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HIV Prevalence Estimates and AIDS Case Projections for the United States: Report Based upon a Workshop

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EXECUTIVE SUMMARY This document presents conclusions and recommendations from a workshop convened to discuss national estimates of human immunodeficiency virus (HIV) prevalence, acquired immunodeficiency virus (AIDS) case projections, and the proportion of HIV-infected persons with laboratory evidence of immune dysfunction. Appendices describe analyses performed before and after the workshop to estimate HIV prevalence and to predict future AIDS cases, the prevalence of persons with AIDS, and deaths among persons with AIDS.

On the basis of these analyses, CDC estimates that approximately 750,000 persons in the United States were infected with AIDS at the beginning of 1986 and that approximately 1,000,000 Americans are currently infected with HIV. At least 40,000 new HIV infections occur each year among adults and adolescents, and an estimated 1,500-2,000 new infections occur each year among newborns as a result of perinatal HIV transmission. Approximately 60% of the estimated 1,000,000 HIV-infected persons in the United States may have T-helper lymphocyte (CD4+ cell) counts of less than 500/mm3 of blood and may benefit from early treatment with zidovudine.

The number of AIDS cases will continue to increase over the next 4 years, with a projection of 52,000-57,000 cases to be diagnosed in 1990. Both AIDS case projections and HIV-prevalence estimates are influenced by the slowing of the rapid upward trend in AIDS incidence that occurred in 1987, particularly among homosexual and bisexual men who are not intravenous drug users. Data available during and after the workshop suggest that medical therapy or a decline in the incidence of new HIV infections among homosexual men in the early 1980s could have contributed to this change in trend, but the relative contributions of these and other factors (including changes in the completeness or timeliness of AIDS case reporting) require further study. INTRODUCTION

The AIDS case surveillance system has been and continues to be the cornerstone of Public Health Service (PHS) efforts a) to monitor the serious morbidity and mortality due to HIV infection in the United States and b) to forecast trends in morbidity and mortality due to HIV infection classified as AIDS. Understanding the extent and distribution of HIV infection in the population and the rate at which new infections occur improves the forecasts and estimates of future needs for services.

National AIDS case projections and HIV-prevalence estimates were made first in 1986 (1) and most recently in mid-1988 (2). CDC planned in 1988 to assess the projections and estimates at roughly 1-year intervals. To that end, a workshop was held October 31-November 1, 1989, in Atlanta, Georgia,

with 70 specialists from federal agencies, state and local health departments, academic centers, and voluntary organizations. Participants in the workshop evaluated the methods used by statisticians and epidemiologists to make AIDS case projections and HIV-prevalence estimates. The participants also reviewed methods for assessing the spectrum of HIV-related immunologic deficiency and estimating the impact of therapeutic interventions on the incidence of AIDS.

Following a plenary session, workshop participants met in four working groups, each charged with reviewing a major issue related to the larger goals of the meeting and making recommendations to the PHS regarding these issues. The four issues were: prevalence and incidence of HIV infection, spectrum of immunologic deficiency, AIDS case projections, and effects of therapy on disease progression. A summary of the conclusions from the workshop, together with current estimates of HIV prevalence and AIDS case projections, has been published (3).

This document provides a more detailed review of the discussions and recommendations of the participants in the four working groups, as well as actions taken during the last year. The statistical methods used to estimate HIV prevalence and future AIDS trends are described in Appendix A. Appendix B provides more detailed information on the results of the analyses used in making the estimates.

In this report, it is sometimes necessary to distinguish between several stages in the natural history of HIV infection. The term "HIV infection" refers to infection with human immunodeficiency virus, regardless of the presence of clinical manifestations, i.e., either symptomatic or asymptomatic infection. The term "symptomatic HIV infection" refers to infection with human immunodeficiency virus and the presence of clinical manifestations that have been linked to HIV infection. These manifestations include some that are not life-threatening, such as oral candidiasis and herpes zoster (4), as well as more serious diseases. The term "life-threatening symptomatic HIV infection" means symptomatic HIV infection and the presence of serious illnesses or conditions that affect HIV-infected persons and are not due to other underlying causes. These illnesses could be opportunistic infections, cancers, or syndromes in the surveillance definition for AIDS (5), or other illnesses such as bacterial pneumonia, pulmonary tuberculosis, other types of pneumonia, septicemia, cardiomyopathy, and nephropathy that apparently cause death for some HIV-infected persons whose illness does not meet the surveillance definition for AIDS (6,7). FACTORS AFFECTING HIV-PREVALENCE ESTIMATES AND AIDS CASE PROJECTIONS Back-calculation

