CHAPTER 5

HOMOSEXUAL MEN IN SAN FRANCISCO: ESTIMATION OF PARAMETERS AND INCIDENCES

San Francisco (SF) has been chosen as the site for modeling HIV transmission in homosexual men because very good data are available there. The large open community of homosexual men in SF has been the source of numerous sexual behavior surveys. Additionally, data are available in SF for AIDS incidence each year and for HIV incidence as early as 1978. In this application of the simulation model, men who have sex with men (homosexual and bisexual men) are called homosexual men. Since most (85%) of the reported AIDS cases in SF have occurred in homosexual men, the modeling here does not include transmission between homosexual/bisexual men and others such as their heterosexual partners or homosexual intravenous drug users.

5.1 Estimation of Parameters Related to the Stages

The model and parameter values in Section 2.1 for staged progression to AIDS based on clinical phases is used here.

5.1.1 Probabilities of Transmission in the Stages

Recall that $\omega_k \times QH$ is the probability of transmission by people in stage k where $\omega_k = 1$ for an asymptomatic stage. Persons in the pre–antibody stage, symptomatic stages and AIDS stage seem to be more infectious than asymptomatic persons (Goedert et al., 1987, 1989; May, 1988; De Gruttola and Mayer, 1987; Padian et al., 1987; Osmund et al., 1988; Burke et al, 1989). Longini et al. (1990), using data on partnerships with HIV–infected persons, have estimated that the transmission rate of AIDS patients is 7.5 times that of symptomatic patients. In the model the factors ω_k are 2 for the pre–antibody stage, 1 for the asymptomatic stages, 2 for the symptomatic stages, and 15 for the AIDS stage.

5.1.2 Behavioral Changes in the Stages

Recall that $\rho_k \times PA$ is the average number of new sexual partners per month in stage k, where $\rho_k = 1$ for asymptomatics. Homosexual men might reduce their (unprotected) sexual activity either because they do not feel well in the symptomatic and AIDS phases or because they know that they have an HIV infection and do not want to infect others. Data presented by Coates et al. (1987) showed that in homosexual men in SF knowledge of HIV positive status resulted in a decrease in unprotected sexual activity from 18% to 12% between 1984 and 1986. Cates and Handsfield (1988) summarized studies showing that counseling and testing for HIV lead to reductions in high–risk behavior and that HIV positive individuals change their behavior more than HIV negative individuals. Thus the values chosen are $\rho_k = 1$ for stages in the pre–antibody or asymptomatic phases, $\rho_k = 0.75$ for stages in the symptomatic phase, and $\rho_k = 0.5$ for the

AIDS stage. There is significant uncertainty in the data leading to the parameter estimates for the $\omega_k \times \rho_k$ values of (2, 1, 1.5, 7.5) in the four phases so the sensitivity analysis in Section 6.4 considers (1, 1, 1, 1) and (10, 1, 1, 1).

5.2 Estimation of Population Sizes and Turnover Rate Constants

The SF Department of Public Health (Lemp et al., 1990) estimated that there were 55,816 homosexual males in the city of San Francisco in 1984. A similar estimate was obtained by Pickering et al. (1986). The size of the homosexual male population probably increased during the 1970s due to the popularity of SF with homosexual men and may have decreased in recent years. However, because precise information is not available, the male homosexual population size in SF is assumed to be constant at 56,000 in the model during the HIV epidemic. The sensitivity analysis considers sizes of 40,000 and 80,000.

A survey by Communications Technologies (Bye, 1987) found that 26% of the homosexual men in SF had lived there for five years or less. The immigration and emigration rates are therefore assumed to be 5% per year, so that $\delta = 0.05/12$ per month. Although the migration rate of 5% per year seems to be a reasonably good estimate, the sensitivity analysis considers migration rates of 0%, 3%, and 8%. Using mortality data (US Bureau of the Census, 1987) for men between 18 and 54, the death rate for homosexual men in the model is $\mu = 0.000532$ deaths per person per month.

The San Francisco City Clinic Cohort (SFCCC) consists of approximately 6700 homosexual men recruited between 1978 and 1980 from a clinic for sexually transmitted diseases to participate in a hepatitis B study. Because of the selection procedures, these men were probably more sexually active than most homosexual men in SF. In the SFCCC, 166 (2.4%) were reported to have AIDS by December 1984; 147 of these men still lived in SF, and 19 had moved to ten other U.S. cities. AIDS cases in the SFCCC were 38.5% of all AIDS cases in SF in the last half of 1981 and 16.4% of the cumulative AIDS cases in SF in December 1984 (Jaffe et al., 1985). Subsets of the SFCCC have been used to examine factors associated with HIV infection (Darrow et al., 1987) and progression to AIDS (Hessol et al., 1989). Data from the SFCCC are used here and in the next section.

