

Chapter 5

Understanding the United States AIDS Epidemic: A Modeler's Odyssey

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5.1 Introduction

This chapter presents a time-indexed investigation of the author's fifteen years of work in studying the AIDS epidemic and attempting to come up with strategies for its defacilitation. This saga of modeling the AIDS epidemic also demonstrates how one poses and solves a problem in a continually changing data environment. Early on in this odyssey (around 1983), a differential equation model was developed based on currently available data to see what might have facilitated the AIDS endemic becoming an epidemic. This model indicated that a "core" high activity subpopulation within the gay community could be the cause — not as a result of increasing total aggregate contacts, but by virtue of their very high contact rate. Such skewed contact rates have the effect of keeping aggregate contacts constant, yet driving the epidemic the same way as if aggregate contacts had more than doubled.

Time passed, and when such results were presented, they were implicitly accepted by professional audiences. However, attempts to instigate control measures in the city of Houston met with political resistance and lack of action. This points out another important (and sobering) lesson of practical modeling: that a convincing mathematical model need not lead to policy change and action.

In the 1990s, joint work with a graduate student produced a much

more complicated model for dealing with the mature epidemic. This model suggested that there was little to be gained in shutting down high contact establishments once the proportion of infectives reached 40%.

In 1998, a really fine data set was obtained from the World Health Organization (WHO). These data showed that there were modest decreases in the incidence of new AIDS cases throughout the First World. A kinetic model based on the data gave the amazing result that the piecewise exponential growth rate was the same for all American and European First World countries. This occurred, in spite of the fact that incidences per 100,000 varied greatly from country to country (by a factor of ten). This led to another model, giving the strong indication that it is cheap travel to and from the USA which drives the epidemic in Canada and Europe.

5.2 *Prelude: The Postwar Polio Epidemic*

Effective immunizations against many of the killing diseases of the 19th century, plus antibiotics massively utilized during World War II, gave the promise of the end to life-threatening contagion in the United States. The killers of the future would be those largely associated with the aging process, such as cancer, stroke, and heart attack.

However, in the postwar years, polio, which already had stricken some (including President Roosevelt), became a highly visible scourge in a number of American cities, particularly in the South, particularly among the young. In 1952, over 55,000 cases were reported. Mortality rates in America, due to good care, had by that time dropped to well under 10%. Nonetheless, the spectacle of children confined to wheelchairs or iron lungs was a disturbing one.

This was in the years before the emigration of the middle classes to suburbia and most schools tended to have representation from a wide range of socioeconomic groups. Incidence rates were the highest in the summers, when the schools were closed. But, at the intuitive level, it was clear that polio was a disease predominantly of school age children, and that there was a fair amount of clustering of cases. Although the causative agent had not been isolated, there was little doubt that it was a virus, that it favored young hosts, that the throat was the likely pathway, and that transmission was greatest in the hot weather.

In such a situation, it might appear that a prudent public health policy would be to discourage summer gatherings of children, particularly in confined indoor settings or in swimming pools. Such an inference

might well be put down as a prejudice of causation where none existed. Indeed, this was the era of the kiddie matinee and new municipal swimming facilities given by city governments to their citizens in celebration of a perceived affluence following the War. Some parents did, to the displeasure of their children, attempt to deprive them of matinees and swimming excursions; but such were in the distinct minority. From time to time, city officials would take such steps as shutting down municipal swimming pools, but this was unusual and always temporary. There was a large economic constituency for matinees and swimming pools. The constituency for shutting them down was acting on intuition and without business support. The results were that the movies and pools generally stayed open all summer. The epidemic flourished.

There was a great deal of expectation that “the cavalry will soon ride to the rescue” in the form of an expected vaccine against the disease. In 1955, the Salk vaccine¹ did appear, and new polio cases, for the United States, became a thing of the past. Of course, a residual population of tens of thousands of Americans remained, crippled by polio.

There was very little in the way of a postmortem examination about how effective public health policy had been in managing the American polio epidemic. In fact, there had been essentially no proactive policy at all. But two effective anti-polio vaccines (Salk and then Sabin) seemed to have brought everything right in the end. If there were serious efforts to learn from the mistakes in management of the American polio epidemic, this author has not seen them.

Polio had, apparently, been simply a bump in the road toward a time in which life-threatening contagious diseases in America would be a thing of the past. However, having spent my childhood in Memphis, Tennessee (one of the epicenters of the postwar polio epidemic), that epidemic was something I would never forget. My parents were among the number of those who forbade matinees and swimming pools to their children. But among my childhood friends there were several who died from polio, and many others crippled by it.

5.3 *AIDS: A New Epidemic for America*

In 1983, I was investigating the common practice of using stochastic models in dealing with various aspects of diseases. When attempting to

¹In 1999, evidence started to appear that contamination of the Salk vaccine by a monkey virus, not unrelated to HIV, was causing many of the recipients of the Salk vaccine to develop a variety of cancers, possibly due to a destruction of parts of their immune system.

model the progression of cancer within an individual, a good case could be made for going stochastic. For example, one matter of concern with solid tumors is whether the primary tumor throws off a metastasis before it has been removed surgically. Whether it has or has not will largely determine whether surgical removal of the primary tumor has cured the patient. Such a phenomenon needs to be modeled stochastically.

On the other hand, when modeling the progression of a contagious disease through a population, the common current practice of using a stochastic model and then finding, for example, the moment generating function of the number $Y(t)$ of infectives seems unnecessarily complicated, particularly if, at the end of the day, one decides simply to extract $E(Y(t))$, the expected number of infectives. Moreover, any sociological data, if available, are likely to be in terms of aggregate information, such as the average number of contacts per day.

I had decided to write a paper giving examples where deterministic modeling would probably be appropriate. I selected the AIDS epidemic because it was current news, with a few hundred cases reported nationally. Although reporting at the time tended to downplay the seriousness of the epidemic (and, of course, the name was pointedly innocuous, the same as an appetite suppressant of the times), there was a palpable undercurrent of horror in the medical community. It looked like a study that might be important.

Even at the very early stage of an observed United States AIDS epidemic, several matters appeared clear to me:

- The disease favored the homosexual male community and outbreaks seemed most noticeable in areas with sociologically identifiable gay communities.
- The disease was also killing (generally rather quickly) people with acute hemophilia.
- Given the virologist's maxim that there are no new diseases, AIDS, in the USA, had been identified starting around 1980 because of some sociological change. A disease endemic under earlier norms, it had blossomed into an epidemic due to a change in society.

At the time, which was before the HIV virus had been isolated and identified, there was a great deal of commentary both in the popular press and in the medical literature (including that of the Centers for Disease Control) to the effect that AIDS was a new disease. Those statements were not only putatively false, but were also potentially harmful. First of all, from a practical virological standpoint, a new disease might

have as a practical implication genetic engineering by a hostile foreign power. This was a time of high tension in the Cold War, and such an allegation had the potential for causing serious ramifications at the level of national defense.

