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THE AIDS EPIDEMIC:
RECENT TRENDS AND FUTURE PROSPECTS

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The Deceleration in AIDS Incidence

Recent evidence suggests a possible slowdown in the growth rate of new AIDS cases (see Figure 1). The apparent slowing in overall AIDS incidence has occurred predominantly among homosexual and bisexual men, who still make up most of the cases (see Figure 2). This slowdown in AIDS diagnoses among homosexual men has been observed primarily in San Francisco, New York and Los Angeles, but also among white men outside these major coastal cities.

There are three competing, but not mutually exclusive, explanations for the observed slowdown in AIDS incidence. First, the trend may be an artifact of increasing underreporting of AIDS cases over the past two years. Second, zidovudine (AZT) and aerosolized pentamidine may have been administered to growing numbers of HIV-infected patients before they manifested AIDS. Third, the slowdown could be the

Figure 1: U.S. AIDS Incidence Estimates, 1979-1989

Source: U.S. Centers for Disease Control, October 1989

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consequence of a decline in the incidence of HIV infection several years earlier.

It is not possible with current data to distinguish sharply among these three competing explanations. An increase in the underreporting of AIDS is not likely to be the sole explanation. Although certain manifestations of AIDS are known to be seriously underreported among intravenous drug users, the apparent slowdown in AIDS incidence has occurred not in that group but among white homosexual men. Still, AIDS has probably been diagnosed increasingly on an outpatient basis, as patients have sought medical care earlier in the course of their disease. It is possible that state and local health departments have been less successful in identifying such outpatient cases.

Zidovudine has been available in the United States since late 1986. At about the same time, oral trimethoprim-sulfamethoxazole and aerosolized pentamidine began to be used to prevent Pneumocystis carinii pneumonia (PCP). Both treatments have now entered into widespread clinical use, at least for patients with confirmed AIDS. Clinical trials have confirmed that zidovudine delays the progression to AIDS in asymptomatic HIV-infected patients with severe immune deficiency (defined as fewer than 500 CD4+ cells per cubic millimeter). The critical unanswered question, however, is how many such HIV-infected patients received treatment during the past two or three years?

Based upon unit sales of zidovudine, an estimated 40,000 to 80,000 patients are currently taking the drug in the United States. About 4,000 eligible patients with AIDS took advantage of the zidovudine compassionate use program during late 1986 and early 1987. For the sake of argument, suppose that 5,000 asymptomatic HIV-infected patients with depressed immune systems (CD4+ counts under 500) had been taking zidovudine during 1987, and that 10,000 were taking the drug in 1988. For such patients,
zidovudine reduces the one-year rate of progression to AIDS five percent to two percent, and the two-year rate of progression is reduced from 15 percent to eight percent. At best, only about 700 or 800 cases of AIDS would have been prevented by such treatment.

In order to explore the third explanation for the slowed AIDS rate—that there was an earlier decline in HIV infection—a simple "back calculation" model of HIV incidence may be used. The idea behind such a model is to reconstruct the number of past cases of HIV infection that would be required to produce the current pattern of new AIDS cases. Making such a calculation requires information on the incubation period of HIV.

Figure 3 repeats CDC's data on actual AIDS incidence from Figure 1 and shows two estimates of AIDS incidence derived from different back calculation models. Model A's estimates were based upon all of the AIDS incidence data from the first quarter of 1979 through the third quarter of 1989. In Model B, the same statistical procedure was employed, but the last six data-points were dropped, so that only the incidence data through the first quarter of 1988 were included. For both models, the fitted incidence of AIDS is also projected forward through 1992.

Published projections of future AIDS cases have changed considerably over the past few years. Comparison of these projections is difficult, because both the projection models and the underlying data have changed. The analysis in Figure 3, by contrast, applies the same statistical model to two different data bases. This figure shows how strongly updated AIDS incidence data influence future AIDS projections.

The differences between Models A and B are substantial. An analyst who used only the AIDS incidence data available as of early 1988 (Model B) would project 142,000 AIDS cases by the third quarter of 1989—
about 11,000 cases more than are currently estimated by the CDC. The same analyst would project a cumulative total of 680,000 AIDS cases by 1996—about 198,000 more than are projected by Model A.

A more detailed look at Model A is shown in Figure 4, which plots the estimated incidence of HIV infection since 1977. Also plotted are CDC’s actual AIDS incidence data and the AIDS incidence projected through 1995. According to Model A, HIV infections peaked in 1983 at about 53,000 cases per quarter-year (95 percent confidence interval, ±2,000) and fell markedly by 1985 to about 12,000 (95 percent confidence interval, ±2,000). A continued linear decline in new HIV infections since 1985 would produce an estimated 6,800 new HIV cases per quarter-year in mid-1989. Moreover, the predicted future incidence of AIDS reaches a relatively flat maximum in the range of 14,000 new cases per quarter-year during 1992-1996.

By contrast, Model B does not produce a downturn in new HIV infections after 1983. The estimated HIV incidence, in fact, increases from 39,000 in 1983 (95 percent confidence interval, ±3,000) to 41,000 in 1985 (95 percent confidence interval, ±2,000). Even if HIV incidence declined linearly thereafter, the estimated HIV incidence would be 23,500 cases per quarter-year in mid-1989.

