

Comments on Receiving the Lilienfeld Award:

Eras in Epidemiology

September 29, 2015

Jonathan M. Samet
Distinguished Professor and Flora L. Thornton Chair
Department of Preventive Medicine
Keck School of Medicine of USC
Director, USC Institute for Global Health
University of Southern California

Before making formal remarks, I begin with my thanks and gratitude:

- To the American College of Epidemiology (ACE) and its Awards Committee for selecting me for this honor. I have valued my relationship with the ACE over a many-year span. I have found many ACE colleagues who share my belief that epidemiologists should make a difference and I have worked under the umbrella of ACE on projects that have proved valuable for our field.
- To those who nominated me—I am grateful for your thinking that I am a deserving candidate for the Lilienfeld Award.
- And finally to the “too many to be counted” colleagues, collaborators, and students who have enriched my career.

Today, I will speak briefly about *Eras in Epidemiology*—hardly a new title, but one that fits with what I intend to present. Don’t be mistaken—I am not talking about “errors” in epidemiology, also a favorite topic for many. I am entitled to talk about eras because I have now reached an age at which introductions begin to sound like obituaries and I am asked to give talks that offer reflections on my career. Understand—that when these invitations start, you are entering the “end-game” of your career.

Back to eras—my career in epidemiology started in 1975 when I went to the Channing Laboratory at Harvard Medical School and started on my master’s degree in epidemiology at the Harvard School of Public Health. This training happened serendipitously; at the time I was seeking an opportunity to train in pulmonary medicine and public health and there were not many programs for doing so. While compulsively reading the *Annals of Internal Medicine*, as I once did before 21st century distractions ended this habit, I found an old-fashioned hard-copy announcement of a new fellowship in “the clinical epidemiology of heart and lung disease” that offered funding to do precisely what I wanted to do. This was the launch of Frank Speizer’s training program at Harvard’s Channing Laboratory—a program that has made extraordinary contributions to our field through the success of its graduates. I wrote Frank, who became a

mentor and lifelong friend, and told him that I was the perfect candidate for the program and that he should take me on. In Frank's low-key style, I eventually received a letter saying that I should come and I did. In the summer of 1975, I started at the Channing, then at Boston City Hospital. Within months I had launched my first research study—of asbestos exposed workers at Electric Boat in Groton—making epidemiology a reality, and 40 years later the fascination of epidemiological research has not waned. My training in epidemiology was with the Department of Epidemiology of the Harvard School for Public Health—there, I learned methods from MacMahon, Miettinen, Monson, and Hutchinson that have stuck.

I am not a historian so that my description of eras in epidemiology is approximate and idiosyncratic. Named inelegantly, they are: 1) the era of tuberculosis and infectious diseases (1900-1940); 2) the transition years with the decline of infectious diseases and the rise of chronic diseases (1940-1960); 3) the chronic diseases era and the return of infectious diseases (1960-1990); 4) the era of speciation with the rise of many epidemiologies (1990 until now); and 5) the next era—to be named. Each was marked by accomplishment and each came to a close as new scientific opportunities and challenges emerged and directions shifted.

Let's start with the first era embodied by Wade Hampton Frost, arguably the original academic epidemiologist. He was first appointed at Johns Hopkins in 1919, four years after the School of Hygiene and Public Health was started. In a career model that prevailed for decades, he moved from the world of application as a member of the US Public Health Service to the new school. His work centered on infectious diseases, particularly tuberculosis, then a leading killer, and he remains linked with methods: birth cohort analysis and the retrospective cohort study. Importantly for our field, he advanced case studies in education and established "population laboratories" in Hagerstown and East Baltimore. These connections persist today at Johns Hopkins in the George W. Comstock Center for Public Health Research and Prevention in Washington County and the Urban Health Initiative in East Baltimore. George Comstock bridged from this first era to the third—beginning his career with studies of tuberculosis and the tuberculin skin test in the early 1940s and ending squarely in the third in 2007, when he died at age 92. He had the foresight to store serum samples in population cohorts, launching studies that fit within the paradigm that we now call molecular epidemiology. There is a lesson here—careers bridge eras and researchers need to be nimble and able to learn and move from one to another. More on that challenge later.

The transition era (1940 - 1960) was largely driven at its start by a single risk factor — cigarette smoking and its enormous consequences. The rise of lung cancer was undeniable by the 1940s and needed investigation to identify its causes. Landmark case-control studies were published in 1950 and soon followed by equally renowned cohort studies. Many early developments in chronic disease epidemiology were driven by research on smoking: the population attributable risk (Morton Levin), the odds ratio (Cornfield), systematic review and causal criteria (the 1964 Surgeon General's report), and large cohort studies (Doll and Hill, Hammond and Horn, and others). Smoking, a devastatingly powerful cause of disease, was a perfect starting point for chronic disease epidemiology. Smoking was an accurately and feasibly measured cause of

disease and so potent that its causal effects for many diseases were readily detected. The new approaches were quickly turned to other non-communicable diseases.