Secondly, treating an unknown disease as a new disease essentially removes the possibility of stopping the epidemic sociologically by simply seeking out and removing (or lessening) the cause(s) that resulted in the endemic being driven over the epidemiological threshold.

For example, if somehow a disease (say, the Lunar Pox) has been introduced from the moon via the return of moon rocks by American astronauts, that is an entirely different matter than, say, a mysterious outbreak of dysentery in St. Louis. For dysentery in St. Louis, we check food and water supplies, and quickly look for “the usual suspects” — unrefrigerated meat, leakage of toxins into the water supply, etc. Given proper resources, eliminating the epidemic should be straightforward.

For the Lunar Pox, there are no usual suspects. We cannot, by reverting to some sociological *status quo ante*, solve our problem. We can only look for a bacterium or virus and try for a cure or vaccine. The age-old way of eliminating an epidemic by sociological means is difficult — perhaps impossible.

In 1982, it was already clear that the United States public health establishment was essentially treating AIDS as though it were the Lunar Pox. The epidemic was at levels hardly worthy of the name in Western Europe, but it was growing. Each of the European countries was following classical sociological protocols for dealing with a venereal disease. These all involved some measure of defacilitating contacts between infectives and susceptibles. The French demanded bright lighting in gay “make-out” areas. Periodic arrests of transvestite prostitutes on the Bois de Bologne were widely publicized. The Swedes took much more draconian steps — mild in comparison with those of the Cubans. The Americans took no significant sociological steps at all.

However, as though following the Lunar Pox strategy, the Americans outdid the rest of the world in money thrown at research related to AIDS. Some of this was spent on isolating the unknown virus. However, it was the French, spending pennies to the Americans’ dollars, at the Pasteur Institute (financed largely by a legacy from the late Duke and Duchess of Windsor) who first isolated HIV. In the intervening fifteen years since isolation of the virus, no effective vaccine or cure has been produced.

5.4 Why An AIDS Epidemic in America?

Although the popular press in the early 1980s talked of AIDS as being a new disease, as noted above, prudence and experience indicated that it was not. Just as new species of animals have not been noted during human history, the odds for a sudden appearance (absent genetic engineering) of a new virus are not good. My own discussions with pathologists with some years of experience gave anecdotal cases of young Anglo males who had presented with Kaposi's sarcoma at times going back to early days in the pathologists' careers. This pathology, previously seldom seen in persons of Northern European extraction, now widely associated with AIDS, was at the time simply noted as isolated and unexplained. Indeed, a few years after the discovery of the HIV virus, HIV was discovered in decades old refrigerated human blood samples from both Africa and America.

Although it was clear that AIDS was not a new disease, as an epidemic it had never been recorded. Because some of the early cases were from the Congo, there was an assumption by many that the disease might have its origins there. Clearly, record keeping in the Congo was not and is not very good. But Belgian colonial troops had been located in that region for many years. Any venereal disease acquired in the Congo should have been vectored into Europe in the 19th century. But no AIDS-like disease had been noted. It would appear, then, that AIDS was not contracted easily as is the case, say, with syphilis. Somehow, the appearance of AIDS as an epidemic in the 1980s, and not previously, might be connected with higher rates of promiscuous sexual activity made possible by the relative affluence of the times.

Then there was the matter of the selective appearance of AIDS in the American homosexual community. If the disease required virus in some quantity for effective transmission (the swift progression of the disease in hemophiliacs plus the lack of notice of AIDS in earlier times gave clues that such might be the case), then the profiles in Figures 5.1 and 5.2 give some idea why the epidemic seemed to be centered in the American homosexual community. If passive to active transmission is much less likely than active to passive, then clearly the homosexual transmission patterns facilitate the disease more than the heterosexual ones.

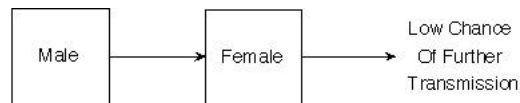


FIGURE 5.1 Heterosexual transmission of AIDS

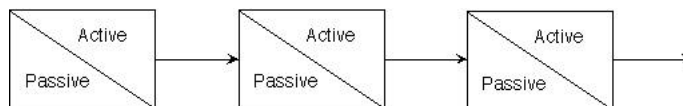


FIGURE 5.2 Homosexual transmission of AIDS

One important consideration that seemed to have escaped attention was the appearance of the epidemic in 1980 instead of ten years earlier. Gay lifestyles had begun to be tolerated by law enforcement authorities in the major urban centers of America by the late 1960s. If homosexuality was the facilitating behavior of the epidemic, then why no epidemic before 1980? Of course, believers in the “new disease” theory could simply claim that the causative agent was not present until around 1980. In the popular history of the early American AIDS epidemic, *And the Band Played On*, Randy Shilts points at a gay flight attendant from Quebec as a candidate for “patient zero.” But this “Lunar Pox” theory was not a position that any responsible epidemiologist could take (and, indeed, as pointed out earlier, later investigations revealed HIV samples in human blood going back into the 1940s).

What accounts for the significant time differential between civil tolerance of homosexual behavior prior to 1970 and the appearance of the AIDS epidemic in the 1980s? Were there some other sociological changes that had taken place in the late 1970s that might have driven the endemic over the epidemiological threshold?

It should be noted that in 1983 data were skimpy and incomplete. As is frequently the case with epidemics, decisions need to be made at the early stages when one needs to work on the basis of skimpy data, analogy with other historical epidemics, and a model constructed on the best information available.

I remember in 1983 thinking back to the earlier American polio epidemic that had produced little in the way of sociological intervention and less in the way of models to explain the progress of the disease. Although polio epidemics had been noted for some years (the first noticed epidemic occurred around the time of World War I in Stockholm), the American public health service had indeed treated it like the “Lunar Pox.” That is, they discarded sociological intervention based on past experience of transmission pathways and relied on the appearance of vaccines at any moment. They had been somewhat lucky, since Salk started testing his vaccine in 1952 (certainly they were luckier than the thousands who had died and the tens of thousands who had been permanently crippled). But basing policy on hope and virological research was a dangerous policy (how dangerous we are still learning as we face the prospect of one million American dead from AIDS).

Although some evangelical clergymen inveighed against the epidemic as divine retribution on homosexuals, the function of epidemiologists is to use their God-given wits to stop epidemics. In 1983, virtually nothing was being done except to wait for virological miracles.

One possible candidate was the turning of a blind eye by authorities to the gay bathhouses that started in the late 1970s. These were places where gays could engage in high frequency anonymous sexual contact. By the late 1970s they were allowed to operate without regulation in the major metropolitan centers of America. My initial intuition was that the key was the total average contact rate among the target population. Was the marginal increase in the contact rate facilitated by the bathhouses sufficient to drive the endemic across the epidemiological threshold? It did not seem likely. Reports were that most gays seldom (many, never) frequented the bathhouses.

But perhaps my intuitions were wrong. Perhaps it was not only the total average contact rate that was important, but a skewing of contact rates, with the presence of a high activity subpopulation (the bathhouse customers) somehow driving the epidemic. It was worth a modeling try.