The most widely used method of estimating future AIDS incidence and historical HIV prevalence is a statistical procedure called back-calculation. An extension of this method permits the estimation of the number of HIV-infected persons in different stages of disease. The back-calculation method uses two types of data to estimate the number of prior HIV infections necessary to account for the AIDS cases that have been diagnosed subsequently and that have been or will be reported (8,9). The two types of data are a) observed AIDS incidence and b) an estimate of the incubation-time distribution (the time from HIV infection to a diagnosis of AIDS). Changes in or limitations of these two types of data will affect estimates derived from back-calculation. Trends in AIDS incidence

Slowing of the rapid upward trend in AIDS incidence that occurred in 1987 has influenced current HIV-prevalence estimates and AIDS case projections (10). The number of AIDS cases diagnosed per month continued to increase in 1987, but the rate of increase declined in the middle of that year, particularly among homosexual and bisexual men who did not use intravenous drugs (Figure 1). Among that group, the change in trends was most apparent in New York City, San Francisco, and Los Angeles (Figure 2). The trend in incidence also appears to have changed during 1987 among white homosexual men outside these cities, with no change in the trend among all other categories of homosexual men, most of whom are black or Hispanic (Figure 3; only the smoothed trends in monthly

incidence are shown in this figure).

The factors considered by the workshop participants as reasons for this change included the following: a) a decline in the incidence of new HIV infections among homosexual men in the early 1980s, leading to a subsequent decline in the incidence of reported AIDS cases (11); b) the use of antiretroviral and other types of therapy by mid-1987, leading to a lengthening of the incubation period from the acquisition of HIV infection to the presence of symptoms of AIDS; and c) possible decreases in the completeness or timeliness of AIDS case reporting. The accuracy of HIV-prevalence estimates and AIDS case projections depends in part on the determination of the relative contribution of these or other factors.

Data related to two of these factors--completeness of reporting and effect of therapy--became available after the workshop. Analysis of preliminary data on mortality for 1988 did not indicate less complete reporting of AIDS cases in 1987 and 1988 than before 1987 (see Appendix A). The availability of data on the use of zidovudine (formerly called AZT) in mid-1987 made it possible to estimate the effect of medical therapy on the change in trend in AIDS incidence occurring in that year. Using a mathematical model, Gail et al. estimated that zidovudine treatment given during early 1987 to 5-7 thousand homosexual or bisexual men with severe immunodeficiency, but without AIDS, could account for the change in the trend in AIDS incidence among men in this category during the last half of 1987 (12). More than 10,000 persons received zidovudine from the Burroughs Wellcome Company under a limited drug distribution system during March-September 1987. Data from a 4% systematic sample of this group indicate that approximately 4,000 homosexual men who were infected with HIV and had low T4 lymphocyte (CD4+ cell) counts, but who had not yet developed AIDS, received zidovudine during that time (13). Although these data suggest that medical therapy could have made a substantial contribution to the change in trend in AIDS incidence among homosexual men during 1987, the relative contribution of this and the other factors noted above can only be determined after further study. Incubation-time distribution

Back-calculation estimates are known to be sensitive to the incubation-time distribution used (11). The incubation-time distribution may have changed recently as a result of improved medical care (delaying a diagnosis of AIDS and lengthening the incubation time), the revision of the AIDS surveillance definition in 1987 (5) (possibly resulting in the reporting of some patients at an earlier stage in their illness), and increased outpatient diagnosis and treatment of persons with symptomatic HIV infection (possibly resulting in the reporting of some patients later in their illness, when they are hospitalized). Therefore, back-calculation may not provide accurate estimates of HIV prevalence and future AIDS trends unless the model uses a distribution for incubation time that incorporates the effect of these possible changes.

Because of the length of the incubation period--with few AIDS cases developing within the first 2 years of infection--back-calculation also cannot detect recent changes in HIV incidence. Estimates of HIV incidence during the last 2 or 3 years are less likely to be accurate than estimates of HIV incidence from at least 4 years ago. Results presented at this workshop confirmed that estimates of recent HIV incidence obtained from back-calculation are subject to much uncertainty (Appendix B).