The sexually very active fraction (F) and the sexual activity ratio (R) can be estimated by using the data from the SFCCC (Darrow, 1989). The choice of F = 0.1 is consistent with the data showing that there is a small percentage of sexually very active men. For 751 SFCCC men, the 10, 25, 50, 75, 90 and 95 percentiles for the average number of nonsteady sexual partners per year from the time of enrollment to the first followup (reinterview of diagnosis of AIDS) were 0, 12, 36, 84, 204 and 329 which make the median numbers of partners per year about 36 for the least active 90% and 329 for the most active 10%. For 500 SFCCC men interviewed between 1978 and 1984−85 the analogous percentiles for the number of partners per month were 0, 1, 3, 8, 18 and 28 so that the median numbers of partners per month were about 3 for the least active 90% and 28 for the most active 10%. For 413 SFCCC men interviewed between 1984−85 and 1986−87, the analogous data were 0, 0, 1, 4, 11, 18 so that the median numbers of partners per month were about 1 for the least active 90% and 18 for the most active 10%. These data suggest that 10% of the homosexual men in SF are approximately ten times more sexually active than the others so that $F = 0.1$ and $R = 10$ are reasonable estimates. The sensitivity analysis considers combinations where F and R are halved and doubled.

Although the information on the distributions of numbers of sex partners of homosexual men in SF is less complete in three other articles (Darrow et al., 1987; Winkelstein, Lyman et al., 1987; Winkelstein, Samuel et al., 1987) the data are consistent with 10% being ten times as active. The Gay Report (Jay and Young, 1979) was a survey of 4212 homosexual men in the U.S. carried out by gay organizations. In this sample, the lifetime median number of sexual partners was 49.5, with 12.5% reporting over 500 sex partners. This suggests that 12.5% were at least 10 times as sexually active as the other homosexual men. Note that data between 1979 and 1989 suggests that $F = 0.1$ and $R = 10$ are reasonable parameter values. Brauer et al. (1992) consider an HIV/AIDS model in which the fraction in the very active (core) group changes as a function of incidence–driven changes in behavior.

The rate constant (ϕ) for moving from the very active to active compartments is chosen to correspond to a 5% inflow and a 5% outflow per year so that $\phi = 0.05/12$ per month. The sensitivity to this choice is examined in Section 6.4.

5.3 Sexual Behavior Parameter Estimates

In the fitting of the simulations the most reliable parameter values are fixed and the six least reliable parameter values are varied to fit the simulation model to the HIV and AIDS incidence data. These six parameters are the epidemic starting date, the four parameters in Chapter 3 defining the average number of new sexual partners per month and the external mixing fraction. The *a priori* estimates or ranges for these six parameter values obtained in this section serve as initial guesses for the fitting iterations and as checks on the best–fitting parameter estimations.

5.3.1 Probability of Transmission Per Partner

Grant et al. (1987) found that the mean probability of infection through unprotected receptive anal intercourse was 0.102 per sex partner for the homosexual contacts of the 672 homosexual men studied. Since asymptomatic individuals in our model have relative infectivity $\omega_k = 1$ and the people in the other stages have higher degrees of infectiousness, the average relative infectivity of the infected persons contacted by the 672 men is assumed to be 2. Thus $2QH = 0.1$ so that the probability of homosexual transmission of HIV to sex partners of active asymptomatic infected persons is $QH = 0.05$. The value of QH based on receptive anal intercourse may be too large since homosexual partnerships can involve many other types of sexual contacts. Since QH and the average number PA of different partners per month always appear as a product in the model, QH is held fixed while PA is varied.

5.3.2 New Partners Per Month

Surveys by Johnson (1988) and Becker and Joseph (1988) cite studies showing that HIV seropositivity in homosexual men is associated with receptive anal intercourse and the number of sexual partners. Like QH above, the number of new sexual partners per month, PA, is really a simplified average over a variety of types of partnerships. Recall that PA is defined in Chapter 3 in terms of the four parameters PAS, STR, STP, and RDN given in Table 3.1.

