

Chronicle of an Epidemic Foretold: A Response to the Wallaces

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ALTHOUGH THERE ARE SOME VOCAL EXTREMISTS — for whom AIDS is either inconsequential or apocalyptic — most AIDS prognostications are based on a thoughtful rationale and a defensible method. But whether their forecasts prove right, wrong, or moot, the process of considering the future is vital. Forecasts demand a response and are an integral part of the way in which society comes to grips with a problem. A case in point is the article in this issue of the *Milbank Quarterly* by Rodrick and Deborah Wallace, who hypothesize a trajectory for AIDS that merits our attention. Their article exemplifies one of two major species of forecast — prediction — that focuses on the long-term future. The other — projection — is more concerned with numbers (of infections, cases, or deaths) and plays a distinctly different role. A comparison of projection and prediction may provide some perspective on the answers various authors have offered to date.

Projection

Since the inception of the epidemic, investigators have tried to “extend the curve” into the future, using simple statistical models. An extrapolation now based on AIDS data compiled before 1981 and extending

through December 1984 (Centers for Disease Control and Prevention 1993) might elicit a laugh at the absurd results. A simple linear regression ($y = a + bx$) predicts 11,068 cases by the end of 1992; a simple exponential regression ($y = ae^{bx}$) predicts 9,311,202 (the provisional number of cases through 1992 is 284,840) (Centers for Disease Control and Prevention 1993). These results would not have been absurd in the early 1980s, however. A virulent and protean illness, a broadening clinical spectrum, a quixotic viral agent, powerful social ramifications—all conspired to augment the confusion and uncertainty.

Despite the uncertainty, a number of the empirical extrapolations in the early to mid 1980s were carefully thought through, fit the existing data well, and were not far off the future mark. Five different approaches, using quadratic, cubic, and logistic formulas and a variety of transformations (summarized by the General Accounting Office [1989]), produced estimates from 185,000 to 324,000 for the cumulative number of AIDS cases through 1991 (the actual number of cases reported by the Centers for Disease Control and Prevention [1993] through 1991 was 230,941) (table 1). Taylor (1989) reviewed a set of empirical extrapolations (exponential, logistic, and quadratic) and, using them as a group, derived an estimate of 192,000 to 224,000 cumulative cases through the end of 1991.

TABLE 1
Projections of Cumulative Number of AIDS Cases through 1991

Method	Number of models	Range of projection	Actual cases	Adjusted actual cases
Extrapolation	5	185,000–324,000		
Back calculation	2	84,000–295,000	230,941 ^c	272,510 ^d
Macro level ^a	4	143,000–750,000		
Micro level ^b	2	240,000–256,000		

^a Defined in the GAO report as models that simulate epidemiologic processes by addressing the individual-level events that constitute them.

^b Defined in the GAO report as models that simulate individual behaviors and estimate the size of groups at risk and the transmission probabilities.

^c From Centers for Disease Control and Prevention (1993).

^d From adjustment cited in Brookmeyer (1991, 6: table 1, note 1).

Source: Adapted from General Accounting Office (1989).

Though a reasonable first approach, extrapolation methods were blind to epidemiologic and biologic factors. In an effort to consider some of these factors, Brookmeyer and Gail (1986) described the method of back calculation that has become the standard for AIDS projections in recent years. In this approach, the number of AIDS cases in year t [$A(t)$] is based on estimates of seroprevalence [$H(t)$] and the density of persons with a given incubation period x [$I(x)$], using the following equation:

$$A(t) = \int_0^t I(x)H(t-x) dx$$

As estimates of seroprevalence and the distribution of incubation periods have improved, so have the projections for AIDS cases. In the four sets of projections issued to date by the Centers for Disease Control and Prevention (CDC) in collaboration with outside consultants, the estimates, originally on the high side, have dropped gradually to meet the reported numbers and adjusted actual estimates (U.S. Public Health Service 1986, 1988; Centers for Disease Control 1990; Centers for Disease Control and Prevention 1992) (table 2). The back-calculation method is apparently sensitive to directional short-term change, and Brookmeyer (1991) predicted that the current plateau would extend from 1991 through 1995. Thus, despite considerable controversy, researchers have developed a set of efficient tools for surveillance and planning.

