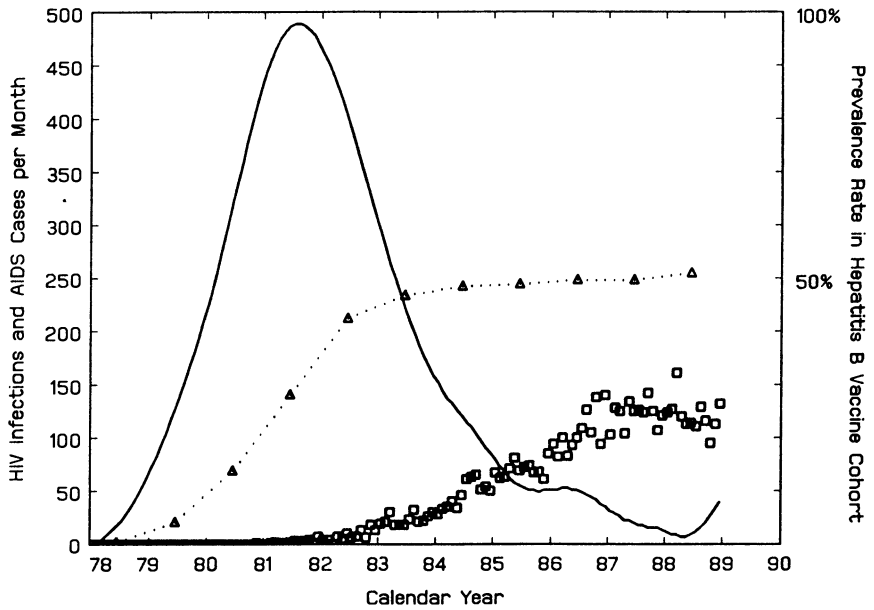
BOOK REVIEWS

The Statistics of HIV

AIDS Epidemiology. A Quantitative Approach. RON BROOKMEYER and MITCHELL H. GAIL. Oxford University Press, New York, 1994. xvi, 354 pp., illus. $49.95. Monographs in Epidemiology and Biostatistics, 22.

The London *Bills of Mortality* were initiated in 1603, and by the late 1600s the "Collector of the Bills," British demographer and tradesman John Graunt, was developing statistical methods to systematically record and analyze the morbidity and mortality statistics of the day. In 1692, he summarized much of this work in his *Natural and Political Observations Mentioned in a Following Index and Made upon the Bills of Mortality*. The modern version of the *Bills of Mortality* in the United States is the *Morbidity and Mortality Weekly Report* (*MMWR*), compiled and published by the Centers for Disease Control and Prevention (CDC) in Atlanta. Since reporting on the first five acquired immune deficiency syndrome (AIDS) cases in 1981, the *MMWR* has deftly chronicled the progress of human immunodeficiency virus (HIV) epidemic in the United States. By the end of 1993, there were 361,509 reported cases of AIDS, 220,871 of them having resulted in death. One might say that the authors of the book under review here became the John Graunts of the HIV epidemic. Working closely with the CDC, they were involved in the development of many of the statistical methods used in the analysis of HIV/AIDS data. Most notably, they developed the method of back-calculation for estimating the size of the HIV epidemic and for predicting the short-term course of the AIDS epidemic. This book gives a careful description of these methods. In addition, it gives much of the quantitative history of the epidemic in the United States.



The estimated monthly infection rate (solid line) and reported monthly AIDS incidence rate (squares) for homosexual and bisexual men in San Francisco, and the plot of HIV prevalence rate (percent) for homosexual and bisexual men participating in hepatitis B vaccine trials in San Francisco (triangles). Note that the HIV epidemic (solid line) drives the AIDS epidemic (squares), but with a time lag dictated by the AIDS incubation distribution. In San Francisco, the HIV infection rate is estimated to have peaked late in 1981, but reported AIDS cases were beginning to flatten out around 1988, when the HIV infection rate was estimated to have dramatically decreased. Nearly half the men in a sample taken from the original hepatitis B vaccine trial cohort had been HIV-infected by 1983. [From *AIDS Epidemiology: A Quantitative Approach*, where references to the original sources are given.]

An important chapter in this history is the effort to estimate the size of the HIV epidemic in the United States. The authors devote several chapters to this subject. Once it was established in the early 1980s that AIDS was caused by the retrovirus HIV and techniques were developed for detecting infection, it became critical to elucidate the natural history of the disease and estimate the magnitude of the growing epidemic. In 1986, at a Public Health Service meeting at Coolfont, West Virginia, medical researchers, epidemiologists, and statisticians estimated, on the basis of seroprevalence surveys from selected populations, that 1 to 1.5 million Americans were then infected with HIV. This estimate was shockingly high, given that a total of only 21,000 AIDS cases had been reported to the CDC at that time. The estimate was produced by multiplying the estimated HIV prevalence among male homosexual and intravenous-drug–using subgroups by the estimated national size of these subgroups. However, the HIV prevalence estimates were not based on representative probability samples, and the subpopulation sizes were hard to estimate—for example, the estimation of the size of the male homosexual population was partly based on the outdated 1948 Kinsey report. In short, there were many potential sources of bias. If the seroprevalence estimate was indeed accurate, then the mean AIDS incubation period, that is, the time from infection to an AIDS diagnosis, would have to be quite long. Although, in 1986, the estimate of the mean AIDS incubation period from transfusion recipients was 4.5 years, this estimate, based on retrospectively recorded AIDS cases, was thought to be too low. By 1989, prospective studies of HIV-infected persons yielded estimates of around 10 years for the median AIDS incubation period. Thus new HIV infections (which were not observed) would appear as newly reported AIDS cases on average 10 years later. This point is aptly demonstrated in the figure (left) that appears on the cover of the book, which shows a plot of the reported AIDS incidence for homosexual and bisexual men in San Francisco along with the estimated HIV infection rate. Mathematically, this meant that reported AIDS incidence was a "convolution" of the HIV infection rate and the AIDS incubation distribution. Since the AIDS incidence and incubation distribution were assumed to be known, the HIV infection rate was estimated by statistically deconvoluting the HIV infection rate from the AIDS incubation distribution. This technique became known as back-calculation, since

