, and welcome them to the search for the positions to which we are applying! I found out while in the Netherlands that I didn't get one of the professorships.

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#### 1986: Visiting Scientist, Center for Mathematics and Computer Science, Amsterdam NL

From January through July, I visited Richard Gill's group at CWI. It was an exciting place, and I enjoyed the professional and interpersonal benefits. That Spring, the Chernobyl disaster occurred and we avoided eating vegetables (especially spinach) that was grown in or near the plume. Dennis Boos visited for a bit and described his travels to avoid getting near the plume. I remarked that he had good material for the travel book *Europe on less than 10 rads a day* (there was a travel book, *Europe on \$10 a day*). Amsterdam was a great jumping off point for trips to England (spent some time with Cox), France and beyond.

CWI was a 25km commute from Aalsmeer, usually by bike, which was almost always a pleasure with devoted bike paths. However, occasionally the crosswinds were so strong that you had to lean the bike at about a 45 degree angle into the wind to avoid being blown over, and needed to be ready for the lull that required a rapid reaction. Back then, maybe still, you could have Heineken delivered to your door, and I counted on having one or two waiting for me at home.

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#### Back at Harvard

In August 1986, I started a job search. There were several possibilities and by the late Spring of 1987, I was considering the division head (aka, chair) position at Minnesota, a professorship in the statistics department at Wisconsin, and a senior position at RAND in Santa Monica CA with John Rolph (my longest term statistical colleague and friend, having met at Columbia when he was a visiting faculty member in 1968).

About then, I received an invitation from UNC to apply for the Biostatistics chair position. I replied (via snailmail, no email yet), that I was considering a few short-deadline offers and wasn't going to apply. It turns out to be the only job to which I didn't apply for which I was rejected, in that about a year later I received a polite letter indicating that someone else (Barry Margolin) had been selected!

#### Off to Minnesota

I accepted the Minnesota offer and let Wisconsin and RAND know. John Rolph wrote a congratulatory note that finished with, "I hope you freeze your ass off!" [I did]. Before I left Harvard, Marvin Zelen gave me two pieces of advice,

- Don't spend too much time and resources trying to (re)ignite under-performing faculty; spend resources on the productive and potentially productive ones.
- Never tell a lie, but that's not the same as telling the whole truth!

I've adhered to both.

**1987–2000:** Professor & Head (Head through mid-1999) of Biostatistics, U of Minnesota SPH  
 There is, indeed, life after Harvard! I arrived in the summer of 1987 as Professor and Head, Division of Biometry in the School of Public Health. I use “department” in what follows, because while initially the SPH was a department of the medical school (divisions within), it has been a free-standing school for many decades with sub-units operating as departments. The department was high-quality and I had the goal (and dean's expectation) of growing statistical research, the doctoral program and other aspects. The department's graduate program was quite small, especially relative to its signature activity as one of the principal statistical and data management centers for NIH-sponsored trials through its Coordinating Centers for Biometric Research (CCBR).

My initial goal was to preserve what was already excellent and to gain credibility and trust of all concerned that I wasn't some carpetbagger from the East Coast, Harvard no less. My first lessons learned were that people listened carefully to what I said (I had to reduce the prevalence of jeux-de-mots!), that many faculty were reluctant to voice opinions in public (I'd leave a faculty meeting thinking there was broad agreement on an issue only to have several faculty state in private that they didn't agree). So, creating a safe environment for frank discussion became a top priority, achieved with reasonable success.

I was fortunate that the department was relatively small, with a small number of moving parts and interest groups, so that my administrative skills could grow as did the department. I did learn that leading a large, diverse group is more challenging.

The CCBR was housed off campus, about a 15 minute walk from the departmental office, which in the winter when the temperature was at  $-10^{\circ}$  Fahrenheit aided by some wind made for infrequent travel. Geography was definitely destiny and one of my first accomplishments was to create a combined phone book for the two locations. Additional integration of research and educational activities did follow. My other, short-term accomplishment was to change the department's name from “Biometry” to “Biostatistics” primarily to improve marketing.

At my arrival the department wasn't very “methodological” and I set the goal of hiring assistant professors who blended methods and applications. It worked out well, and I spent a fair amount of time mentoring.

#### **Relations with the School of Statistics**

When I arrived, the department had mixed relations with the School of Statistics. For example, several students who didn't pass the Statistics qualifying exam, migrated to our Masters or Doctoral programs, reinforcing the view that the Biometry department was of lower quality. Though several of these students were very good, I established the rule that at least until we upgraded our credentials, we wouldn't admit such students. Seymour Geisser, head of the School (e.g., department) of Statistics, and I knew each other well and relations between the groups improved to the point where Stat. students took our courses (the reverse had always happened), and faculty engaged

in joint research. I was occasionally asked if I worried that the degree of integration would prompt the Provost to merge the departments. I stated and believed that it would be silly to do so, we ran efficient and effective operations. I know that Provosts can do silly things, but up to now that bit of silliness hasn't happened.