The model developed in [2] considered the situation in which there are two subpopulations: the majority, less sexually active, and a minority with greater activity than that of the majority. We use the subscript “1” to denote the majority portion of the target (gay) population, and the subscript “2” to denote the minority portion. The latter subpopulation, constituting fraction p of the target population, will be taken to have a contact rate τ times the rate k of the majority subpopulation. The following differential equations model the growth of the number of susceptibles X_i and infectives Y_i in subpopulation i ($i = 1, 2$).

$$\begin{aligned}\frac{dY_1}{dt} &= \frac{k\alpha X_1(Y_1 + \tau Y_2)}{X_1 + Y_1 + \tau(Y_2 + X_2)} - (\gamma + \mu)Y_1 \\ \frac{dY_2}{dt} &= \frac{k\alpha\tau X_2(Y_1 + \tau Y_2)}{X_1 + Y_1 + \tau(Y_2 + X_2)} - (\gamma + \mu)Y_2 \\ \frac{dX_1}{dt} &= -\frac{k\alpha X_1(Y_1 + \tau Y_2)}{X_1 + Y_1 + \tau(Y_2 + X_2)} + (1 - p)\lambda - \mu X_1 \\ \frac{dX_2}{dt} &= -\frac{k\alpha\tau X_2(Y_1 + \tau Y_2)}{X_1 + Y_1 + \tau(Y_2 + X_2)} + p\lambda - \mu X_2,\end{aligned}\tag{5.1}$$

where

k = number of contacts per month,
 α = probability of contact causing AIDS,

Table 5.1 Extrapolated AIDS cases: $k\alpha = 0.05, \tau = 1$

year	cumulative deaths	fraction infective
1	1751	0.00034
2	2650	0.00018
3	3112	0.00009
4	3349	0.00005
5	3571	0.00002
10	3594	0.000001

Table 5.2 Extrapolated AIDS cases: $k\alpha = 0.02, \tau = 16, p = 0.10$

year	cumulative deaths	fraction infective
1	2,184	0.0007
2	6,536	0.0020
3	20,583	0.0067
4	64,157	0.0197
5	170,030	0.0421
10	855,839	0.0229
15	1,056,571	0.0122
20	1,269,362	0.0182

λ = immigration rate into the population,
 μ = emigration rate from the population,
 γ = marginal emigration rate from the population due
to sickness and death.

In [2], it was noted that if we started with 1,000 infectives in a target population with $k\alpha = 0.05, \tau = 1$, a susceptible population of 3,000,000 and the best guesses then available ($\mu = 1/(15 \times 12) = 0.00556, \gamma = 0.1, \lambda = 16,666$) for the other parameters, the disease advanced as shown in Table 5.1.

Next, a situation was considered in which the overall contact rate was the same as in Table 5.1, but it was skewed with the more sexually active subpopulation 2 (of size 10%) having contact rates 16 times those of the less active population. Even though the overall average contact rate in Table 5.1 and Table 5.2 is the same ($(k\alpha)_{\text{overall}} = 0.05$), the situation is dramatically different in the two cases. Here, it seemed, was a *prima facie* explanation as to how AIDS was pushed over the threshold to a full blown epidemic in the United States: a small but sexually very active subpopulation.

I note that nothing more sophisticated than some numerical quadrature was required to obtain the results in these tables. In the ensuing ar-

guments concerning why AIDS became an epidemic in the United States, everything beyond the rather simple deterministic model (5.1) will be, essentially, frosting on the cake. This was the way things stood in 1984 when I presented the paper at the summer meetings of the Society for Computer Simulation in Vancouver. It hardly created a stir among the mainly pharmacokinetic audience who attended the talk. And, frankly, at the time I did not think too much about it because I supposed that probably even as the paper was being written, the “powers that be” were shutting down the bathhouses. The deaths at the time were numbered in the hundreds, and I did not suppose that things would be allowed to proceed much longer without sociological intervention. Unfortunately, I was mistaken.

In November 1986, the First International Conference on Population Dynamics took place at the University of Mississippi where there were some of the best biomathematical modelers from Europe and the United States. I presented my AIDS results [4], somewhat updated, at a plenary session. By this time, I was already alarmed by the progress of the disease (over 40,000 cases diagnosed and the bathhouses still open). The bottom line of the talk had become more shrill: namely, every month delayed in shutting down the bathhouses in the United States would result in thousands of deaths. The reaction of the audience this time was concern, partly because the prognosis seemed rather chilling, partly because the argument was simple to follow and seemed to lack holes, and partly because it was clear that something was pretty much the matter if things had gone so far off track.

After the talk, the well-known Polish probabilist Robert Bartoszyński, with whom I had carried out a lengthy modeling investigation of breast cancer and melanoma (at the Curie-Sklodowska Institute in Poland and at Rice), took me aside and asked whether I did not feel unsafe making such claims. “Who,” I asked, “will these claims make unhappy?” “The homosexuals,” said Bartoszyński. “No, Robert,” I said, “I am trying to save their lives. It will be the public health establishment who will be offended.”

And so it has been in the intervening years. I have given AIDS talks before audiences with significant gay attendance in San Francisco, Houston, and other locales without any gay person expressing offense. Indeed, in his 1997 book [1], Gabriel Rotello, one of the leaders of the American gay community, not only acknowledges the validity of my model but also constructs a survival plan for gay society in which the bathhouses have no place.

5.5 A More Detailed Look at the Model

A threshold investigation of the two-activity population model (5.1) is appropriate here. Even today, let alone in the mid-1980s, there was no chance that one would have reliable estimates for all the parameters k , α , γ , μ , λ , p , τ . Happily, one of the techniques sometimes available to the modeler is the opportunity to express the problem in such a form that most of the parameters will cancel. For the present case, we will attempt to determine the $k\alpha$ value necessary to sustain the epidemic when the number of infectives is very small. For this epidemic in its early stages one can manage to get a picture of the bathhouse effect using only a few parameters: namely, the proportion p of the target population which is sexually very active and the activity multiplier τ .