the HIV infection rate is estimated from AIDS incidence that occurs later in time. Once the HIV infection rate was estimated, then short-term AIDS incidence could also be projected forward from this rate with reasonable accuracy. In a 1986 *Lancet* article, Brookmeyer and Gail used back-calculation to predict that the number of cumulative AIDS cases would increase by at least a factor of five over the next five years, a prediction that proved to be accurate. By 1988, they and their colleagues used back-calculation to estimate that approximately one million Americans were currently infected with HIV, validating the Coolfont estimates as well as similar estimates from ongoing subpopulation surveys. This number has not changed much since then.

The book contains many other intriguing chapters on the development of statistical and mathematical methods for dealing with HIV/AIDS epidemiological problems. There is a very good chapter detailing new statistical methods for estimating important indicators of disease progression from "prevalent cohorts," that is, cohorts of HIV-infected persons, for many of whom times of infection onset are unknown. The authors include an interesting chapter on the use of epidemic transmission models in the qualitative analysis of the dynamics of HIV/AIDS epidemics. They close with a chapter on the statistical analysis of therapeutic and vaccine trials. Of special interest is the story of the testing of the antiviral drug zidovudine (AZT). The need to rapidly deploy AZT for the treatment of critically ill AIDS sufferers, augmented by pressure from AIDS activist groups, helped change the accepted statistical paradigm for conducting clinical trials to a more humane and responsive form.

This book should be of particular interest to biostatisticians and epidemiologists who deal with epidemiological data, but should also be of interest to infectious-disease scientists who are not necessarily quantitatively oriented. There is plenty of mathematical development for those who like to follow the various arguments and ideas in this form, but there are also plenty of tables and graphs for those who do not care to follow the equations. I would recommend the book both as a text and as a reference. Finally, the statistical methods presented along with the myriad cautionary notes should be of use in the analysis of infectious diseases other than HIV that possess long and variable incubation periods and natural histories.

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Vignettes: Retrospective on Washington

From 1989 to 1993 D. Allan Bromley was science adviser to President George Bush. Below are excerpts from his recently published assessment of the experience, *The President's Scientists: Reminiscences of a White House Science Advisor* (Yale University Press).

One of the most useful pieces of advice I received in Washington came from . . . an experienced administrator [who] said, "Bromley, you have to get away from this idea that you are supposed to transmit some information. Hearings in the Congress are pure theater—and you don't get any of the good lines."

Some members of the scientific community feel that the Presidential Science Advisor is their lobbyist in the White House. It bears emphasis that the moment the Advisor is perceived to be functioning as such or engaging in special pleading on behalf of the scientific community rather than as a member of the President's inner circle committed to implementing the President's goals, his effectiveness and the cooperation that he receives from the other senior staff members disappear.

Dick Darman is one of the brightest individuals with whom I have ever interacted. He and John Sununu each scored the maximum 1,600 points on their Scholastic Aptitude Tests at the end of secondary school; neither was at all reluctant to remind others of the fact. . . .

John Sununu had asked me to see him in his office for what I assumed would be a one-on-one meeting . . . . When I arrived . . . , however, I found Darman, [Michael] Boskin, [Roger] Porter, [Boyden] Gray and [Andrew] Card there as well. Darman, it developed, had requested the meeting, and he was obviously furious about something. Moreover, it soon became clear that the notebook that he had with him . . . contained copies of every article mentioning my name published anywhere since my arrival in Washington, as well as copies of all my congressional testimony and publications.

Darman's thesis was that I was getting favorable publicity at his expense . . . . It took months [for our relations] to get back to a superficially friendly basis.

In retrospect the [White House Conference on Science and Economic Research Related to Global Climate Change] was successful in achieving its primary goals. But at the time, the Bush Administration received major negative press treatment concerning the Conference: in large measure this reflected the fact that we had been forced, by political experts in the White House, to take on some public relations consultants whose experience had been with political conferences and conventions. The problem was that in a political convention the losers disappear after the convention and are expected to rally behind the winner; casting an international scientific conference in a winners-and-losers framework inevitably results in a group of very unhappy "losers" who do *not* disappear . . . but instead go home to foment all manner of national and international difficulties.

Shortly after I arrived in Washington a Bush-Gorbachev summit in Washington resulted in an invitation to a rather peculiar luncheon at the Soviet Embassy. . . . The stated intent was to invite the "intelligentsia" of the United States. But because Raisa Gorbachev was a fan of old Hollywood movies there was a somewhat strange guest list [including] Gregory Peck, Jane Fonda, Harry Belafonte, Henry Kissinger, John Kenneth Galbraith, Jesse Jackson, David Rockefeller. . . . As President and Mrs. Gorbachev were seated in front of a huge fireplace, the staff rolled an enormous bullet-proof plate-glass panel between them and the remaining guests. Gorbachev was much embarrassed and quickly got rid of the panel.

Too great a fraction of the scientific community [believes] that if they join in killing the funding for a large project like the SSC . . . the funding so liberated will find its way to areas of science of greater interest to them. Nothing could be more wrong . . . . When an investment in the future disappears, the funding does not go to other investments in the future but rather to satisfy immediate consumer demands.