PREVALENCE AND INCIDENCE OF HIV INFECTION Estimates of HIV prevalence

The estimated prevalence of HIV infection in the U.S. population is an important measure of the extent of the nation's HIV-related problem. The PHS has used a working estimate of 1-1.5 million infections in the United States, but arguments have been presented for both lower and higher estimates (1). Workshop participants assessed the 1986 PHS estimate and evaluated the range of current estimates derived from back-calculation and from direct estimation using data from HIV seroprevalence surveys.

On the basis of information provided at the workshop, CDC estimates that approximately 1 million persons in the United States are currently infected with HIV. Previous estimates.

In 1986, a workshop of medical researchers, epidemiologists, and statisticians in Coolfont, West Virginia, estimated that a total of 1-1.5 million HIV infections existed in the United States (1). To arrive at this range, the workshop participants used an estimate of the sizes of the various populations at risk and the estimated HIV seroprevalence in the groups. Since the HIV antibody test had been licensed only a year earlier, seroprevalence data were limited, and little was known about the long-term natural history of HIV infection. At the time of the Coolfont workshop, 21,000 cases of AIDS had been reported to CDC. The Institute of Medicine, National Academy of Sciences, reviewed and did not challenge the estimate of 1-1.5 million HIV infections (14).

By 1987, more seroprevalence data were available, and the direct estimate of the number of HIV infections was revised to a slightly lower range of 945,000-1.4 million (11). Estimates from back-calculation included a wider range (420,000-1.65 million). Current estimates derived from back-calculation.

Since 1987, the back-calculation method has been further refined, more information has become available on the distribution of incubation times, and the change in trends of AIDS incidence has become apparent. In addition, more extensive seroprevalence data on sentinel populations are now available from CDC's surveys and studies.

Four workshop participants summarized current estimates of HIV prevalence based on the back-calculation method and presented analyses for more detailed discussion (Brookmeyer, Hay, Hyman, and Rosenberg). Additional analyses were done after the workshop. CDC adjusted all estimates for previous deaths, underreporting of AIDS cases, and deaths due to HIV infection in persons not meeting the AIDS surveillance definition* (see Appendices A and B).

*CDC estimates that 70%-90% of all HIV-related deaths among men 25-44 years of age (the group most affected by the HIV/AIDS epidemic) are reported through AIDS surveillance (7) and that 85% of all diagnosed cases of AIDS (as defined by national surveillance criteria) are reported (see Appendix A).

On the basis of these back-calculation analyses, CDC now estimates that approximately 750,000 persons in the United States were infected with HIV at the beginning of 1986 (Table 1). Estimates of current HIV prevalence based on these analyses range from 650,000 to 1.4 million. The median of these estimates is greater than 900,000, and only one estimate is less than 850,000. The wide variation among the estimates for recent years reflects the sensitivity of the back-calculation approach to more recent surveillance data reports and to varying estimates of the distribution of incubation times.

The group agreed that back-calculation provides a basis for estimating past HIV-infection prevalence and future AIDS incidence. However, the accuracy of this method depends on the validity of the necessary assumptions and adjustments made, especially those concerning the completeness of AIDS case reporting and the estimated distribution of incubation periods. Current estimates derived from empirical data.

The group also reviewed estimates of total HIV prevalence derived from seroprevalence data from CDC's family of surveys. Participants evaluated a framework of age- and sex-specific HIV-prevalence rates derived from data from the sentinel hospital network (15). Prevalence data from civilian applicants for military service, childbearing women, ambulatory patients, Job Corps entrants, and federal prisoners were compared with the expected rates, with consideration given to the probable

biases involved. The results of these preliminary analyses were consistent with prevalence estimates ranging from a minimum of approximately 300,000 (based on rates from applicants for military service) to a maximum of approximately 1.5 million (based on rates from federal prisoners). Considering both the biases in the seroprevalence data that determine the extremes and the bulk of empirical prevalence data, a plausible range is approximately 800,000-1.2 million HIV infections (15). Further quantitative evaluation of the biases inherent in several of the data sets is necessary.