Subsets of men from stratified random samples of the SFCCC (see Section 5.2) were interviewed in 1978, 1984, 1985, and 1987 (CDC: 1985e; 1985f; 1987d; Doll et al., 1987; Doll, 1988). The mean numbers of nonsteady partners (defined as individuals with whom the participant had sexual contact just once or twice) during a four–month period were 29.3 per person (median = 16) in 1978, 14.5 (median = 3) in 1984 and 5.5 (median = 1) in 1985. The medians yield a yearly reduction factor of $0.67 = (1/16)^{1/7}$. In these studies, the risk index of a sexual activity is the product of the percentage of time the participant engaged in this type of activity and the number of nonsteady male partners during the same period. The risk index for receptive anal intercourse with ejaculation with nonsteady partners was 10.9 in 1978, 3.3 in 1984, 0.4 in 1985 and 0.09 in 1987. These data yield a yearly reduction factor of $0.59 = (0.09/10.9)^{1/9}$. The risk index for insertive anal intercourse with nonsteady partners was 12.9 in 1978, 3.5 in 1984, 1.0 in 1985, and 0.35 in 1987 so the yearly reduction factor was $0.67 = (0.35/12.9)^{1/9}$.

In the SFCCC, of the 25% who were negative for hepatitis B, 359 took part in hepatitis B vaccine trial. Of these men, 313 agreed to participate in a HIV study (Hessol et al., 1989). Although the SFCCC men were probably more sexually active than other homosexual men in SF, those in the vaccine trial cohort were probably less active than others in the SFCCC, since they were negative for hepatitis B. Hessol et al. (1989) suggest that these vaccine trial men might be typical of SF homosexual men, since the decrease in HIV seroconversion in this cohort parallels a decrease in their high–risk sexual behavior and a city–wide decrease in gonococcal proctitis. In this vaccine trial cohort, the estimated average number of partners with whom the index cases engaged in receptive anal intercourse was approximately constant at about 17 per year (1.4 per month) through 1981, and then decreased to about 0.1 in 1987. This suggests a yearly reduction factor of $0.43 = (0.1/17)^{1/6}$ in high–risk sexual behavior.

The San Francisco Men's Health Study (SFMHS) was started in June 1984 to study the epidemiology of AIDS in a six square kilometers area (19 census tracts), in which the early AIDS incidence had been highest. It was estimated that there were approximately 18,000 homosexual men living in this area. The initial cohort in the SFMHS consisted of 1034 single men aged 25 to 55 recruited by area probability sampling (Winkelstein, Lyman et al., 1987). In a sample from the SFMHS the average lifetime number of sex partners was 200 so that there may have been about 20 partners per year or about 1.7 per month (Winkelstein, Samuel et al., 1987). Winkelstein, Wiley et al. (1988) report behavior changes in the SFMHS participants. Among HIV–positive men, insertive anal intercourse with 2 or more partners in 6 months declined from 40% in early 1984 to 15% in early 1985, was approximately constant through late 1986, and then declined to 5% in early 1987. Among HIV–negative men, receptive anal intercourse with 2 or more partners in 6 months decreased from 15% in early 1984 to 5% in late 1984 and remained low, with a value of 3% in early 1987. These data suggest large decreases in high–risk sexual behavior in 1984, and smaller decreases since 1985.

The decreases in high–risk sexual activity reported above are consistent with observed decreases in gonococcal proctitis cases per year in SF (Pickering et al., 1986; Hessol et al., 1989; Kohn, 1990). As shown in Figure 3.2, cases were approximately level from 1978 to 1981, decreased rapidly between 1982 and 1987, and then decreased slowly in 1988 and 1989. Since gonorrhea incidence responds rapidly to changes in behavior (Hethcote and Yorke, 1984), the changes in gonorrhea incidence are a good indication of behavior changes. Decreases in high–risk sexual activity starting in 1982 are consistent with the increasing awareness of AIDS among homosexual men in SF at about that time (Darrow et al., 1987; CDC: 1985f; 1987d).

A simplified version of the model in Chapter 3 can be used for gonorrhea transmission in homosexual men in SF. This gonorrhea model has only one infectious phase with an average infectious period of one year, after which the recovered men are susceptible again. Figure 3.3 shows the monthly gonococcal proctitis incidence in the simulation model when the average contact rate decreases by a factor of 0.70 each year from January 1982 to December 1984. The similarity of the simulation incidences to the observed gonorrhea incidences suggest that decreases in the average number of sexual partners started in about 1982 and occurred for several years.