For $Y_1 = Y_2 = 0$ the equilibrium values for X_1 and X_2 are $(1-p)(\lambda/\mu)$ and $p(\lambda/\mu)$, respectively. Expanding the right-hand sides of (5.1) in a Maclaurin series, we have (using lower case symbols for the perturbations from 0)

$$\begin{aligned}\frac{dy_1}{dt} &= \left[\frac{k\alpha(1-p)}{1-p+\tau p} - (\gamma + \mu) \right] y_1 + \frac{k\alpha(1-p)\tau}{1-p+\tau p} y_2 \\ \frac{dy_2}{dt} &= \frac{k\alpha\tau p}{1-p+\tau p} y_1 + \left[\frac{k\alpha\tau^2 p}{1-p+\tau p} - (\gamma + \mu) \right] y_2.\end{aligned}$$

Summing then gives

$$\frac{dy_1}{dt} + \frac{dy_2}{dt} = [k\alpha - (\gamma + \mu)] y_1 + [k\alpha\tau - (\gamma + \mu)] y_2. \quad (5.2)$$

In the early stages of the epidemic,

$$\frac{dy_1/dt}{dy_2/dt} = \frac{(1-p)}{p\tau}.$$

That is to say, the new infectives will be generated proportionately to their relative numerosity in the initial susceptible pool times their relative activity levels. So, assuming a negligible number of initial infectives, we have

$$y_1 = \frac{(1-p)}{p\tau} y_2.$$

Substituting in (5.2) shows that for the epidemic to be sustained, we must have

$$k\alpha > \frac{(1-p+\tau p)}{1-p+\tau^2 p} (\gamma + \mu). \quad (5.3)$$

Accordingly we define the *heterogenous threshold* via

$$k_{\text{het}}\alpha = \frac{(1-p+\tau p)}{1-p+\tau^2 p} (\gamma + \mu).$$

Now, in the homogeneous contact case (i.e., $\tau = 1$), we note that for the epidemic to be sustained the following condition must hold:

$$k\alpha > \gamma + \mu.$$

Accordingly we define the *homogeneous threshold* by

$$k_{\text{hom}}\alpha = \gamma + \mu.$$

The heterogeneous contact case with k_{het} has the average contact rate

$$k_{\text{ave}}\alpha = p\tau(k_{\text{het}}\alpha) + (1-p)(k_{\text{het}}\alpha) = \frac{(1-p+\tau p)^2}{1-p+\tau^2 p}(\gamma + \mu).$$

Dividing the sustaining value $k_{\text{hom}}\alpha$ by the sustaining value $k_{\text{ave}}\alpha$ for the heterogeneous contact case then produces

$$Q = \frac{1-p+\tau^2 p}{(1-p+\tau p)^2}.$$

Notice that we have been able here to reduce the parameters necessary for consideration from seven to two. This is fairly typical for model-based approaches: the dimensionality of the parameter space may be reducible in answering specific questions. Figure 5.3 shows a plot of this “enhancement factor” Q as a function of τ . Note that the addition of heterogeneity to the transmission picture has roughly the same effect as if all members of the target population had more than doubled their contact rate. Remember that the picture has been corrected to discount any increase in the overall contact rate which occurred as a result of adding heterogeneity. In other words, the enhancement factor is totally due to heterogeneity. It is this heterogeneity effect which I have maintained (since 1984) to be the cause of AIDS getting over the threshold of sustainability in the United States.

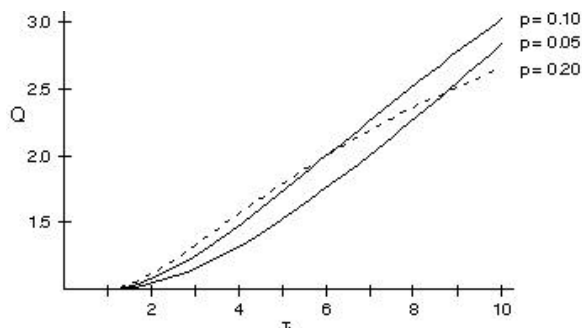


FIGURE 5.3 Effect of a high activity subpopulation

If this all still seems counterintuitive, then let us consider the following argument at the level of one individual infective. Suppose, first of all, that the disease is such that one contact changes a susceptible to an infective. Then let us suppose we have an infective who is going to engage in five contacts. What number of susceptibles (assuming equal mixing) will give the highest expected number of conversions of susceptibles to infectives? Note that if the number of susceptibles is small, the expectation will be lessened by the “overkill effect”: i.e., there is the danger that some of the contacts will be “wasted” by being applied to an individual already infected by one of the other five contacts. Clearly, here the optimal value for the size N of the susceptible pool is infinity, for then the expected number of conversions from susceptible to infective $E(\mathcal{I} | N = \infty)$ is five.

Now let us change the situation to one in which two contacts, rather than one, are required to change a susceptible to an infective. We will still assume a total of five contacts. Clearly, if $N = 1$ then the expected number of conversions is $E = 1$; there has been wastage due to overkill. Next, let us assume the number of susceptibles has grown to $N = 2$. Then the probability of two new infectives is given by

$$P(2 | N = 2) = \sum_{j=2}^3 \binom{5}{j} \left(\frac{1}{2}\right)^5 = \frac{20}{32}.$$

The probability of only one new infective is $1 - P(2 | N = 2)$. Thus the expected number of new infectives is

$$E(\mathcal{I} | N = 2) = 2 \left(\frac{20}{32}\right) + 1 \left(\frac{12}{32}\right) = 1.625.$$

Now when there are $N = 3$ susceptibles, the contact configurations leading to two new infectives are of the type $(2, 2, 1)$ and $(3, 2, 0)$. All other configurations will produce only one new infective. So the probability of two new infectives is given by

$$P(2 | N = 3) = \binom{3}{1} \frac{5!}{2!2!1!} \left(\frac{1}{3}\right)^5 + \binom{3}{1} \binom{2}{1} \frac{5!}{3!2!} \left(\frac{1}{3}\right)^5 = \frac{150}{243}$$

and the expected number of new infectives is

$$E(\mathcal{I} | N = 3) = 2 \left(\frac{150}{243}\right) + 1 \left(\frac{93}{243}\right) = 1.617.$$

Further calculations give $E(\mathcal{I} | N = 4) = 1.469$, $E(\mathcal{I} | N = 5) = 1.314$. For very large N , $E(\mathcal{I})$ is of order $1/N$. Apparently, for the situation where there are a total of five contacts, the value of the number in the

susceptible pool that maximizes the total number of new infectives from the one original infective is $N = 2$, not ∞ . Obviously, we are oversimplifying, since we stop after only the contacts of the original infective. The situation is much more complicated here, since an epidemic is created by the new infectives infecting others and so on. As well, there is the matter of a distribution of the number of contacts required to give the disease. We have in our main model (5.1) avoided the complexities of branching process modeling by going deterministic. The argument above is given to present an intuitive feel as to the facilitating potential of a high contact core in driving a disease over the threshold of sustainability.

In the case of AIDS, the average number of contacts required to break down the immune system sufficiently to cause the person ultimately to get AIDS is much larger than two. The obvious implication is that a great facilitator for the epidemic being sustained is the presence of a subpopulation of susceptibles whose members have many contacts. In the simple example above, we note that even if the total number of contacts were precisely five, from a standpoint of facilitating the epidemic, it would be best to concentrate the contacts into a small pool of susceptibles. In other words, if the total number of contacts is fixed at some level, it is best to start the epidemic by concentrating the contacts within a small subpopulation. Perhaps the analogy to starting a fire, not by dropping a match onto a pile of logs, but rather onto some kindling beneath the logs, is helpful.