Thus, although based on independent data sources and subject to different biases, both methods--back-calculation and extrapolation from empirical data--provide national HIV prevalence estimates that overlap and center around 1 million (Table 1). Estimates of HIV incidence

The incidence of HIV infections in the U.S. population indicates growth of the epidemic at a given time. Unfortunately, it is extremely difficult to measure the incidence of an infection that is often initially not accompanied by symptoms. The incidence of new HIV infections can be either observed directly in groups that are repeatedly screened for HIV infection or estimated from serial prevalence measurements.

Workshop participants reviewed directly observed annual incidence rates for specific groups, including the following:

- Red Cross blood donors who have donated at least twice since HIV screening began--approximately 0.003% (1 of every 30,000 donors) infected per year from 1988 through 1989
- active-duty military personnel--approximately 0.06% to 0.08% (1 of every 1,200-1,700 personnel) infected per year from 1987 through 1989
- homosexual men in observed cohorts--1%-3% infected per year from 1987 through 1989
- intravenous drug users in New York City--3%-9% infected per year from 1987 through 1989

Incidence estimates derived from HIV serosurveys of blood specimens from newborn infants indicate that 1,500-2,000 HIV-infected infants were born in 1989 (approximately 30% of births to HIV-infected women, or approximately 0.05% of all infants born in the United States) (Table 1).

Annual incidence has been inferred from data on serial prevalence among applicants for military service. Evaluations of these data (for persons who are on average younger than active-duty personnel) yielded an estimate of 0.5/1,000/year for males and 0.14/1,000/year for females (J. McNeil et al., Walter Reed Army Institute of Research, unpublished data). Additional years of observation as well as further theoretical work on analytic methods will be needed to derive similar estimates from other sources of prevalence data.

Extrapolation of incidences for active-duty military personnel to the U.S. population at large provides a minimum estimate of HIV incidence for adults and adolescents. Observed incidences for these personnel were 0.77/1,000/year from 1985 through 1987 (16) and approximately 0.6/1,000/year (J. McNeil et al., Walter Reed Army Institute of Research, unpublished data) to 0.7/1,000/year (17) from 1988 through 1989. Preliminary extrapolation to the U.S. population from age-, sex-, and race-adjusted data for active-duty military personnel (using the lowest observed incidence of 0.6/1,000) suggests that at least 40,000 new HIV infections occurred among adults and adolescents in the United States during 1989 (Table 1). The principal assumption for these extrapolations is that the risk of new infection is at least as high for young adult civilians as for military personnel of comparable age. This is a plausible assumption because the military actively discourages homosexual and bisexual men and intravenous drug users (IVDUs) from applying for service, screens applicants for HIV antibody and excludes those

found to be infected prior to enlistment, and enforces policies against homosexual and drug-using behavior by military personnel.

Currently, an estimated 1,500-2,000 new infections occur each year among newborns as a result of perinatal transmission, and at least 40,000 new infections occur each year among adults and adolescents. Comparing the estimate of approximately 750,000 HIV-infected persons alive at the beginning of 1986 with the current estimate of approximately 1 million alive in mid-1989 suggests that an average of greater than 80,000 new infections have occurred each year since 1986.

Recommendations

The working group made the following recommendations to improve the accuracy of estimates derived from back-calculation:

1. Reports of HIV-prevalence estimates derived from back-calculation should clearly state the year(s) that the estimates were made and the approach taken to adjust for the following:
    - delays in reporting of AIDS cases
    - incomplete reporting of diagnosed AIDS cases and nonreporting of symptomatic HIV infection that is life-threatening but does not meet the AIDS case definition
    - changes in the distribution of the incubation period
    - changes in the AIDS case definition 2. Back-calculation models should incorporate all available AIDS surveillance data, including data for persons diagnosed as having AIDS after mid-1987. The models will, however, require modifications to allow for changes in the distribution of the incubation period that reflects the results of early therapy. 3. Separate back-calculation estimates of prevalence should be made for distinct transmission categories and demographic and geographic subgroups. 4. The statistical imprecision of estimates of the distribution of the incubation period should be incorporated into the back-calculation models. Studies should be carried out to characterize more accurately the distribution of the incubation period in populations other than homosexual men (e.g., IVDUs and perinatally infected infants). 5. Estimates of the statistical precision of back-calculations should accompany all point estimates--with the sources of error clearly stated. Additional uncertainty should be assessed by sensitivity analysis and synthesized into an overall estimate of uncertainty. 6. Researchers using back-calculation should be encouraged to share informally their adjusted data on AIDS incidence before publication. Sharing these data will make it easier to determine whether differing results are caused by different adjustments for reporting delays or by different methodologies.