#### **Degrees of Separation**

When I arrived, the department was the data center for the National Marrow Donor Program (NMDP), including the role of searching for HLA matches or near matches between donors and potential recipients. Admiral Elmo Zumwalt, head of the Pacific fleet during most of the Vietnam war, was the motive force in establishing the NMDP, because his son had died of leukemia almost surely caused by exposure to agent orange. There were "issues" between the data center and the NMDP executive board, and a meeting to address them was held at a hotel near MSP airport. There I was, having coffee with Zumwalt, discussing NMDP issues; a stark contrast to my previous "relationship" with him when I participated in anti Vietnam war protests. Life does have intriguing arcs.

#### **Research**

The department had a distinguished record in hosting coordinating centers for multi-center clinical trials, and that signature continued to grow. Most notable for me, was our becoming the coordinating center for the Community Programs for Clinical Research in AIDS (CPCRA)—the community-based alternative to the AIDS Clinical Trials Group (ACTG). Jim Neaton was director and I co-director, definitely in an apprentice role. The CPCRA's mission was to implement large, relatively simple trials in community settings, primarily for the under-served. From the start, we included community representatives in designing the trials, and held retreats with a focus on developing understanding of the statistical and other aspects of them. It was one of the most satisfying, inspiring and impactful professional activities I have done.

We collaborated with the Epi department on a Cancer Prevention and Research Unit focused on colon cancer. I directed the statistical and data management component. We held weekly meetings to discuss statistical issues, and these morphed into the principal venue for discussing and addressing a broader range of issues, almost the scientific nexus.

#### **Financial Mangement**

As the department grew in size and complexity, our management system grew and became a trusted source of financial information. We actually knew our financial status on a day-to-day basis, and that came in very handy one year when the NIH stated that we would be flat-funded for the next project year based on expended funds for the current. Their number was about \$1 million less than our accounting system showed. Amazingly, the NIH trusted us, I suppose in part because soon thereafter the university acknowledged that they had failed to submit bills to the NIH in a timely manner (go figure). An offshoot of our reputation for accurate and proper financial management was that a medical school investigator asked that we take over financial management of his projects.

#### **Allocation of ICR**

Biostatistics departments frequently have problems obtaining their of Indirect Costs Recovery (ICR), especially if they collaborate as co-PI and the PI is in a different department. However, it would be mission-compromising, and likely impossible, to

work solely on projects on which a department faculty member was PI. Bean counting to the rescue—I was a leader in implementation of a formula-based approach for the school through which collaborating departments receive a share of the ICR based on participation of co-PIs. This allocation of resources allowed collaboration decisions to be based on the scientific merits, with the financial aspects less dominant. In the same spirit, there was a formula-based allocation of tuition dollars.

#### **Bill Brody**

Bill Brody was the provost of the Health Sciences and caused all sorts of trouble, wanting to eliminate tenure, radically consolidate departments, break an emerging faculty union. I was definitely in the opposing camp, and there was considerable tension. During my sabbatical in the Netherlands (see below), I was invited by Hopkins to apply for the Biostatistics Chair position. I wasn't ready to leave Minnesota, but was scheduled to return to Minnesota for few days, I agreed to visit Hopkins on the condition that wasn't a candidate, but would write a report on what I considered the principal issues for the department. Nevertheless, in June I got a call from Dean Al Sommer who started with, "I know you stated that you weren't a candidate, but we want to offer you the job . . ." It turns out that a few weeks before that call, the announcement had been made that Bill Brody would be the next president of Hopkins. Al knew of the troubles at Minnesota and so I had a pretty easy time turning down the offer with, "With all of the problems Brody caused at Minnesota, can you imagine my following him to Hopkins?" Al had no argument against that, and the great benefit to Biostatistics at Hopkins was that Scott Zeger agreed to leave his position as Academic Dean and chair the department.

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#### **1995–1996: Visiting Professor, Afdeling Medische Statistiek, U of Leiden, NL**

Needing a break, I spent about 9 months in the department of Medical Statistics. Hans van Houwelingen was chair, and environment was very welcoming. In addition to academic pursuits, happily the winter was sufficiently cold to allow long-distance skating on the chain of lakes. And, the weather was also warm(ish), inviting frequent bike rides to the North Sea sand dunes (18km), to Amsterdam (43km), and once to Utrecht (55km). Each of these confirmed the statement, "When you are biking in the Netherlands, the wind is always in your face!"

My Dutch was rudimentary, but I could understand basic conversations reasonably well, especially seminars delivered in the home language. However, my production of Dutch was very limited and in a seminar I was careful not to ask a question until the very end (difficult for me) because as soon as I did, the session would switch to English.

In February of 1996, a Vermeer exhibit opened in The Hague and I had a ticket to attend. Wei Shen, one of my graduate students, and I were working on what would become "Triple-goal estimates in two-stage hierarchical models." I was working out the least favorable shrinkage factor, the one with the biggest MSE "payment" for estimating individual parameters, while also well-estimating the parameter histogram and parameter ranks. On the day before I went to the Vermeer exhibit, I found the least favorable to be the reciprocal of the golden ratio,

$1/\phi = (\sqrt{5} - 1)/2 = 0.618$ , a nearly religious revelation because the golden ratio is ‘all over’ Vermeer’s paintings. For sure, the exhibit was even more interesting than it would have been.