5.6 Forays into the Public Policy Arena

The senior Professor of Pathology at the Baylor College of Medicine in the 1980s was Raymond McBride. McBride had been one of the pioneers in immunosuppression for organ transplantation and was the Chief of Pathology Services for the Harris County (Houston) Medical District. Distressed to see the ravages of AIDS on autopsied victims, he was quite keen to have municipal authorities act to close down the bathhouses. He and I co-authored a front page op-ed piece for the *Houston Chronicle* entitled “Close Houston’s Gay Bathhouses” [7], taking care not to mention the names and addresses of the two major offending establishments lest some vigilante act be taken against them. Hardly a ripple of interest, even though Houston, with less than one-tenth the population of Canada, had more AIDS cases than that entire country. We tried to motivate members of the City Council. When interviewed by a reporter, the office of the Councilman in whose district these two bathhouses were situated shrugged the whole matter off by asking, “What’s a bathhouse”? I served on the American Statistical Association’s Ad Hoc

Committee on AIDS from its inception until its demise. But our mandate was never allowed to extend to modeling. Only the methodology of data analysis was permitted. Nor were we allowed, as a committee, to compare America's AIDS incidence with that from other countries.

The situation was not unlike that of the earlier polio epidemic. There were specific interests for not addressing the bathhouse issue, but there was only a nonspecific general interest for addressing it.

Although I myself had no experience with the blood-testing issue, it should be noted that early on in the epidemic, long before the discovery of HIV, it was known that over 90% of the persons with AIDS tested positive to antibodies against Hepatitis-B. For many months, the major blood collecting agencies in the United States resisted employing the surrogate Hepatitis test for contaminated blood. The result was rampant death amongst hemophiliacs and significant AIDS infections among persons requiring large amounts of blood products for surgery.

The statistician/economist/sociologist Vilfredo Pareto remarked that Aristotle had made one mistake when he presented to the world the system of logical thinking. The mistake was Aristotle's assumption that once humankind understood logical consistency, actions, including public policy, would be made on the basis of reason. Pareto noted that the historical record showed otherwise. The more important the decision, Pareto noted, the less likely was logical inference based on facts — a significant concern in decision making. So, it has unfortunately been with policy concerning AIDS.

5.7 *Modeling the Mature Epidemic*

In the United States, the AIDS epidemic crossed the threshold of viability long ago. Consequently, we should investigate the dynamics of the mature epidemic. Unfortunately, we then lose the ability to disregard five of the seven parameters and must content ourselves with picking reasonable values for those parameters. A detailed analysis is given in [6]. In the following, we will make certain ballpark assumptions about some of the underlying parameters. Suppose the contact rate before the possible bathhouse closings is given by

$$(k\alpha)_{\text{overall}} = (1 - p + \tau p)(\gamma + \mu). \quad (5.4)$$

This represents an average contact rate for the two-activity model. We shall take $\mu = 1/(180 \text{ months})$ and $\lambda = 16,666$ per month. (We are assuming a target population, absent the epidemic, of roughly 3,000,000.) For a given fraction π of infectives in the target population, we ask what

is the ratio of contact rates causing elimination of the epidemic for the closings case divided by that without closings.

Figure 5.4 shows the ratio of contact rates (with closings relative to without closings) as a function of π for $p = 0.1$ and $\gamma = \frac{1}{60}$. It would appear that as long as the proportion of infectives π is no greater than 40% of the target population, there would be a significant benefit from bathhouse closings. The benefit decreases once we get to 40%. However, because of the fact that there appears to be a continuing influx of new entrants into the susceptible pool, there is good reason to close these establishments. Generally, restoring the sociological *status quo ante* is an effective means of stopping an epidemic; often this is difficult to achieve. Closing the bathhouses continues to be an appropriate action, even though a less effective one than if it had been taken early on in the history of the epidemic.

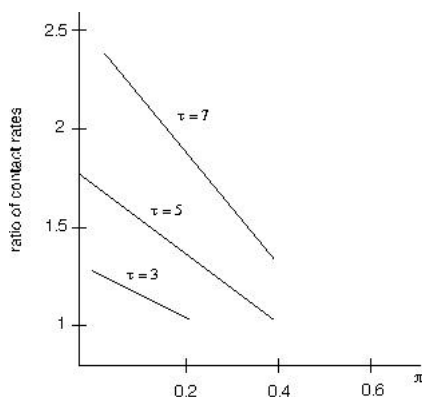


FIGURE 5.4 Effect of bathhouse closings in a mature epidemic

Next, we look at the possible effects on the AIDS epidemic of administering a drug, such as AZT, to the entire infective population. Obviously, infectives who die shortly after contracting a contagious disease represent less of an enhancement to the viability of an epidemic than those who live a long time in the infective state. In the case of AIDS, it is probably unreasonable to assume that those who, by the use of medication, increase their T cell count to an extent where apparently normal health has returned, will decide to assume a chaste life style for the rest of their lives. We shall assume that the drug increases life expectancy by two years. Figure 5.5 demonstrates the change in the percent infective if the drug also increases the period of infectivity by two years for various proportions π of infective at the time that the drug is administered. The curves plot the ratio of the proportion infective using

AZT to the proportion infective if AZT is not used (with $\gamma = \frac{1}{60}$) and they asymptote to $1.4 = 84/60$, as should be the case. The greater pool of infectives in the target population can, under certain circumstances, create a kind of “Typhoid Mary” effect, where long-lived infectives wander around spreading the disease. Clearly, it should be the policy of health care professionals to help extend the time of quality life for each patient treated. However, it is hardly responsible to fail to realize that, by so doing, in the case of AIDS, there is an obligation of the treated infective to take steps to ensure that he does not transmit the disease to susceptibles. To the extent that this is not the case, the highly laudable use of AZT to improve the length and quality of life for AIDS victims is probably increasing the number of deaths from AIDS.

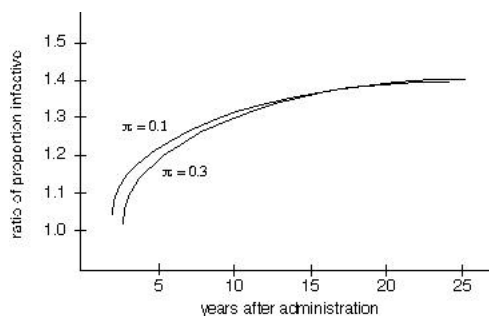


FIGURE 5.5 AZT effect on sustaining an AIDS epidemic

5.8 AIDS as a Facilitator of Other Epidemics

In 1994 Webster West [9] completed a doctoral dissertation attempting to see to what extent AIDS could enhance the spread of tuberculosis in America. Since we are primarily concerned here with the spread of AIDS itself, we shall not dwell very long on the tuberculosis adjuvancy issue. The reader is referred to relevant papers elsewhere [11, 10].

West did discover that if one used stochastic process models and then took the mean trace, one obtained the same results as those obtained simply by using deterministic differential equation models. In the United States, since the Second World War at least, tuberculosis has been a cause of death mainly of the elderly (for example, Mrs. Eleanor Roosevelt died of it). Tuberculosis is carried by the air, and its epidemiological progression is enhanced by infected persons who are well enough to walk around in elevators, offices, etc. When tuberculosis is confined to elderly persons, essentially not moving freely about, it is largely self-contained. But HIV infected persons are generally young, and generally employed,

at least before the latter stages of full blown AIDS.