Additional recommendations included the following:

1. For direct estimation of total HIV prevalence, the direction and impact of the biases inherent in observed seroprevalence data from CDC's seroprevalence surveys--especially those from childbearing women--should be further evaluated.

2. Results of the feasibility phase of the National Household Seroprevalence Survey (NHSS) should be reviewed, and information that could be collected to give more precise estimates of HIV prevalence and/or help refine model-based projections should be identified.

3. Further analysis should be done to make minimum--and, if possible, maximum--estimates of the

number of new infections per year (annual HIV incidence), using both observed seroconversion data and back-calculation models.

4. Analytic approaches should be explored for inferring incidence from serial cross-sectional prevalence data as the information becomes available from CDC's seroprevalence surveys.

Actions taken since meeting

1. A description of the methods used in CDC's HIV seroprevalence surveys was published (18).

2. In October 1990, a summary of descriptive data from CDC's family of seroprevalence surveys was published (19).

SPECTRUM OF IMMUNOLOGIC DEFICIENCY AMONG HIV-INFECTED PERSONS

Monitoring the CD4+ cell counts of persons with HIV infection provides a measure of HIV-related immune dysfunction. To help quantify HIV-related morbidity and to estimate the potential need for antiretroviral and other therapies, the workshop group evaluated the need for surveillance of immune-status indicators to augment data on HIV/AIDS incidence and prevalence in projecting the impact of the epidemic.

The distribution of measures of immune status among HIV-infected persons can be estimated from data obtained in surveys, from ongoing cohort studies, and from such statistical methods as back-calculation. Surveys can directly measure both the number of infected persons in a sample of the population and the distribution of CD4+ cell counts among those infected. Cohort studies of selected risk groups provide historical data regarding changes in CD4+ cell-count distributions over time that can be used in conjunction with estimates of rates of decline of CD4+ cell counts, HIV incidence, and cause-specific mortality rates to project current and future CD4+ cell-count distributions.

Workshop participants reviewed data from immunologic studies of active-duty military personnel with HIV infection (20; National Naval Medical Center, unpublished data) and in cohorts of homosexual and bisexual men (21,22). Using the Army data (20) and projection method, it was estimated that by 1989 approximately 17% of HIV-infected persons evaluated between 1985 and 1989 had less than 200 CD4+ cells/mm3 and that an additional 41% had 200-500 CD4+ cells/mm3. The Navy data and projection method yielded corresponding estimates of 19% and 45%, respectively. Thus, 58%-64% of persons with HIV infection may have CD4+ counts of less than 500/mm3. These estimates are consistent with those reported from cohort studies among homosexual and bisexual men (21,22).

To estimate CD4+ cell-count distributions, modeling methods such as back-calculation use data on the incidence of end-stage disease (e.g., AIDS case reports, HIV-associated deaths), together with estimates of the distribution of times from infection to various stages of immune suppression. An extension of the back-calculation method permits estimation of the number of infected persons in various stages of disease. Using adjusted data on AIDS incidence and a median of 3.6 years from low CD4+ cell counts to AIDS estimated from cohort studies of males with hemophilia (23), Brookmeyer estimated that as of July 1987, there were approximately 150,000 adults infected with HIV who did not yet meet the CDC AIDS case definition, but who had less than 200 CD4+ cells/mm3; these persons accounted for approximately 15% of his estimate of 987,000 HIV-infected adults who had not yet progressed to AIDS (24).

The back-calculation method is sensitive to estimates of median time from low CD4+ cell counts (less than 200 cells/mm3) to AIDS. Various cohort studies estimate the median time to range from 1 to 3 years (e.g., studies of males with hemophilia and studies of homosexual and bisexual males).

Therefore, if the incubation period differs by risk group or is affected by therapy, estimates of the distribution of immune-status indicators based on back-calculation may have to be adjusted. Presently, however, estimates of the proportion of HIV-infected adults with less than 200 CD4+ cells/mm3 are consistently 15%-20%, regardless of the projection method used.