Prediction

Both current reports and short- to intermediate-term projections suggest a leveling of incidence nationally, but a cogent description of the long-term trajectory remains elusive. There are competing thoughts on the matter—a sizable body of literature, in fact, has emerged in the past few years. Most attempts to describe the AIDS epidemic, or some portion thereof, have used compartment models (Gail and Brookmeyer 1988). The original concept divided a population into three groups: those susceptible, those infected, and those removed (either by death or by recovery with immunity) (Bailey 1975). The interaction of these groups (compartments) could be described using a set of partial differential equations. Early work in the transmission of gonorrhea used this ap-

1991 (cum)	270 (201-311)				230,941	272,510
1992	80 (13-119)	84	86	58-85	47-77	48,996
1992 (cum)	365 (205-440)	380				284,840
1993				61-98	47-85	-
1993 (cum)				390-480		-
1994					43-93	-
1994 (cum)					415-535	-

^a Scanning across permits comparison of all estimates made for a given year with the actual number of cases reported for that year (using provisional data as of May 1993). Scanning down provides the trajectory of cases estimated by each of the projections.

^b For the years estimated, "cum" signifies the estimate of cumulative number of cases through the end of the given year. The year alone indicates that the estimate is for the number of cases occurring within that calendar year. In most instances, the ranges provided are projections of the likely general area for the estimate, rather than true confidence limits.

^c *Sources for columns:* 1986: U.S. Public Health Service (1988); 1988: Centers for Disease Control (1990), using methods of extrapolation or back calculation as noted; 1990: Centers for Disease Control and Prevention (1992) for both columns. The left-hand column updates the 1988 estimates based on adjustment for underreporting and the right-hand column uses the method of back calculation; 1992: Brookmeyer (1991), using the method of back calculation; actual: Centers for Disease Control and Prevention (1993); adjusted actual: Brookmeyer (1991, 6: table 1, note 1), applying the undercount estimate of 85 percent to the actual reports.

proach to model the existence of “core” groups whose intense transmission was responsible for the majority of infections that occurred (Hethcote and Yorke 1984). Anderson, May, and their colleagues linked the compartment model approach to concepts of population ecology (May and Anderson 1987, 1988; Anderson and May 1988; Anderson et al. 1989). They modeled the interaction between groups as a function of the probability of transmission of HIV, the frequency with which members of the group changed sexual partners, and the duration of infectiousness. As Gail and Brookmeyer (1988) pointed out, such modeling does not permit quantitative projection, but does allow a detailed examination of transmission scenarios: the effect of altering parameters, the potential impact of interventions, and the ultimate demographic effects of uncontrolled spread of HIV (Anderson et al. 1991). Most scenarios predict rapid short-term growth, steady state in the long term (measured in decades), and ultimate population contraction.

A host of other compartment-based models, using a variety of statistical and computer techniques, has appeared in recent years. Many use sophisticated mathematical concepts to verify intuitive conclusions. Hyman and Stanley (1988), for example, conclude that random mixing of sexual partners leads to rapid exponential growth and saturation, whereas mixing of like with like leads to much slower epidemic growth in which those at lowest risk are still not infected after 40 years. Jacquez et al. (1988), with similar sophistication, demonstrate that spread of infection to members of low-risk compartments directly depends on the extent of their contact with members of high-risk compartments. Several of these models have focused specifically on drug use (Kaplan 1989; Peterson et al. 1990; Allard 1990); their results confirm that prediction of the progression of the epidemic is sensitive to which parameters are chosen. Although not inclusive, this brief review of predictive models points to an emerging pattern—lots of interesting ideas and thoughtful exploration, but a collective hedging of bets in the face of uncertain parameters. Few, if any, make an unqualified prediction.