Although the four parameters defining the average number PA of different partners per month are varied to satisfy the fit criteria, initial estimates and reasonable ranges are necessary. In the paragraphs above, the yearly reduction factors in sex partners per month are 0.59, 0.67, 0.43, and 0.70, which makes 0.4 to 0.7 a reasonable range for the yearly reduction factor RDN in the HIV simulations. The data above indicate that a good estimate for the reduction starting date STR would be January 1982, but other dates in 1981 or 1982 are also considered acceptable in the simulations. Reductions in high–risk sexual behavior may be continuing in recent years, but they are probably smaller than in previous years. The initial guess for the reduction stopping date STP is December 1984, but other stopping dates are also acceptable.

Values for the average number of partners per month in the paragraphs above are $29.3/4 = 7.3$ (median $= 4$) in 1978 for the SFCCC, 1.4 before 1981 for the SFCCC vaccine trial sample, and 1.7 before 1984 for the SFMHS. Thus a reasonable initial guess for PAS, the average number of partners per month before STR, is 2. This corresponds to an average number of partners per month of 1.05 for active individuals, and 10.5 for very active individuals when 10% are ten times as active.

5.3.3 Other Parameters

The blood samples in the SFCCC indicate that some men were HIV positive in 1978 so that the HIV epidemic probably started several years earlier. Hence the epidemic starting date STD might be in 1974, 1975 or 1976. In the model for heterosexual transmission of gonorrhea which had sexually active and very active subpopulations (Hethcote and Yorke, 1984), the external mixing fraction was 0.8, so that the *a priori* estimate of the external mixing fraction η in this model is $\eta = 0.8$.

5.4 Estimation of HIV and AIDS Incidences

5.4.1 HIV Incidence in San Francisco

More information is available on HIV seroconversions in SF than in any other location. Because blood samples were saved for participants in a hepatitis B vaccine trial starting in 1978 (Hessol et al., 1990), SF is the only place where data on HIV incidence is available before 1984. Two other sources of HIV incidence data are the SF Men's Health Study (Winkelstein, Lyman et al., 1987) and the SF General Hospital Cohort (Moss et al., 1988). Using three data sets, Bacchetti and Moss (1989) estimated the HIV seroincidence for homosexual men in SF from 1978 to 1989. Bacchetti (1990) refined this approach and obtained monthly HIV seroincidence estimates. His HIV seroincidences were found by scaling up a seroincidence curve estimated from the cohort studies so that the cumulative HIV seroconversions through September 1984 matched his city–wide estimate of 20,060. Since HIV infection occurs approximately 2 months before HIV seroconversion, the HIV incidence estimates before 1985 in Figure 5.1 are obtained by shifting the Bacchetti seroincidence estimates back 2 months.

Because Bacchetti's HIV seroconversion estimates in 1985 to 1988 were based on closed cohorts of aging men, they may not reflect the higher HIV incidence occurring in younger men. Based on the low seroincidence in the SF City Clinic Cohort (SFCCC) and the SF Men's Health Study, Lemp et al. (1990) assumed that 0.8% of the susceptible homosexual men would become HIV–infected each year from 1988 to 1993. In the Multicenter AIDS Cohort Study consisting of 3095 initially seronegative homosexual men recruited in mid–1984, the overall annual HIV infection rate over 5 years was 1.4%, but the seroconversion rate in the younger men was significantly higher (Kingsley et al., 1990). Thus the HIV seroconversion rate of about 1% per year may be correct for older homosexual men in these closed cohorts, but seroconversion rates are higher in younger homosexual men.

Among homosexual men visiting STD clinics in SF, Kellogg et al. (1990) found 40.7% HIV seroprevalence in 59 men ages 20–24 and 60.7% seroprevalence in 125 men ages 25–29. They suggested that previously uninfected young men may have seroconverted since 1983 when the annual incidence of new infections began to decline in SF. Clearly, the HIV seroconversion rates in these younger homosexual men (one third of the sample survey) must have been much higher than 1% per year in recent years in order to reach the observed HIV seroprevalence levels of 40.7% and 60.7%. If the annual HIV seroconversion rates in recent years were 4% for the susceptible homosexual men in SF under 30 and 1% for those over 30, then the average seroconversion rate in recent years for all homosexual men in SF would be $(1/3)4\% + (2/3)1\% = 2\%$. These estimates are consistent with other estimates (Hessol et al., 1990; Winkelstein, Wiley et al., 1988). The HIV seroprevalence is approximately 20,000 out of about 56,000 homosexual men in SF (Bacchetti, 1990), so that the annual number of seroconversions may have been about 2% of 36,000 susceptibles, or 720 per year. This 720 HIV seroincidence per year is plausible