When CD4+ cell counts for HIV-infected persons can be obtained, the workshop participants judged such counts to be the most useful predictors of stage of disease currently available. Although CD4+ cell counts are used clinically to indicate the need for and timing of therapeutic interventions, additional research is needed to evaluate the usefulness of changes in CD4+ cell counts as markers of therapeutic efficacy and to correlate such changes with the prevention or remission of clinical symptoms. Because there is inherent variability in CD4+ cell counts, other parameters (e.g., CD4+/CD8+ ratio, percentage of total lymphocytes that are CD4+, clinical signs and symptoms) may ultimately be more reliable and valid indicators of immune status, alone or in combination. Also, because different specimens are required for CD4+ cell counting than for serum antibody testing, and since the technology for CD4+ cell counting is not currently widely available, the workshop participants concluded that it would be desirable to identify an alternative indicator of immune dysfunction that is measurable in serum and is also highly correlated with stage of disease. Serologic markers (e.g., beta-2 microglobulin and neopterin levels) should be further explored.

Recommendations

1. Ongoing and planned PHS-sponsored studies of demographically, geographically, and behaviorally defined subgroups of the infected population (e.g., homosexual and bisexual men, IVDUs, women, children, adolescents, and racial/ethnic minorities) should be supplemented to identify markers of immune status for all stages of disease. Studies should also be designed or augmented to a) measure rates of decline in CD4+ cell counts, b) identify surrogate markers of immune status that can be measured in serum, and c) measure the effects of various types of therapy on rates of decline of CD4+ cell counts and on changes in other indicators of immune status.

2. Surveys should be conducted to describe the spectrum of immune deficiency among infected persons.

3. CDC's HIV-infection classification system should be modified or appended with a system based on indicators of immune status, including CD4+ cell measures (e.g., count, ratio, percentage).

4. Surveys designed to measure seroprevalence should, when possible, include CD4+ cell counts for persons identified as being infected with HIV. If CD4+ cell assays are not feasible, the use of markers of immune status that can be measured in serum should be evaluated for use in survey designs.

5. Modeling methods designed to project distributions of immune status among infected populations should be further developed. These should include methods to model a) the decline of CD4+ cell counts, b) the progression of other markers of infection, and c) the effects of treatment on the rates of change of CD4+ cell counts and other markers. Actions taken since meeting

6. The CDC HIV classification system is being revised to include indicators of immune status (i.e., CD4+ cell counts or percent) as well as clinical symptoms. This will fulfill recommendation 3.

7. Programs to facilitate the standardization of CD4+ cell testing, evaluate the effects of CD4+ cell-

count variability and measurement error, and make recommendations regarding specific quality-control procedures have been put in place under the aegis of PHS agencies.

8. Plans have been made to supplement serosurveys at chosen sentinel locations with assessments of immune status within the next year. This is related to recommendations 2 and 4.

9. Longini and Clark, in collaboration with staff at the Walter Reed Army Institute of Research, have developed a staged model for the decline in CD4+ cell counts in persons with HIV infection. In general, the results agree with the U.S. Army data summarized in this section. This partially fulfills recommendation 5.

AIDS CASE PROJECTIONS

AIDS case projections are based on the incidence of AIDS, adjusted for estimated reporting delays. The charge to the workshop group was to review methods for forecasting future AIDS cases and to recommend how AIDS case projections should be made. The 1986 and 1988 projections (1,2) were obtained by extrapolating recent trends in the incidence of AIDS. Recent changes in these trends, shown in Figures 1-3, indicate the need to reconsider the earlier projections. Interpretation of the change in trends of AIDS incidence is an important factor in the choice of a model for projecting AIDS cases and in the ultimate projected ranges.

Workshop participants concluded that the number of AIDS cases diagnosed in the United States will continue to increase through 1993 (Table 2). An estimated 41,500 cases diagnosed during 1989 eventually will be reported--a 19% increase over the corresponding count for 1988, greater than the earlier report of a 14% increase for a similar period based on less complete data (10). After adjustments for underreporting, it is estimated that 52,000-57,000 cases of AIDS will be diagnosed during 1990 and that this figure will rise to 61,000-98,000 cases diagnosed during 1993 (Table 2). The group also concluded that the number of AIDS cases diagnosed in the United States will continue to increase through 1993 for each of the current principal transmission categories (homosexual and bisexual men, IVDUs, persons infected through heterosexual transmission, and children infected perinatally; see Table 3). These projections include an adjustment for the estimate that approximately 85% of diagnosed AIDS cases (i.e., 85% of all persons with diagnosed diseases meeting the current surveillance criteria for AIDS) are eventually reported.