West discovered that the result of AIDS facilitating tuberculosis was likely to be only a few hundred additional deaths per year. His model further revealed that modest resources expended in the early treatment of persons infected with tuberculosis could bring even these relatively modest numbers down.

5.9 *Comparisons with First World Countries*

As noted in Section 5.3, the position of other developed countries toward defacilitating contacts between infectives and susceptibles was quite different from that in the United States. In a very real sense, these other countries can be used as a “control” when examining the epidemic in the United States. Good data for new cases did not become easier and easier to obtain as the epidemic progressed. Whereas in the earlier time span of the epidemic fairly good data for all First World countries could be obtained via “gopher” sites, increasingly it became more and more disconnected as data bases supposedly moved to the Internet. The reality was that the information on the gopher sites stayed in place but was not brought up to date, while data on the Internet appeared temporally disconnected. Great patience was required to follow a group of countries over a period of time, and because of holes in the data, it was not at all clear whether anything but snippet comparisons could be made. I published one of these at a conference in 1995 [5], but the data available to me at the time gave only suggestions of what was happening. There seemed to be something important going on that went to the issue of the United States being a source of infection for other First World countries.

I kept sending out queries to the Centers for Disease Control and the World Health Organization (WHO), but without much success. Finally, in early 1998, Ms. Rachel Mackenzie of the WHO contacted me and provided me, not with a URL, but with the data itself, which was in the hands of the Working Group on Global HIV/AIDS, and STD Surveillance which is a joint Working Group between WHO and UNAIDS. I wish to acknowledge my gratitude to Ms. Mackenzie and her colleagues for allowing me to use their data base.

Figure 5.6 shows the staggering differences in cumulative number of AIDS cases between the United States and France (FR), Denmark (DK), the Netherlands (NL), Canada (CAN), and the United Kingdom (UK). The pool of infectives in the USA dwarfs those of the other First World countries. Whenever I would bring up the enormous differential between the AIDS rate in the United States and those in Europe, my

European colleagues would generally attribute all this to a time lag effect. Somehow the United States had a head start on AIDS, but in time the European countries would catch up. If other First World countries were lagging the USA, then one would expect some sort of variation in new AIDS cases such as that depicted in Figure 5.7. However, Figure 5.8 demonstrates that the time lagging hypothesis is not supported by the data. No other First World country is catching up to the USA. Moreover, a downturn in new case rates is observable in all the countries shown.

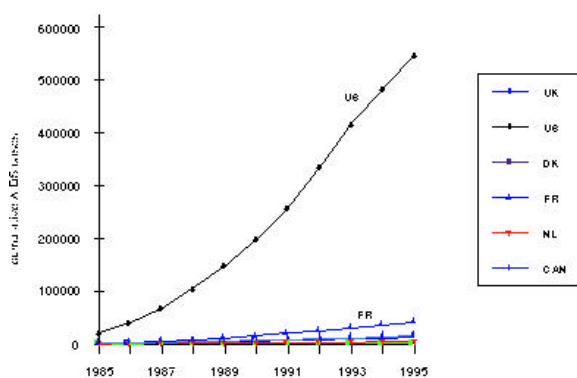


FIGURE 5.6 Cumulative AIDS cases 1985–1995

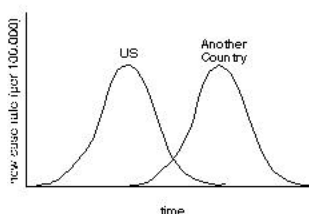


FIGURE 5.7 A time-lagged scenario

Further insight is provided by Figure 5.9, in which we divide the annual incidence of AIDS per 100,000 in the USA by that for various other First World countries. Note the relative constancy of the new case ratio across the years for each country when compared to the USA. Thus, for the United Kingdom, it is around 9, for Denmark 6, etc. It is a matter of note that this relative constancy of new case rates is maintained over the period examined (eleven years). In a similar comparison, Figure 5.10 shows that the cumulative cases of AIDS per 100,000 in the USA divided

by that for other First World countries gives essentially the same values observed for the new case rates in Figure 5.9.

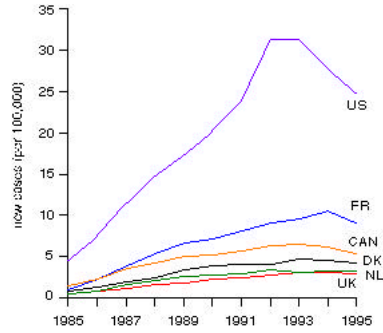


FIGURE 5.8 New case rates by country

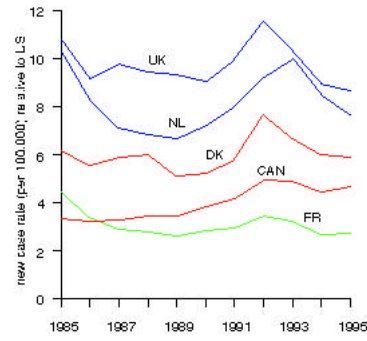


FIGURE 5.9 Comparative new case rates

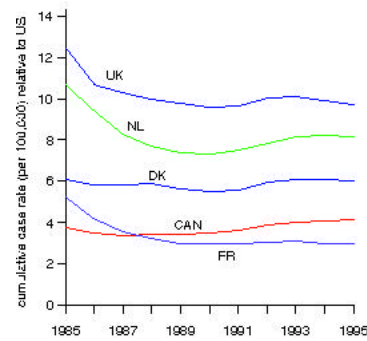


FIGURE 5.10 Comparative cumulative case rates

To investigate further, let us consider a piecewise in time exponential model for the number of AIDS cases, say in Country A:

$$\frac{dy_A}{dt} = k_A(t)y_A.$$

Figure 5.11 gives estimates for the rates k on a year-by-year basis using

$$k_A(t) \approx \frac{\text{new cases per year}}{\text{cumulative cases}}.$$

Note the apparent near equality of rates for the countries considered. To show this more clearly, Figure 5.12 displays the ratio of the annual estimated piecewise national rates divided by the annual estimated rate of the USA.