I was an examiner on a PhD defense, a wonderful experience. All defenses took place in a historic building, in room with wall lined with paintings of distinguished (male) faculty and administrators. The demand for the room was high, and it felt a bit like it must feel to get married in Las Vegas: the defense took place, the group went downstairs for a brief wine toast, meanwhile the next defense had filled the room. According to tradition, the person who was defending had a named “second” so if the candidate fainted or otherwise could not continue, the second would step in a finish the job!

A convenience of being near Amsterdam was that the 1996 IBC took place there in July 1996. I stayed around for it and then returned to Minnesota.

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#### Lance Waller’s promotion

In the Spring of 1997 Lance Waller’s promotion to Associate Professor was unanimously approved by the department and the school. It was then forwarded to the, recently created (by former health sciences provost Bill Brody) health sciences review board before then going on to the university level. The health science provost rejected the promotion, stating in a communication on Wednesday, April 9th, that Lance is on a fine trajectory, but needs more time. The University-level AP committee was meeting the following week, and I had very little time to get the decision reversed. I spent the next several days obtaining testimonials from internationally renowned statisticians (D. R. Cox, Brad Efron, . . .) and on Monday the 14th sent a letter to the University’s Senior VP for Academic Affairs that included the background and testimonials. Happily, the health science’s rejection was reversed at the university level and Lance was promoted. He left for Emory in a year or so later, but it was a win for the department and the school.

David Cox, in his cover email to me noted that, if I went through with the attempt and it failed, possibly even if it succeeded, my position as department chair would be at risk. I agreed, but of more importance was that my credibility and the school’s regarding faculty development was at even greater risk. Indeed, I would have had a hard time assuring potential hires and current faculty that if they were productive and excellent, they would be promoted.

#### Stepping down/aside

I believe in term limits and in 1997, after 10 years as chair, I was ready to step down/aside). A search was initiated, and in the Spring of 1999, Richard Tweedie became chair. We discussed current projects, and I listed some goals that I wasn’t able to achieve, but were still on my “to do” list. As a testimonial to term limits and succession, he successfully dealt with several of them before his untimely death June 2001. He was playing badminton at lunchtime, collapsed and never recovered.

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**July–December 1999:** Visiting Scholar, NAS Committee on National Statistics

To get out of Richard's way and have some space to consider my future, I took a six-month sabbatical in DC as a visiting scholar with the National Academies' Committee on National Statistics. During that period, I got the "DC bug" and was interested in returning as a resident. I came back to Minnesota just in time to celebrate the new millennium, and headed back to DC in July of 2000.

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**July 2000–June 2002:** Senior Statistical Scientist, The RAND Corporation

I wanted to be in DC and decided to try a .org. I accepted an offer from RAND to build up the statistics group in the DC office (actually in Pentagon City, VA), which is very close to the Pentagon. It was interesting and challenging to learn a new culture. RAND rewarded standard, academic productivity (articles, books, talks), but also policy briefings and position papers; of course also from bringing in business. I continued some methods research including optimal ranking, including application to Value Added Modeling (VAM) of teaching effectiveness, and got involved in several policy-related projects.

RAND has both domestic and defense sides, with the latter offices behind doors that only certain key cards will open (not mine). Some of RAND's components are FFRDCs (Federally Funded Research and Development Centers), but accounting rules apply to the entire organization. You need to record hours on a daily basis, post no more than or less than 40 per week (for full time). Occasionally, inspectors will roam through the offices unannounced to check your time sheets, to make sure you are up to date.

The accounting rules made hours the local currency: "Tom, could you advise on this, I can give you 5 hours, bill account ##." That had the positive effect of people paying for your time, the negative of injecting too much of time-keeping, consulting culture. I note that academe appears to be moving steadily towards this model.

The morning of September 11, 2001 I was working in my Cleveland Park, DC house, about ready to leave for the office, when a colleague called and told me not to come in, but definitely turn on the TV. I did, and watched the twin towers collapse and the aftereffects of the plane hitting the Pentagon, a quarter mile or so from the RAND office.

After a year or so at RAND, I realized that I missed having teaching and research advising, helping to educate the next generation of (bio)statisticians as a hard-wired part of my professional activities. As a result, in July 2002 I joined Hopkins Biostatistics and continued to live in DC.

Living in DC I had to be careful in accepting invites to be on committees, panels, etc. in the DC area. I was a cheap date (no travel, no hotel), so almost no matter my quality, I was cost-effective. I developed the strategy of asking myself if I would have accepted the invite, if I still lived in Minneapolis. The approach protected me from over-committing to the bounteous available opportunities.

**2002–present:** Professor/Professor Emeritus, Biostatistics, Johns Hopkins Bloomberg SPH

I had, and to a degree still have, a productive and fulfilling professional and personal life with Hopkins Biostatistics. The department is world-class with equally impressive collegiality. The department's and school's research and educational programs go from lab, through clinic, to the field; domestically and internationally. I've benefitted from this broad and deep set of opportunities.

An amusing situation occurred in 2003. I was invited to a new to JHU faculty reception hosted by the then-president Bill Brody (see my Minnesota write-up). Germaine and I were in the reception line and as we approached the "grip and grin" with the president, Brody checked my name tag and stated, "I was wondering if you were **that Tom Louis.**" I simply stated, "Hi Bill," and enjoyed it immensely.