The current projections are lower than those made in 1988 (the midpoint of the current projected range is 10% lower for 1989 and 17% lower for 1992; see Table 4), reflecting the change in the trend in the incidence of AIDS that occurred in 1987. A discussion of possible reasons for the change in the rate of increase did not yield firm conclusions, but the group thought that the change was too abrupt to have been caused solely by past changes in HIV incidence.

The current range of projections was derived from extrapolation and from back-calculation, with two of the back-calculation models incorporating plausible estimates of the effect of currently available medical therapy and of the proportions of infected persons receiving therapy (see Appendices A and B). Predictions after 1990 are especially uncertain, however, because little information exists on the future extent and duration of the therapeutic effect of zidovudine, prophylactic therapy for Pneumocystis carinii pneumonia, or other treatments in delaying AIDS, or when these treatments began to be used extensively, and the number of persons receiving such treatments.

Recommendations

1. AIDS case projections should continue to be made and should be based on reported AIDS cases

adjusted for national underreporting. Projections should also be made for patient subgroups defined by geography, gender, race/ethnicity, and mode of HIV exposure.

2. Projections should be made by stage of disease for the number of living patients with HIV-associated health problems, with stage based on a clinical indicator such as CD4+ cell count.

3. Statistical methods used to project the future course of the epidemic should continue to be based on surveillance data. To improve projections, more data should be obtained on the completeness and timeliness of AIDS case reporting. More data are also needed on the incidence of HIV, the spectrum and natural history of HIV infection, the prevalence of types of behavior associated with HIV acquisition and transmission, and the effect and use of various types of therapy. These data should be obtained for both children and adults and for the major HIV-transmission categories.

4. Statistical methods should be developed for making more accurate AIDS case projections. These methods should incorporate empirical data on HIV incidence, effects of therapy, and changes in the incubation period.

Actions taken since meeting

1. Brookmeyer and Liao (24) have extended their back-calculation procedure to incorporate empirical estimates of recent HIV incidence. This fulfills recommendation 4 and is related to recommendation 2.

2. Longini and W.Y. Tan (Memphis State University) extended a model for the stages of HIV infection (25) to include effects of therapy. Longini, R. Byers (CDC), and Tan incorporated this extension into back-calculation (26). This work is related to recommendations 2 and 4.

3. CDC, in collaboration with selected health departments, is now conducting special surveillance projects to describe the spectrum of HIV-associated health problems among adults and children, the completeness of AIDS case and death reporting, and the extent of HIV-related morbidity and mortality not included in AIDS surveillance criteria. In addition, another project is being initiated to collect supplemental data through AIDS and HIV surveillance on social/economic status, drug use, sex behaviors, access to health services, and, for women, reproductive history. This will fulfill recommendation 3.

EFFECT OF THERAPY ON DISEASE PROGRESSION

This group was asked to estimate the impact of AIDS therapy on past and future incidence of AIDS. Getting that estimate required assessing the magnitude of the treatment impact and the prevalence of persons taking AIDS therapies (specifically, zidovudine and prophylactic therapy for P. carinii pneumonia), both currently and in 1987 when there was a decline in the rate of increase in numbers of diagnosed AIDS cases reported to CDC.

Data presented at the workshop indicated that the use of zidovudine initially reduces the risk of developing AIDS for some HIV-infected persons who are asymptomatic or mildly symptomatic but who have CD4+ cell counts of less than 500/mm3. Current data indicate that, in a clinical trial setting, the risk of progression to AIDS among treated patients is approximately one-third the risk for untreated patients (27). Although the use of zidovudine delays the onset of AIDS only temporarily, the therapeutic benefit may be extended by new types of therapy currently being evaluated.

The group's opinion was that access to AIDS/HIV drugs differs among population groups. Some

groups--such as homosexual men on the East and West Coasts--have greater access, whereas other groups--such as minority persons and IVDUs not in treatment programs--have much lower access. Data from the San Francisco City Clinic Study (conducted by the San Francisco Health Department and CDC) show that 73% of homosexual men who would most likely benefit from therapy (i.e., men who knew they were HIV-seropositive and who had CD4+ cell counts of less than 200 cells/mm3) were taking zidovudine in 1989 (28). No data were available to indicate the percentage of HIV-infected persons among low-access groups receiving zidovudine or other appropriate therapies.