Table 5.1. Estimates of yearly HIV and AIDS incidences for homosexual men in SF

year	HIV incidence	AIDS Incidence: all cases adjusted for reporting delays	Consistent Cases: cases adjusted for reporting delays	Consistent Cases: modified non–consistent cases	Consistent Cases: total adjusted cases
1978	439	0	0	0	0
1979	1963	0	0	0	0
1980	4390	2	2	0	2
1981	5721	22	22	0	22
1982	4337	86	86	0	86
1983	2362	228	228	0	228
1984	1269	443	442	0	442
1985	762	681	678	0	678
1986	720	1029	1009	1	1010
1987	720	1320	1272	3	1275
1988	720	1354	1276	9	1285
1989	720	1449	1321	17	1338
1990	720	1635	1522	29	1551

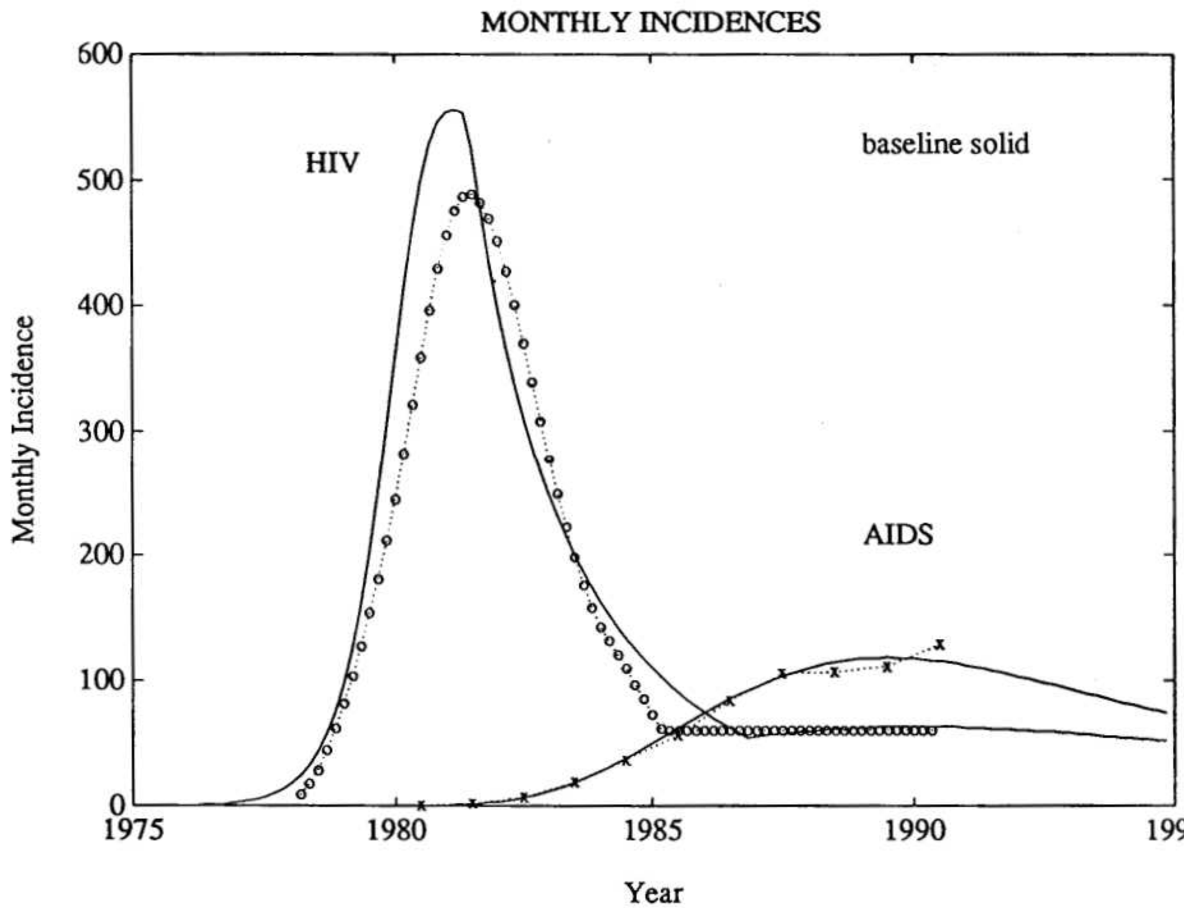

Figure 5.1. The HIV incidence curve (circles) and the AIDS incidence curve (x symbols) correspond to the estimates in Table 5.1. Baseline simulations for HIV and AIDS incidences corresponding to Tables 6.1 and 6.2 from Chapter 6.