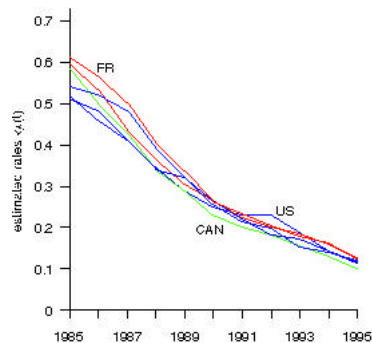


FIGURE 5.11 Estimates of k_A by country

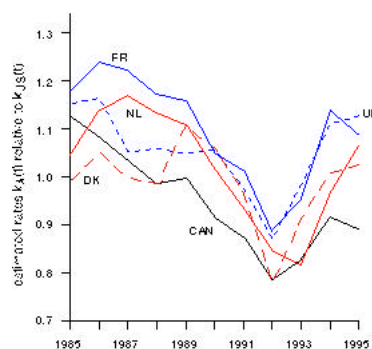


FIGURE 5.12 Ratios of k_A estimates

It is a matter of some interest that the k values are essentially the same for each of the countries shown in any given year. How shall

we explain a situation where one country has a much higher incidence of new cases, year by year, yet the rate of increase for all countries is the same? For example, by mid-1997, the United Kingdom had a cumulative total of 15,081 cases compared to 612,078 for the United States. This ratio is 40.59 whereas the ratio of populations is only 4.33. This gives us a comparative incidence proportion of 9.37. On the other hand, at the same time, Canada had a cumulative AIDS total of 15,101. The US population is 9.27 times that of Canada, so the comparative incidence proportion for the USA versus Canada in mid-1997 was 4.37. The comparative incidence of the USA vis-a-vis the UK is over twice that of the USA vis-a-vis Canada. Yet, in all three countries the rate of growth of AIDS cases is nearly the same. This rate changes from year to year, from around 0.54 in 1985 to roughly 0.12 in 1995. Yet it is very nearly the same for each country in any given year. One could therefore predict the number of new cases in France in a given year, just about as well knowing the case history of the United States instead of that in France. The correlation of new cases for the United States with that for each of the other countries considered is extremely high, generally around 0.96. It is hard to explain this by an appeal to some sort of magical synchronicity — particularly since we have the fact that though the growth rates of AIDS in the countries are roughly the same for any given year, the new case relative incidence per 100,000 for the United States is several times that of any of the other countries.

Recall from Section 5.4 the conjecture made in the mid-80s that it was the bathhouses which caused the stand-alone epidemic in the United States. But, as we have seen, the bathhouse phenomenon really does not exist in the rest of the First World. How is it, then, that there are stand-alone AIDS epidemics in each of these countries? I do not believe there are stand-alone AIDS epidemics in these countries.

To model this situation, let us suppose there is a country, say Country Zero, in which the sociology favors a stand-alone AIDS epidemic. From other First World countries there is extensive travel to and from Country Zero, as indicated by Figure 5.13. If AIDS, with its very low infectivity rates, breaks out in Country Zero, then naturally the disease will spread to the other countries. But if the infectivity level is sufficiently low, then the maintenance of an apparent epidemic in each of the countries will be dependent on continuing visits to and from Country Zero.

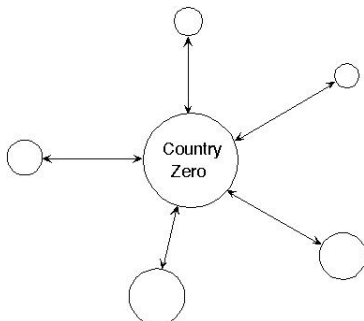


FIGURE 5.13 Model for spread of disease from Country Zero

Now let us suppose the fraction of infectives is rather low in country j . Thus, we shall assume that the susceptible pool is roughly constant. Let x_j be the number of infectives in country j and let z be the number of infectives in Country Zero. Let us suppose we have the empirical fact that, both for Country Zero and the other countries, we can use the same β_t in the growth models

$$\frac{dz}{dt} = \beta_t z \quad (5.5)$$

$$\frac{dx_j}{dt} = \beta_t x_j. \quad (5.6)$$

Let the population of country j be given by N_j and that of Country Zero be given by N_Z . Suppose the new case rate in Country Zero divided by that for country j is relatively constant over time: namely,

$$\frac{z/N_Z}{x_j/N_j} = c_j. \quad (5.7)$$

Let us suppose that, at any given time, the transmission of the disease in a country is proportional both to the number of infectives in the country and the number of infectives in Country Zero. Then from (5.6)–(5.7)

$$\frac{dx_j}{dt} = \alpha_{jt} x_j + \eta_{jt} z = \left(\alpha_{jt} + \frac{N_Z}{N_j} c_j \eta_{jt} \right) x_j = \beta_t x_j, \quad (5.8)$$

where α_{jt} and η_{jt} are the transmission rates into country j from that country's infectives and Country Zero's infectives, respectively. We are assuming that infectives from other countries will have relatively little effect on the increase of infectives in Country Zero. Thus, for a short time span, (5.5) gives

$$z(t) \approx z(0)e^{\beta_t t}$$

and (5.8) is roughly

$$\frac{dx_j}{dt} = \alpha_{jt}x_j + \eta_{jt}z(0)e^{\beta_t t}.$$

Now, we note that the epidemic in a country can be sustained even if α_{jt} is negative, provided the transmission from the Country Zero infectives is sufficiently high. If we wish to look at the comparative effect of Country Zero transmission on country j vis-a-vis country i , we have

$$\eta_{jt} = \frac{c_i}{c_j} \frac{N_j}{N_i} \eta_{it} + \frac{\alpha_{it} - \alpha_{jt}}{c_j} \frac{N_j}{N_Z}.$$

If for two countries i and j we have $\alpha_{it} = \alpha_{jt}$, then

$$\eta_{jt} = \frac{c_i}{c_j} \frac{N_j}{N_i} \eta_{it}.$$

Using (5.7) this can be expressed as

$$\frac{x_j}{x_i} = \frac{\eta_{jt}}{\eta_{it}}.$$

If η_{jt} doubles, then according to the model, the number of infectives in country j doubles.

Let us see what the situation would be in Canada if, as a stand alone, the epidemic is just at the edge of sustainability: i.e., $\alpha_{CAN,t} = 0$. Then, going back to a universal β_t for all countries including Country Zero (America) and using the c_{CAN} value of 4.14 for 1995, we have from (5.8)

$$\begin{aligned} \eta_{CAN,t} &= \frac{N_{CAN}}{N_{USA}} \frac{1}{c_{CAN}} \beta_t \\ &= \frac{26,832,000}{248,709,873} \frac{1}{4.14} \beta_t \\ &= 0.026\beta_t. \end{aligned}$$

Thus, according to the model, activity rates from USA infectives roughly 2.6% of that experienced in the USA could sustain a Canadian epidemic at a comparative incidence ratio of around 4 to 1, US to Canadian. (If someone would conjecture that it is rather the Canadian infectives who are causing the epidemic in the United States, that would require the activity rate of Canadian infectives with American susceptibles to be $1/0.026 = 38.5$ times that of Canadian infectives with Canadian susceptibles.) If this activity rate would double to 5.2%, then the Canadian

total infectives would double, but the rate $(1/x_{CAN}) dx_{CAN}/dt$ would still grow at rate β_t . Similar calculations show that

$$\eta_{FR,t} = 0.076\beta_t, \eta_{UK,t} = 0.024\beta_t, \eta_{DK,t} = 0.0034\beta_t, \eta_{NL,t} = 0.0075\beta_t.$$

In summary, we have observed some surprises and tried to come up with plausible explanations for those surprises. The relative incidence of AIDS for various First World countries when compared to that of the United States appears, for each country, to be relatively constant over time and this incidence appears to be roughly the same for cumulative ratios and for ratios of new cases. The rate of growth β_t for AIDS changes year by year, but it seems to be nearly the same for all the First World countries considered (Figure 5.11), including the USA. The bathhouse phenomenon is generally not present in First World countries other than the United States. Yet AIDS has a continuing small (compared to that of the USA), though significant, presence in First World countries other than the United States. The new case (piecewise exponential) rate there tracks that of the United States rather closely, country by country. We have shown that a model where a term for "travel" from and to the USA is dominant does show one way in which these surprises can be explained. Some years ago [2, 3, 8, 4], I pointed out that the American gay community was made unsafe by the presence of a small subpopulation which visited the bathhouses, even though the large majority of gays, as individuals, might not frequent these establishments. The present analysis gives some indication that the high AIDS incidence in the United States should be a matter of concern to other First World countries as long as travel to and from the USA continues at the brisk rates seen since the early 1980s.