Both Model A and Model B were applied to CDC’s AIDS incidence data that are uncorrected for underreporting of AIDS cases. If the extent of underreporting has been 20 percent over the course of the epidemic, then the estimates all need to be adjusted upward by a factor of 1.25. Still, comparison of the models suggests that the recent AIDS incidence falls short of that which could have been predicted in early 1988 by at least 11,000 cases. Moreover, the slowdown is consistent with a downturn in HIV infections after 1983.

**Figure 4: Estimated U.S. Incidence of HIV Infection and AIDS, 1979-1995**

<table>
<thead>
<tr>
<th>Year</th>
<th>HIV Incidence (thousands)</th>
<th>Predicted AIDS</th>
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<td>1975</td>
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**NOTE:** The error bars on the HIV incidence curve show the estimated 95 percent confidence intervals.
Seroprevalence data from selected cohorts of homosexual men suggest that the incidence of new HIV infections was declining after 1982. However, these cohorts are small. Taken together, they contain only about 5,000 subjects who were initially seronegative, and there is no guarantee that these cohorts are representative of HIV infection among homosexual men generally. Although there is evidence that sexual practices among homosexual men were changing as early as 1982, even without such behavioral change, HIV infection rates could still decline, as the very highest risk groups of homosexual men became almost fully infected.

If the recent slowdown in AIDS cases is a real consequence of an earlier peaking in HIV incidence, can we be confident that it is permanent? Figure 2 shows that heterosexual AIDS cases continue to increase among both intravenous drug users and their heterosexual partners. While AIDS incidence in these groups is still a minority of all cases, this situation may change in the late 1990s.

The Improvement in Survival of AIDS Patients

Recent studies have shown a trend toward improved short-term survival from AIDS, at least since 1986. The gain in survival, however, has been seen only in AIDS patients initially manifesting PCP. The reduced mortality among PCP patients was seen in every risk group. Among homosexual men the increase in median survival for PCP patients was particularly pronounced, increasing from 10.5 months in 1984 to 18.0 months in 1987.

The apparent improvement in survival could conceivably be due to the growing difficulties in ascertaining AIDS-related mortality. Even in a carefully followed cohort of AIDS patients in San Francisco, mortality status could not be determined in 10 percent of cases. But it is hardly clear how such a bias in mortality follow-up would be confined to PCP patients in every risk group. Alternatively, the apparent gain in survival could be the consequence of earlier diagnosis of AIDS, when patients are at a less advanced stage of HIV infection; however, this hypothesis is weakened by the fact that very little of the mortality decline was observed immediately after diagnosis. The observed improvements in survival in the 1986 and 1987 cohorts are most consistent with the introduction of new medical therapies in 1986 and 1987. Zidovudine, in particular, was approved by the U.S. Food and Drug Administration in 1987 for use in AIDS patients with a confirmed episode of PCP.

Will the initial decline in mortality continue? If so, what will the prevalence of AIDS be as we approach the mid-1990s? Preliminary data from 1988 and 1989 do indeed suggest a continued mortality decline, but these improvements continue to be confined to PCP patients. If the gain in survival actually reflects the increased use of zidovudine, and if the drug is also effective in AIDS patients without PCP, then future gains in survival for non-PCP patients are possible. Whether zidovudine will improve long-term survival and whether other antiviral agents will soon enter widespread clinical use are questions critical to any future mortality projections.

To gain some understanding of the potential impact of future improvements in survival, I used the estimates from Models A and B to project AIDS incidence and prevalence through the first quarter of 1996. My key assumption was that median survival progressively increased from about 15 months in 1987 to 30 months by 1996. If so, the great majority of patients who contracted AIDS during 1976-1996 will be alive in 1996. Under Model A, about 482,000 AIDS cases will have occurred by 1996, of which about 315,000 will still be alive.

What will be the impact of over 300,000 people living with AIDS? That is about one AIDS patient for
every three acute care hospital beds in the United States. But the issue for the medical care system—and for our economy generally—is really the health status of AIDS patients and not merely their number. If antiviral therapy decreases the frequency and severity of AIDS-associated opportunistic infections, then conceivably many AIDS patients will remain out of the hospital and in the workplace.

Model A gives a cumulative incidence of HIV infection of nearly 780,000 cases by 1996. A reasonable correction for underreporting of AIDS cases would boost the HIV infection estimate to about one million. If HIV infection rates continue to decline, then about 60 percent of the cumulative total of HIV-infected persons will have already contracted AIDS by 1996, and the remaining 40 percent will be in various pre-AIDS stages in the natural history of HIV infection. Accordingly, it is reasonable that by 1996, there could be well over a half-million HIV-infected persons in need of some form of treatment. We need to think now about the potential impact of such a large population of HIV-infected people on our medical system and our society more generally.

NOTES

1. The data in Figures 1 and 2 are estimates made by the Centers for Disease Control (CDC) as of October 1989. (Refer to US Centers for Disease Control. Division of HIV/AIDS. Report of the HIV/AIDS Projections Workshop. October 31-November 1, 1989. Atlanta: US Centers for Disease Control, January 1990. These estimates have been corrected for reporting delays.) Additional estimates are provided in an upcoming 1990 article by JE Harris “AIDS Incidence and Reporting Delays” in the Journal of the American Statistical Association. (These data have not been corrected for underreporting.)

2. Similar slowdowns in AIDS incidence among homosexual men have been observed in England, Australia, and the Federal Republic of Germany.


7. Volberding, op. cit.


10. The details of the statistical method are given in Harris JE. op. cit., note 1.


12. See note 1, supra.


17. Harris, op. cit., note 16.

18. Lemp, op. cit., note 16.