Although the number of pediatric cases is comparatively small, members of the group thought that previous modeling exercises had not addressed differences in prognosis and therapies among children compared with others. Limited data suggest that symptomatic children who take zidovudine have favorable outcomes that are comparable to those for adults who take zidovudine. For example, a 2- to 3-fold reduction in deaths was observed among 20 children in a Phase I study of zidovudine. The proportion of children diagnosed as having HIV infection who are being treated with zidovudine is not known but probably does not exceed 50%. HIV-infected children are still a comparatively low-access group.

Data available at the workshop were insufficient to estimate the relative contribution of therapeutic interventions such as zidovudine or prophylactic therapy for P. carinii pneumonia to the slowing in the rate of increase among reported AIDS cases that occurred in the middle of 1987. Although therapy could substantially reduce the development of AIDS in the short term, there were few data available to the working group to indicate that zidovudine and prophylactic therapy for P. carinii pneumonia were widely used in 1987 by persons who had not yet developed AIDS, even among high-access groups. The group estimated that approximately 7% of HIV-seropositive, non-AIDS members of the Multicenter AIDS Cohort Study (MACS) were taking any drug for AIDS therapy or prophylaxis in 1987, although this figure may be modified or augmented on the basis of ongoing data analysis.

National reporting in 1987 was similar to or more complete than that in previous years, so underreporting was not thought to be a major contributor to the downturn in reported AIDS cases. However, increasingly more homosexual men and others with AIDS have been receiving ambulatory, out-of-hospital diagnosis and treatment. This trend may be causing some decrease in the completeness and/or timeliness of AIDS case reporting in some areas.

The observed change in trend in reported cases of AIDS may represent, at least in part, a true diminution in HIV infection among homosexual and bisexual men. The number of reported AIDS cases has begun to level off and/or decline among adult and pediatric transfusion recipients and persons with hemophilia, for whom HIV incidence drastically declined in the mid-1980s. The group thought that models assuming substantial infection rates after 1982 or 1983 might be inaccurate given the sharp drop in new infections among homosexual men among recruited cohorts in the 1980s, the greater than or equal to 50% decrease in rectal gonorrhea cases among men in several U.S. cities between 1982 and 1984, and various calculations that show a peaking of HIV infections among homosexual men as early as 1981. Despite the long incubation period from acquisition of HIV infection to development of symptoms of AIDS, one might still have expected to see some leveling in AIDS case trends among homosexual and bisexual men in San Francisco, Los Angeles, and New York by 1987. More conservative assumptions in back-calculation models may be useful to assess the robustness of any putative impact of treatment as well as other factors.

Future research needs to address several issues. Whether zidovudine, dideoxyinosine (ddI), and other new drugs might diminish the infectiousness of HIV-seropositive persons for their sex partners is unknown. If such drugs do reduce infectiousness, effective therapy could contribute to an eventual decrease in reported AIDS cases. Conversely, considerable data indicate that therapy (including that for

drug addiction) can substantially increase survival. Unless therapy reduces infectiousness, a larger pool of living patients with AIDS and other persons infected with HIV will increase the number of infectious persons and, without changes in behavior, could ultimately increase AIDS cases. Researchers need to use behavioral studies and models to address this possibility.

Recommendations

1. Data from on going studies on treatment effects should be released as soon as possible to allow the most current data to be incorporated into models of the epidemic.

2. Existing data regarding prevalence of use of HIV/AIDS therapeutic agents should be analyzed promptly.

Actions taken since meeting

1. Data from current cohort studies have been used to estimate the use of therapy by homosexual men at different stages of HIV infection (28,29). This fulfills recommendation 2.

2. Data from current studies funded by CDC, National Institutes of Health (NIH), and the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA), have been used to estimate the types of HIV/AIDS therapy used by persons with HIV infection (28-30).

3. CDC staff have begun efforts to estimate the proportion of HIV-infected children whose HIV infection has been diagnosed, by comparing AIDS case surveillance and HIV reporting with data from the national survey of childbearing women.

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