I participated in the school's administration via service on the Faculty Senate (including president), the Appointments and Promotions Committee, the Committee on Academic Policy, several searches in Biostatistics and other departments, including searches for chairs. Also, I served on a few professional mis-conduct committees, chaired one; important but "not-fun" assignments.

I enjoyed collaborating on a wide variety of laboratory, clinical and field projects, with the International Centers of Excellence for Malaria Research (ICEMR) being the longest duration and most recent. The ICEMR funded my last doctoral student, Sophie Bérubé, with native French speakers bookending my doctoral advising (Guy Van Melle, PhD from BU, was my first advisee).

Commuting from the DC area to Baltimore was challenging, with constant attention to driving and sufficient lead time required. Unfortunately, travel time somewhat limited my in-person attendance at Hopkins social events, and eliminated Germaine's and my ability to host department events.

I moved to emeritus status in 2018, kept up the ICEMR collaboration and fully (ha) retired in 2021.

**2013–2015:** Associate Director, Research & Methodology, Chief Scientist, U. S. Census Bureau

My most recent sabbatical was 17 years ago, in 1996, and it was time for another, temporary change of context. Bob Groves, then Census Director called and asked if I'd be interested in serving for three years as Associate Director for Research and Methodology (ADRM) and Chief Scientist, under an Interagency Personnel Agreement (IPA) for 80% time. Under an IPA you remain an employee of your home institution, are paid by it, similar to being on a grant. I gave it some thought and agreed in April 2012 to start in January 2013.

Bob had set up a three-year rotation for this position with the goal of bringing fresh ideas to the research directorate. Rod Little was finishing up his three-year term and I would be next. I had some Census cred, via National Academy work via CNSTAT, including panels on Small Area Income and Poverty Estimates (SAIPE) and Formula Allocation of federal funds projects. Rod and I are former chairs of Biostatistics departments, which turns out to be quite logical in that the role of R&M is cognate to that of a Biostatistics department with a blend of collaborations and methodological development.

In late July, Bob called and announced that in early August he was leaving the Census Bureau to be the Provost at Georgetown University. He hoped that I would still take

the ADRM job in 2013. It was an election year, and if Romney won, I wasn't sure the Groves culture at Census would persist. However, I decided that since it was an IPA, if things got really bad (as they did under Trump), I could head back to Hopkins. And, it might be even more important to serve when the executive branch wasn't so supportive of research and methodology.

I quickly learned that the place was hierarchical and even more siloed than academe. My position, one level below the director and deputy director, conferred some benefits including rapid IT service, and a driver (from a driver pool, not my personal driver!) to take me from Suitland, where Census is located, to/from DC for meetings at the department of commerce, to the airport and to other locations.

One evening I was heading to attend a Monday evening event at the State Department, Germaine was meeting me there, so I took advantage of the driver pool. It turned out that this was his first day driving for Census, until the previous Friday he was a State Department driver. All of the security people knew him, so rather than being dropped off outside "the perimeter," I was dropped off at the front door. I felt quite special for about one minute; then had to deal with the usual vetting.

Microsoft Outlook drives the culture. All meetings are scheduled that way with very little asking around for availability. If I wanted to schedule a meeting, my secretary might ask a few key people for availability, but usually just issued the invite, knowing that unless a person had a scheduled meeting with someone higher on the pecking order, my invite was accepted.

I had many administrative responsibilities, and also had the time and pleasure to do some research with colleagues. The latter included a simulator to help assess approaches to the 2020 decennial census, CIs for the American Community Survey based on the Bayesian formalism, the relations between and potential tech transfer between adaptive survey design and adaptive clinical trials, issues in self-selection into surveys.

I chaired the Methods & Standards council, served on the management committee, on the disclosure review committee, the decennial census advisory committee, signed agreements with state statistical agencies, etc., etc.

To poke some holes into silos, starting with R&M I initiated "What's Up," a monthly seminar where one of the six centers within R&M would present their recent research and development activities.

Though the Bureau has several directorates (Communications, Admin/Finance, IT, Research & Methodology, Decennial Programs). Decennial Programs is the 800 pound Gorilla, because it's the only constitutionally-mandated activity. Ramping up to it takes a full 10 years, and if push comes to shove, all else serves its needs.

Continuing resolutions and the government shutdown in October 2013 induced considerable costs in time, productivity and dollars. It takes a lot to stop and start field work and to make up for lost time in all operations. These challenges are especially acute when there are legally mandated deadlines to meet, and challenging in that the ramp-up to the decennial census is, indeed, a ramp-up. Flat funding doesn't work; fortunately Congress recognized this and even with official flat funding, the Bureau was granted an anomaly (additional funding), though not at the requested levels.

I had a great opportunity substituting for the director at the opening of the Launch of the Gulf Cooperative Council Statistics Center in Muscat Oman. It was a grand affair with scientific and political presentations, receptions (ETOH-free); without question a new and unforgettable experience for me.

After my three years as Associate Director and Chief Scientist at 80% time, in 2016 I remained on the IPA at 20% time to help with analyses that support Section 203 of the voting rights act, determining which jurisdictions need to provide ballots in something other than English by using decennial census and American Community Survey information. There are about 8000 jurisdictions and 70 candidate languages, with the criterion for the “need to provide an alternative language” based on legislation with several, “if, but, then, however . . .” criteria. Very little or no data were available for many jurisdictions $\otimes$ languages, and use of the Bayesian formalism was absolutely necessary.