Lilienfeld's career spans the second (transition 1940-60) and third (chronic diseases 1960-90) eras—he published no papers on infectious diseases and is often referred to as “the father of chronic disease epidemiology”. He was the fourth chair of the Department of Epidemiology at what was the Johns Hopkins School of Hygiene and Public Health—now the Johns Hopkins Bloomberg School of Public Health. His tenure as Chair was from 1970-1975 and he took the position when the Department of Chronic Diseases, which he chaired from 1961-1970, was merged with the Department of Epidemiology. The 1960s and 1970s were distinguished by the emergence of research on risk factors for chronic disease as a principal focus for many epidemiologists. In my view, we are now well beyond end of the era of “chronic disease epidemiology.” Lilienfeld's CV illustrates what could be done at the time—he studied many different problems—and he also formally brought genetics into epidemiology, hiring Bernice Cohen, a geneticist as a faculty member at Hopkins, and carrying out pioneering studies—such as that on familial aggregation of lung cancer done with Tokuhata.

By the end of the third era, epidemiological research had identified many opportunities for prevention. While “risk factor epidemiology” has been decried, the “black box” offered opportunities for disease prevention that were to be further refined in the fourth era of speciation (1990 – now). The fourth era was marked by the proliferation of many different kinds of epidemiology—cancer, genetic, pulmonary, CVD, diabetes, reproductive, and more. Some fields became so specialized that researchers defined themselves by particular risk factors and diseases, such as hormones and breast cancer. Disease hopping became impossible and discouraged. My turn to epidemiology from clinical medicine was facilitated by receiving a Research Career Development Award from NHLBI in the early 1980s—my proposed five-year slate was labeled as diffuse because it included cancer, respiratory diseases, and air pollution. Epidemiology has done well during this fourth era and looking back, we should be pleased by the advances and the foundation for prevention that has been established. What are seen as failures—perhaps GWAS and diet and health—should also be viewed as advances. We have learned that we will need to probe deeper and that the questions under study are more complicated than originally framed. New, immediate, and easy gains for prevention, as with smoking, may not be so often identified as in the past.

The resurgence of infectious diseases during this fourth era was also critical for the field. There was an interlude during the 1970s when tuberculosis could be treated and cured, and antibiotics had become available for previously challenging gram negative and positive bacterial infections. Viruses seemed to be well behaved for the moment. As a fledgling pulmonologist, I declared in about 1980 that infectious diseases were conquered (at least in my narrowly defined world). I saw my first case of AIDS a few years later and witnessed the 1993 hantavirus outbreak firsthand while in New Mexico. Infectious diseases epidemiology was resurgent during the 1980s. By 1994, when I went to Johns Hopkins as the sixth chair of the Department of Epidemiology, infectious disease epidemiology was the largest element of the department. I was amazed by its scope and ready to recognize how wrong I had been only 15 years earlier. I

learned much from my colleagues who had the foresight to start the Multi-Center Aids Cohort Study (MACS or SHARE) and ALIVE cohorts. I need to mention Frank Polk here, a friend from the Channing Lab, who led the resurgence of infectious disease epidemiology at Johns Hopkins; he was another leader who anticipated future directions with accuracy.

The new era is definitely underway—quoting Dylan (Bob)—“the times they are a-changin’” but most disconcertingly to all—we don’t know in what way. Back to Dylan: “You don’t need a weatherman. To know which way the wind blows.” Here are some of the wind directions—new cohorts, use of existing data sets, and more and more “inter-disciplinary team science.” Research technologies are setting the directions for research—quite contrary to the hypothesis-driven studies of the past. We are moving away from the days when individual researchers had the privilege of establishing cohorts to an era when many epidemiologists may never collect data themselves, other than via downloading. At this point in my “natural history” where the research winds are blowing is not personally relevant, but I do care because of its implications for our field and particularly for the new cohort of epidemiologists—*whom* I hire and mentor. The new era will also involve team-based research. The new generation is anxious, concerned about what the future holds for their research. Funding is ever more difficult—we are not just on the downside of a funding cycle but in the midst of a fundamental change in public support for investigation. Yet, the opportunities for innovation as the era changes are intriguing and likely to bring a new wave of insights. I will not be a participant but I hope to be around long enough to see what happens.

A few “lessons learned :”

- Our field’s leaders, like Lilienfeld, have been able to anticipate the next era. Here I would like to highlight Brian Henderson as well, the recently deceased founder of my USC department. Brian moved from infectious diseases to cancer epidemiology and then cancer genomics. This is era-spanning
- There are some constants—the methodological core—that will always underlie solid research. In that regard, I am pleased to be here with Steve Cole, a former Hopkins faculty member and friend, who is leading in advancing the methods of epidemiology.
- But, the need for lifelong learning is mounting and a researcher can quickly become out-of-date. I recall Frank Speizer telling me some years ago: “Now that my trainees are middle-aged, I have to tell you that the hard part of your career is not the first half, but the second.” Having now been there—I agree.
- There will always be interesting questions and new ways to address them. Inevitably, there is a leading cause of death.
- Be ready for what may come next—even if you don’t know what it is.
- And in every era, the best have made a difference.

A last thanks—the American College of Epidemiology provides a generous sum with the Lilienfeld Award. A few weeks ago, one of the giants of our field died—Leon Gordis—the fifth Chair of Epidemiology at Johns Hopkins. Leon, of course, was a renowned educator who taught “Epi 1” to thousands and authored a leading introductory text based on this experience. David

Celentano, the current chair, and I have joined to start a fund to support innovation in education in Leon's honor—My award will go to that fund—consider joining David and myself as we establish it (and, if interested, details are at the link below):

<http://www.jhsph.edu/departments/epidemiology/giving/professor-leon-gordis.html>