Developing a model requires risk taking. The model, if it is to be useful, will be developed almost always without anything approaching a full data set. We could always find, as the fuller story comes in, that we were wrong. Then, in the case of epidemiology, we might find that by the time we publish our results, the virologists will have come up with a vaccine, perhaps rendering our model interesting but less than relevant. Most perilous of all, however, is to neglect the construction of a model.

5.10 Conclusions: A Modeler's Portfolio

This chapter has given an overview of around fifteen years of my work on the AIDS epidemic. I did not treat this work as an academic exercise. Rather, by public talks, articles in the popular press, service on the ASA AIDS Committee, and meetings with public officials, I tried to change the public policy on the bathhouses, without effect. So it is correct to

say that I have not been successful in influencing public policy as I had wished. I well recall, by the late 1980s certainly, that things were not going as I had wished.

I never had the experience of somebody getting up at a professional meeting and poking holes in my AIDS model. I would get comments like, “Well, we see that you have shown a plausible way that the epidemic got started. But that does us little good in providing a plan of action now that the epidemic is well under way.” Of course, this statement is not correct, for two reasons. First of all, I have addressed what the effect of closing the bathhouses would be during the mature epidemic. Secondly, effective restoration of the *status quo ante* will, almost always, reverse the course of an epidemic. In the case of polio, for example, closing of the public swimming pools and the suburban cinemas would have greatly defacilitated the epidemic, even after it was well under way.

To my shock, some colleagues took me aside to say that AIDS might be a very good thing, since it was discouraging a lifestyle of which neither these colleagues nor I approved. I always responded that our obligation in health care was to improve the lives of all persons, whether we liked their lifestyles or not. Moreover, I noted that a continuing entry of young males into the sociologically defined gay communities showed that the discouragement induced by the dreadful deaths generally associated with AIDS was not working the way they supposed. For example, in Houston, most of the leadership of the gay community had died off by the early 1990s. The death toll in Houston was staggering, more than in all Canada which has over ten times Houston’s population. And yet, the people who died were replaced by a new wave of infectives.

Perhaps most significantly of all, I would hear amazement that my modeling research was receiving any government support since there seemed to be little statistical interest in such public policy consequential modeling. Vast sums had been spent, for example, in support of the design of procedures whereby blood samples could be anonymously dumped into a pool with that of, say, nine other individuals and this exercise repeated many times in such a way to determine the fraction of AIDS infectives in the USA, while ensuring the privacy of those tested. But modeling the progression of the epidemic was not receiving much NIH or PHS support. I was fortunate indeed that the Army Research Office has allowed me to work on modeling problems generally.

The notion of becoming some sort of full-time activist for modification of government policy toward defacilitating the epidemic was tempting. Some hold that, like an entrepreneur with a good idea for a product, the researcher should put all his/her energy into one enterprise at a time. Certainly, to save the hundreds of thousands of lives which have been

needlessly lost to AIDS, such single-minded fanaticism would have been more than justified. However, based on the considerable effort that I had expended, it seemed to me that public policy was not going to be changed. If there had been some sort of focused attack on my AIDS model, then I might simply have hoped that a better explanation or a more complete model might win the day. But I had received the worst possible response — “We see your model, find no mistakes in it, and concede that it squares with the data, but it must be flawed because it does not square with policy.”

So I continued my general career policy, which is somewhat similar to that of an investment portfolio. The basis of portfolio theory is that putting all of one's assets in one stock, even one with enormous expected return, is generally not a good idea. One is much better advised to use the weak law of large numbers and put one's capital in several enterprises of reasonably good expectation of return, so that the variability of the return of the overall portfolio will be brought down to much better levels than those associated with a single stock. It seems to me that this is a good idea for modeling researchers in allocating their intellectual assets.

During the period since the start of my work on AIDS, I founded the Department of Statistics at Rice, which now has eight faculty, four of them Fellows of the ASA. Again, during this period, I wrote eight books (AIDS figured in only three of these and only as chapters). I produced seven doctoral students during the interval, only one of these writing on AIDS. I managed to obtain United Nations funding to start a Quality Control Task Force in Poland following the fall of Russian domination of that country. I developed computer intensive strategies for simulation based estimation and continuous resampling, largely in connection with modeling work in cancer. I did a modest amount of consulting, saving in the process one or two companies from bankruptcy. I started the development of anti-efficient market theory models which work fine as stochastic simulations, but cannot be handled in closed form. And so on. If AIDS was part of my professional “portfolio,” it accounted for only, say, five percent of the investment.

Since I have so far been unable to find political support for closing down bathhouses in America, it could be argued that the AIDS modeling part of the portfolio was not productive. I disagree. Our business as modelers is, first of all, to understand the essentials of the process we are modeling. Only rarely, and generally in relatively simple situations, such as changing the quality control policy of a corporation, should we expect to be able to say, “There; I have fixed it.”

The optimism concerning a quick discovery of an AIDS cure has dimmed. No doubt, one will be found at some time in the future.

However, after tens of billions of dollars already expended without a cure or vaccine, it is unwise to continue on our present route of muddling through until a miracle occurs. By this time, so many hundreds of thousands of American lives have been wasted by not shutting down high contact facilitating establishments that changing policy could leave open a myriad of litigious possibilities. The families of the dead or dying might have good reason to ask why such policies were not taken fifteen years ago.

Modelers are not generally members of the political/economic power structure, which Pareto termed the “circle of the elites.” We cannot ourselves hope to change public policy. But it is certainly our business to develop models that increase understanding of some system or other which appears to need fixing. We should follow the path of Chaucer’s poor Clerk of Oxford: “. . . gladly would he learn and gladly teach.”

Following the American polio epidemic of the postwar years, no modeler appears to have attempted to describe what went wrong with its management. Had that been done, perhaps a totally different response might have taken place when AIDS came on the scene. At the very least, I hope that my modeling of AIDS will have some impact on public policy concerning the next plague when it comes, and come it surely will.

Acknowledgments

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