#### **2018–2020: Expert Statistical Consultant, FDA’s Center for Drug Evaluation and Research**

The FDA’s Center for Devices and Radiological Health (CDRH) had successfully given Bayesian ideas and procedures at least co-equal status to traditional frequentist, but the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) lagged far behind. I was brought in on an IPA to help energize Bayesian approaches in CDER; Frank Harrell, a far more committed Bayesian than I, was serving in a similar role, so there was a sufficient presence to make progress. We did make some, but not much and it remains to be seen if the benefits of Bayes in some situations will be realized.

In addition to fostering Bayes, I helped review study designs and results (including several COVID protocols) in an advisory capacity. I was on the the advisory committee for the Complex, Innovative Design initiative (encouragement for such designs with increased availability of feedback on early versions of a protocol), gave several internal and a few external presentations, got to know the staff and the complexities of their jobs. In addition to the scientific and to a degree political challenges of the job, staffing is well-below what is needed.

During my time at the FDA, there was a small-world event in that Sylva Heghinian Collins (one of my doctoral students at BU) was appointed head of CDER’s Biostatistics Branch.

COVID-19 made the last 10 months of my IPA remote-only; after early March 2020, I entered the building only once, in December to turn in my computer and badge (and take my coffee mug!).

### **3 Selected Professional Service**

**Editorial:** In my roles as referee, associate editor and editor (*JASA & Biometrics*), I have reviewed  $\approx$  1500 original submissions to various journals, reviewed  $\approx$  1000 revisions for a total of  $\approx$  2500 reviews.

**ENAR President:** During 1991–1993, I served as (President-elect, President, Past President) of the Eastern North American Region (ENAR) of the IBS. ENAR’s funds balance was growing at a rate that could attract the attention of the IRS and threaten our tax exempt status. So, we increased the number of student travel awards, producing a win/win.

While the IBS central office helped with financial accounting, ENAR had, on its own, negotiated hotel contracts and related annual meeting arrangements. I proposed and the executive committee agreed that it was time to end this amateur status (I was negotiating with hotels) and also to put ENAR on a solid, management basis. So, we proposed to the membership that ENAR contract with a management firm. Thank goodness, the proposal passed, but not without considerable contention.

I helped negotiate arrangements between the IBS (Niels Keiding was President) and the American Statistical Association (ASA) to jointly jointly the new, *Journal of Agricultural, Biological and Environmental Statistics, JABES*.

**Committee to Review the Health Consequences of Service during the Persian Gulf War:**

During 1994–1996, I served on this Medical Follow-up Agency committee (the MFUA is a component of the National Academy of Medicine; at that time called the Institute of Medicine. We reviewed available information and took testimony to judge whether service induced what became known as the “Persian Gulf War Syndrome;” also to recommend additional studies and specify the necessary information systems. As with all National Academies panels, payment is delivered by the opportunity to learn a lot, affect science and policy, to get to know a broad spectrum of experts (and the occasional lunch or dinner). I learned a lot about depleted uranium ammunition, desert diseases, nerve gas (the munitions storage bunker in Khamisiyah); the list goes on and on. One committee member had been and likely still was an undercover operative. Several military people would come to testify, would see him and hug him. Later, we’d ask why and the usual answer was, “ I saved his life in [location].”

**NAS Panel on Small Area Income and Poverty Estimates (SAIPE):**

During 1996–1999, I served on this panel with the charge of improving statistical approaches to determining poverty estimates in small areas such as school districts. Every Fall the Census Bureau delivers estimates of school district specific poverty estimates to the department of education, which then distributes them under a formula associated with the Elementary and Secondary Education Act to support free and reduced lunch programs and other approaches to reduce the impact of poverty. The panel began work in the Summer of 1996, and had to recommend a new approach by that Fall. We weren’t ready to “bless” our initial, empirical Bayes models, but also knew that they were better than the current approach. What to do? After much discussion, we decided to recommend a 50/50 solution, an equally weighted average of estimates using the old and the new models, with the proviso that this was a transitional approach to an improved model the next year. NAS report reviewers wanted justification of 50/50 (why not 60/40, 40/60, ...?). Because I had recommended the 50/50, I was asked to respond. With nothing much to go on I stated that 50/50 was the most robust against a broad range of underlying best weights because  $p(1 - p)$  is flat near  $p = 0.5$  and the regret is controlled). Happily, that seemed to satisfy the reviewers.

Historically, the Census Bureau was strongly against any modeling, relying on “design-based” approaches that depend on the sampling plan to produce unbiased estimates and valid uncertainties. However, the design-based approach to small area estimation, while unbiased, produces unacceptably big uncertainties (very broad CIs) and the Bureau was essentially forced into a model-based approach.

**NAS, Committee on National Statistics:**

From 1997–2003, I was a member of CNSTAT. While focusing on “national statistics” (e.g., Federal Statistical Agency activities and prod-

ucts), the portfolio was far broader. Being on the committee was educational and interpersonally rewarding, with enduring professional and personal relationships. It wasn't all work, for example the "take no prisoners," lunchtime turbo croquet at the Beckman Center in Irvine CA.