since it is about one–fourth of the estimated 2800 (5% of our 56,000 estimate) homosexual men immigrating to SF each year. Thus the best approximation of HIV incidence in homosexual men in SF seems to be the Bacchetti's HIV incidence curve in Figure 5.1 until May 1986, and then about 60 per month between 1986 and 1990. The yearly estimated HIV incidences are given in Table 5.1.

5.4.2 AIDS Incidence in San Francisco

In the United States, AIDS cases meeting a surveillance definition (CDC: 1982, 1985c, 1987j) are reported locally and then forwarded to the Centers for Disease Control (CDC). The reported AIDS incidence in SF has been obtained from these case reports sent to CDC through May 1991. (Note that the data used throughout this chapter is for the city of SF, not the SF Metropolitan Statistical Area.) Lindan et al. (1989) found that the reporting delay pattern did not change from 1985 through 1988; consequently, methodical adjustments are possible. Cases diagnosed after March 1985 have been adjusted for reporting delays after grouping cases by quarters of diagnosis (Karon et al., 1988, 1989). The resulting estimates are shown in Table 5.1.

The AIDS surveillance definition was expanded in September 1987 (CDC: 1987j). The expansion allowed patients with a positive HIV antibody test to be reported if they had presumptive (instead of definitive) diagnoses of certain diseases in the previous definition, or if they had certain other diseases indicating severe morbidity associated with HIV infection. Patients satisfying what is called the consistent case definition (Karon et al., 1988) are those with a diagnosis (definitive or presumptive) of a disease in the pre–1987 case definition. The expansion of the surveillance definition increased the number of patients reported with AIDS by adding some patients who die before satisfying the consistent definition and allowing others to be reported earlier in the course of the disease. For homosexual men in SF, 3%, 4%, 8%, and 7% of the cases diagnosed in the years 1987–1990 respectively, were not consistent with the pre–1987 surveillance definition.

The effect of the 1987 change in the AIDS surveillance definition has been estimated (Lemp, 1991). There were 477 persons diagnosed with AIDS in SF between September 1, 1987, and December 31, 1989, based on diseases not consistent with the pre–1987 definition. In seven of these persons, the AIDS diagnosis was not made before the date of death. Of the remaining 470 patients, about half died before developing a disease consistent with the pre–1987 definition, and 130 (28%) had developed such a disease by December 31, 1990. The Kaplan–Meier procedure estimates the median time for progression to the consistent case definition to be 27 months. Of those who reach the consistent case definition before death, the estimates are that 21, 29, 38, 47, and 58% would develop a disease in the consistent case definition at 6, 12, 18, 25, and 31 months, respectively.

The total consistent case estimates in Table 5.1 of annual AIDS incidence are obtained as follows. Monthly incidences (cases diagnosed through December 1990) are adjusted for estimated reporting delays based on cases reported through March 1991 (Karon et al., 1989), both for cases consistent with the pre–1987 definition and for cases not consistent with that definition that did not die during the month of diagnosis. Based on the progression data from SF, the non–consistent cases are modified by assuming that 10% would satisfy the consistent definition six months after the month of diagnosis, and that 5% more would satisfy the consistent definition at the end of each of the following six–month intervals up to three years (i.e., after 12, 18, 24, 30, and 36 months.) For example, the estimate that 10% would satisfy the consistent definition six months later is based on half of the persons with non–consistent diagnoses dying before meeting the consistent definition, and 20% of the remaining persons satisfying the consistent definition within six months. The estimates in Table 5.1 of the total consistent AIDS incidences are obtained as the sums of the consistent and modified non–consistent cases.

One study (Lindan et al., 1989) found that approximately 10% of the total cases in homosexual men in SF from 1985 through 1988 were not reported. A previous study (Rauch et al., 1989) found that at least 98% of the AIDS cases diagnosed in SF before 1987 were reported. Since the extent of underreporting is unclear, the adjusted consistent AIDS cases in Table 5.1 are not further adjusted for underreporting. Thus the HIV and AIDS incidences found by fitting the simulation model to this data need to be scaled up by a factor to account for underreporting.