Thus, projection seems to have been a satisfying exercise, with gradual, sustained improvement in short-term accuracy. Prediction has been more of a cautionary tale, perhaps because of the understandable scientific reluctance to overstate the case. Enormous energy and talent have been invested in defining the difficulties and in providing tentative conclusions about potential alternatives. The reluctance has merit, but it de-

prives us of a vigorous debate based on models and data, and leaves us vulnerable to a media debate based on conjecture and agenda.

An important aspect of the Wallaces' article is that they propose a trajectory and face squarely the possibility of being wrong. They claim that AIDS will spread to more affluent, noncentral areas from the decaying, inner-city epicenters. Using a considerable body of work to which they and collaborators have contributed, as their reference list indicates (Wallace 1991; Wallace and Fullilove 1991), they structure a straightforward argument: the inner cities have undergone systematic dissolution that has impaired or destroyed existing interpersonal and social networks. Such destruction, in the context of populations already marginalized and disadvantaged, has led to the metastasis of dangerous behavior. The inevitable interaction of other social networks with those of such an epicenter will lead to transmission of HIV. Spread of HIV (by any route, including heterosexual contact) will be a function of the ratio of propagation in the epicenters (high) to propagation in more affluent areas (low), of the starting level in the epicenters (high), and of the degree of interaction between the social networks (nonzero). (Perhaps the Wallaces are willing to take this stance because their fundamental thesis does not depend on parameters, although the timing of interaction between social groups may.)

Such a bold prediction may lend their work the appearance of diverging more sharply from previous efforts than is truly the case. In this current article, they restrict themselves to classic epidemic theory (Bailey 1975) and draw the same inferences that others have reported. For example, Jacquez and colleagues (1988) emphasize the importance of the particular pattern of contact mixing between low- and high-risk groups. These authors note that the rapidity of spread will be a function of the mixing pattern between (in the Wallaces' terminology) affluent suburban and disadvantaged inner-city groups. May and Anderson (1988), among others, offer a detailed consideration of how the various groups' interactions affect the reproductive rate (propagation of the epidemic). Although their terminology differs, many of the same concepts obtain in the Wallaces' work (see Wallace 1991). The Wallaces' thesis is also based to some extent on the gradual spread of heterosexually transmitted HIV in a non-drug-using community. Brookmeyer (1991), in predicting a plateau during the early 1990s, also foresaw a doubling in heterosexually transmitted infection. Increases in heterosexual transmission have al-

ready occurred (Holmes, Karon, and Kreiss 1990), although the specific connection of this transmission with the use of injectable drugs may require better delineation. Finally, the Wallaces' consideration of the role that social networks serve in HIV transmission has been a concern to other researchers (Peterson et al. 1990; Klovdahl et al. n.d.; Woodhouse et al. n.d.). A network approach to evaluating surveillance for HIV/AIDS indicates that AIDS is underestimated among whites and in nonepidemic areas such as the Midwest (Laumann et al. 1989), although the conclusions based on this model have been questioned on technical grounds (Berkelman et al. 1989).

The Wallaces may well be wrong. Significant inroads into more prosperous areas have been slow, and it seems likely that control efforts, biologic advances, and perhaps even a modicum of economic recovery will conspire to confine the epidemic. However, the proposition must be considered carefully and debated seriously. To gainsay the argument runs the risk of rejecting the confirmatory observations of others and of dismissing the geographic spread that has already occurred. It runs the risk of contravening an AIDS education program that has been addressed to the nation. Finally, rejecting this prediction out of hand may have a certain ironic expediency. If HIV does not spread to affluent suburban neighborhoods, are we relieved of the burden of reconstituting our inner cities?

The real purpose of prediction is to avoid such irony by invigorating the debate and forging an agenda that helps those at greatest risk and, by natural extension, those at lesser risk. In truth, it does not ultimately matter that the epidemic is correctly foretold, but that it is foreclosed.

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