**NAS panel on Formula Allocation of Federal and State Program Funds:** From 2000–2002, I chaired this study of the statistical and related aspects of allocation of funds by formula. Work on the SAIPE project motivated this more general assessment of programs including school lunch, highway funding, and Medicaid. The premise of all such allocations is to have Congress argue out the details during the legislative process and then let the formulas take over from there. Formula inputs are primarily based on statistical estimates and non-linearities in the formulas amplify the impact of estimation uncertainty, ergo the CNSTAT interest. Formulas include features such as thresholds (e.g., no funds will be allocated unless the percentage of [attribute] is greater than P%), hold harmless provisions (an entity will get at least F fraction of what it got last time), small state minima (a state will get at least \$\$ amount), etc. We asked about the rationale that supported this last and were told, "because there is a Senate."

**NAS Committee on use of third party toxicity research with human participants:** From 2002–2004, I served on this committee that evaluated the quality and use of non-EPA (usually industry) sponsored toxicity research. Suffice to state, in general the research was a statistical wasteland. We recommended new quality standards for EPA to accept third-party produced information, some of which have been implemented.

**Drinking Water Committee, EPA Science Advisory Board:** From 2003–2004, during the second Bush administration, I served on this board, and resigned before the end of my term. Politically appointed EPA staff, generally not fans of regulation, would mis-represent our conclusions and advice or simply imply that they were following it when they were not. So, I pulled the plug.

**IBS President:** During 2005–2008, I served as (president-elect, president, past president) of the International Biometric Society (IBS). It combined challenges and satisfactions in an international context. Interactions were quite intense, including  $\approx 13,500$  ( $\approx 9$  per day) emails during my four-year term. Success as president is measured in small steps (turning the oil tanker is difficult). I did initiate the Prose Editing Project (PEP), that offers free editorial advice (not technical refereeing) to IBS members. Service as president opened up the world with trips to Europe, sub-Saharan Africa, Japan, Brazil and Argentina. Many friendships were a consequence as were a few not so friendly relations on challenging issues.

**Board of Scientific Counselors, NIH-National Institute of Environmental Health Sciences:** I served from 2007–2012, and was the first statistician on the board. Each NIH institute has a BSC that at regular intervals reviews the contributions of "labs" and individual researchers. Reviews focus on scientific productivity and training the next generation via pre- and post-doc programs. No surprise, I contributed most to the reviews of the Biostatistics and the Epidemiology branches, but did add some value to the other reviews and learned a lot by participating.

**AAAS, Section U President:** During 2011–2013, I served as (chair-elect, chair, past chair) of Section U (Statistics) of the American Association for the Advancement of Science (AAAS). Duties included organizing fellow nominations and participating (moderately) in developing

the program for the annual meeting. The organization was (and to a large degree, is) very hierarchical and centralized, almost to the point where the leadership tolerated the sections, but acted as though they were a necessary nuisance. I did help make Statistics more visible in the organization, pestering to include “statistics” in a variety of communications that formerly had only “mathematics.” More broadly, section chairs lobbied for sections to have larger role, and that has succeeded to some degree.

**Citizenship Amicus brief:** In 2018 I represented the American Statistical Association on a working group that also included representatives from the American Sociological Association and the Population Association of America to prepare amicus briefs supporting the lawsuits in, New York, California, and the Supreme Court (SCOTUS) to block including a citizenship question on the 2020 census. Inclusion was barred by the SCOTUS, it felt very good to contribute to the court cases, but I don’t know if there was a causal relation between the decision and our briefs (presumably they didn’t hurt). It was only a partial victory, because the very act of the Trump administration’s attempt likely chilled participation in the 2020 census. Furthermore, almost immediately President Trump ordered federal agencies to provide citizenship-relevant data to the Census Bureau so it could subtract non-citizens from the census totals.

**Expert Declarant in National Urban League et al., vs. Ross & Dillingham:** From 2020–2021 I prepared a declaration and provided continuing advice to the plaintiffs in case #20-CV-5799-LHK, United States District Court for the Northern District of California, San Jose Division: National Urban League and other Plaintiffs vs. Wilbur L. Ross, Secretary of the U. S. Department of Commerce; Steven Dillingham, Director of of the U. S. Census Bureau. Soon after COVID struck, Census proposed the “COVID Plan” delaying termination of Non-response Follow-up (NRFU) to October 31, 2020, delivery of apportionment counts to the president from December 31, 2020 to April 30, 2021, etc. However, in late July the Trump administration contracted the time line to September 30 for termination of NRFU and December 31 for delivery of apportionment counts (with non-citizens subtracted). Enter the Urban League et al. with a court case to restore the COVID plan dates. We got NRFU termination moved to October 15th; the practical impossibility of delivering high-quality apportionment counts by December 31, coupled with Biden’s victory saved the day.

**American Statistical Association’s 2020 Census Quality Indicators Group:** During 2020–2021, I served as a member of this group (visit [our initial report](#)). The 2020 census faced a variety of challenges and it was important to evaluate quality. The Bureau conducted several assessments, but evaluation by an external group was important to increase credibility.

**National Academies’ Panel to Evaluate the Quality of the 2020 Census:** From the Summer, 202 through the Fall of 2023, I served on this Committee on National Statistics (CNSTAT) panel. Unlike most NAS projects, a subset of the panel conducted original data analysis on process indicators (i.e., geography and demography specific counts of self-response, field interviewer response, data obtained by proxy, etc.), all protected by the Census Bureau’s firewall. We had to be vetted for “special sworn status,” went through considerable training and re-training. A very small subset of humans know how to deal with the full database, and we relied on Bureau staff to create analysis data sets and to explain the provenance of each. Each table and graph that we wanted to bring outside the

firewall had to be privacy protected (via differential privacy) and vetted by Census staff. The report will be available on the CNSTAT web in the Fall of 2023.

## 4 Selected Community Service

### Lexington MA school enrollment projections

In 1984, I co-chaired the Lexington MA, School Enrollment Projection & Reorganization Committee. Starting in the late 1970s, enrollments declined and a naive projection suggested that by the mid-1990 enrollment in some grades would be negative! The school board constituted the committee to advise on dealing with these declines.

We obtained fifteen years of enrollment history, birth records and input from real estate companies on the attractiveness of Lexington MA. Interestingly, even for (potential) buyers who wouldn't have children in the schools, high-quality public schools was an important factor in choosing Lexington. Buyers knew that quality schools helped maintain house prices, etc.

We projected the longitudinal evolution of grade-specific enrollments through the mid-1990s via a Poisson arrivals, binomial departures model, initiated by the birth data for feeding into kindergarten and grade 1, accompanied by a model-based uncertainty assessment (no additional uncertainty from model uncertainty). Our first finding was that, no, enrollments were not going to go negative (duh). The 95% confidence intervals for 1990–1995 were so wide as to be essentially useless for planning, and we needed to decide how to communicate signal and noise in a public meeting and what to recommend to the board. To communicate that there was at least some information, we plotted the model-based projection line (the year-specific, maximum likelihood values) and the year-specific 50% coverage limits.

Our recommendations to the board emphasized that “uncertainty” was our principal finding and that re-organization plans should be based on that feature. Ultimately, the board decided to close a few schools, but lease them for private school use. This approach allowed that if the building was brought back into the public system, it wouldn't have to comply with possible new building codes.

This project highlights the importance of uncertainty in making decisions. However, in this specific instance, “Uncertainty, rest in peace,” the 1995 actual enrollment was very close to our maximum-likelihood value!

### Boston University extension course at Norfolk Prison

From 1975–1978 I volunteered with BU's Norfolk Prison Education Program in Norfolk MA to teach mathematics & statistics. The program was a component of the university's extension program, and to get in a prisoner had to have a high-school degree or a GED. Generally, only those with long sentences were in the classes. Once a week, I went to the prison, made my way through the vetting process (ensuring that my hand stamp was sufficiently prominent that I'd be able to get out!), and taught a combination of intro mathematics and statistics. Some students were in the class to avoid other options such as laundry detail, but many were there to learn, and many were street-savvy and intelligent. Occasionally, one of my students would appear at my BU office door, and I'd say something like, “ You on furlough, right?” The answer was always, “yes,” which was quite comforting.

I presented several examples of the need for mathematics to adjust intuition, for example regarding exponential growth or decay. Folding paper was the headliner:

1. "How many times do you think you can fold a sheet of paper in half?"
2. "If you could fold a very thin sheet of paper in half 50 times, how thick would it be?"

The answer to (1.) is 7-8 at most, to (2.) thicker than the distance to the sun; the actual value depending on paper thickness in each case. Disbelief filled the classroom, so I suggested that to see (1.) in action, unroll toilet paper and see how many times you can fold it, forgetting for a moment that I was in a prison! That evening I got a call from the prison superintendent, "Professor Louis, inmates are in the cell block unrolling and folding toilet paper; they stated it was a homework assignment! I said (to myself, OMG!) and let the superintendent know that I could see how the inmates would interpret what I said that way. Prisoners weren't sent to solitary, and neither was I. In that no cell phone era, it was fortunate that I was home!

Many of the attendees were very intelligent, had made a tragic mistake (or more) and were to a large degree wasted lives. I had a wide variety of very interesting conversations during breaks, learning as much or more from them as they learned from me.

The prison was built in early 20th century with a stated rehabilitation goal. There were several "dorms," a classroom building, etc.; of course all surrounded by a high wall with guard towers. When you entered the complex, after vetting they stamped your hand and cautioned not to wash it off, if you wanted to get out at the end of the afternoon.

## 5 Vignettes & Pronouncements

### **Sometimes, statistical inference isn't relevant**

In the early 1970s, I wasn't involved in the early stages of a gender-equity, salary dispute at Tufts University, but was called in by the female faculty part-way through. All parties, myself included, endorsed the validity of the analysis model which estimated salary shortfalls for women. However, the administration argued that the results weren't statistically significant (at 0.05) and so no salary adjustments were needed. I communicated that if the goal were to indict the administration for purposeful discrimination, then statistical significance was relevant. However, if the goal was to redress observed salary discrepancies without assigning blame, then the data analysis without inferential embedding is the way to go. Ultimately, all parties agreed with that view and salary adjustments were made.

### **Timely & Accurate Data**

Ethical monitoring of a clinical trial or other study requires timely, complete and accurate data with informative "paradata" (context such as whether censoring implies no news is good news or no news is no news).

#### *The envelop, please*

Consider a randomized clinical trial comparing an innovation designed to reduce the side-effects of chemotherapy with placebo. Blinded interim results showed that it was almost impossible for the estimated treatment comparison to reverse, but the estimated advantage was not yet sufficiently stable to stop the trial unless the interim estimate favored the placebo group (no hope for the innovation). If the interim result favored the innovation, the trial should continue.

The monitoring board asked to be unblinded and the statistical center revealed the code (“the envelope please”). The treatment codes indicated that results favored the placebo and the trial was stopped.

This story comes from an actual clinical trial with the monitoring board decision occurring on a Saturday. The small company sponsoring the innovation had one other product in its portfolio. They notified the securities and exchange commission of the bad news, the stock opening was delayed to allow all to know the results and the stock dropped by 50% by the end of the day. Imagine the clinical, financial and ethical consequences if the treatment coding were in error.

### **Dealing with results from outside the trial**

The Community Programs for Clinical Research on AIDS (CPCRA) CMV PROPHYLAXIS STUDY provides a second example. The goal was to prevent CMV retinitis using oral Ganciclovir (at the time a standard treatment for the disease). Diagnosis in this community setting was via standard screening assessments, not high-tech. The study close accrual in June of 1994.

The similar Syntex Study comparing oral Ganciclovir to placebo had more intensive screening using high-tech methods that detected subtle, peripheral disease. In July 1994, the Syntex study was stopped by the monitoring board with a 50% reduction relative to placebo with a suggestion of increased survival.

What should the CPCRA do?! We needed to react quickly and in one week prepared a comprehensive report (impossible if we hadn't had timely and accurate data!). We ended up continuing the trial because our data didn't support the Syntex result regarding the CMV endpoint or the hint of a survival advantage. We informed all clinicians and patients, allowing the option of switching Ganciclovir. Very few did so and at the end of the study there wasn't a statistically significant reduction in *clinical* disease, though there was a suggestion of a survival advantage.

### **Research Roles**

Nothing is purely statistical, but most of science and policy has a statistical aspect. (Almost) every scientific and policy enterprise requires collaboration; mutual education is essential. Statisticians need to understand the subject area; collaborators need to understand at least the broad aspects of statistical science. We are the experts, but should promote co-ownership of all aspects of a study and avoid messaging the collaborative equivalent of, “Only historians are allowed to reminisce.”

### **Rules of Engagement**

To be effective scientific and policy collaborators, we must insist on proper relations, roles and resources. We need to be at the table from the beginning of collaborative projects, then proactively participate and communicate. We must clarify expectations, rewards and responsibilities including whether the relationship is to be consulting or collaboration, who does what (ensuring that staffing is sufficient to the tasks) administrative roles. We need to participate in decision-making and resource allocation. The expectations in a consulting relationship are somewhat different, but clarity is no less important. We must reject the demeaning, unethical, destructive and,

happily, reduced in prevalence, practice of being offered the choice between payment or authorship. We need to insist that authorship be based on substantive , irrespective of administrative arrangements.

### **Stage 0 design**

We commonly think of design as it relates to choice of interventions, measurement of covariates, analytic methods, sample size, including follow-up time, and the like. However, assembling an investigative team, stage 0 design, has high leverage on the quality of an investigation as illustrated by the following example.

#### *Review of the use of r-TPA in treating acute stroke*

Randomized trials reported a positive treatment effect for the use of IV t-PA in the treatment of acute ischemic stroke patients within 3 hours of symptom onset. However, clinicians, especially emergency department clinicians, raised concerns about baseline imbalance on important risk factors and also expressed interest in a finer-grained analysis of the role of time from symptom onset and in subgroup analyses. Also, there was concern about some conflicts of interest. In response to these concerns and interests, in May 2002 the National Institute of Neurologic Disorders and Stroke (NINDS) appointed a committee to address the *statistical* aspects of these issues. The three statisticians who agreed to conduct the review knew that though the issues were termed “statistical,” the issues were equally “clinical.” Therefore, we insisted that three clinicians be added to the team, one of whom was critical of the studies. In addition, we insisted that we operate completely independently of the NINDS (get the full datasets, conduct our own analyses, be granted permission to publish what we found, ...). These requirements induced nervous tremors in the NINDS, but were granted, and so we had a high quality level 0 design. Clinician participation was essential. Without them, our analyses would have been far less valid and less credible. Furthermore, complete independence substantially increased trust in our findings, findings that pretty much supported the those in the original articles.

Our results were published in *Stroke*<sup>1</sup>; one letter in response to it by a perennial critic of the original studies, was highly critical of our work. We wrote a short reply, closing with, “No amount of polemic will change biology.”

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<sup>1</sup>Ingall T, O’Fallon M, Asplund K, Goldfrank L, Hertzberg V, Louis TA, Christianson TJH (2004). Findings from the reanalysis of the NINDS tissue plasminogen activator for acute ischemic stroke treatment trial. *Stroke*, 35: 2418-2424. PMID: 15345796