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May 15, 1995

MEMORANDUM FOR DISTRIBUTION LIST

FROM: Patsy Fleming, Director
Office of National AIDS Policy

SUBJECT: Developing the national plan

I want to thank all of you who attended our first meeting of the Interdepartmental Task Force on AIDS on January 25th and welcome those newly identified to participate in our efforts. It was a productive meeting. I hope we have laid the ground work for important cooperation and collaboration to meet the President's directive to have a national plan outlining the federal government's response to the HIV epidemic.

This memo summarizes what we discussed and outlines for you a proposed format for developing the national plan. I have also attached a list of attendees and others who have been designated as members of the task force by their agencies.

Structure and Function of the Task Force. It was generally agreed that the role of this task force is to assure coordination and communication among all government agencies working on AIDS – and to also assure that our resources are well focused and avoid duplication. The task force will be task-oriented and will meet only on an as-needed basis.

The Task Force will function largely through working groups. We have already agreed to form working groups in the following areas: prevention, research, services (including housing), international, and civil rights. It is our hope that in developing the national plan, review of the programs of the individual agencies can occur through the working groups.

Developing the plan. The President has asked for a national plan reflecting the goals and objectives of the federal government in combatting AIDS. It is our intention to develop this plan from the ground up – that each department will articulate its own plan through consultation within the department and, just as importantly, with constituency groups affected by its programs. Once the department plans are developed (see format discussion below), the relevant work groups of the task force will meet to integrate the plans and discuss programs and projects in common. Office of National AIDS Policy staff will work with the working groups and the full task force to assure a logical and accurate merging of these departmental efforts.

It is our goal to have department plans submitted to this office by June 30, 1995, with working group discussion and revisions occurring over the summer, with a final plan ready for review by the President's Advisory Council no later than September 1, 1995. It is critical that this process be completed by then so that we can integrate this effort into the FY 1997 budget.

Format for the plan. We propose a straight-forward approach to this plan. We want our first effort to be an accurate summation of the direction of current federal efforts, as well as to provide some guidance as to where additional resources might be directed. The plan will be arranged by the areas of our work groups (prevention, research, services, international, civil rights, and any others that might be relevant). Within each area, broad goals should be identified. For each goal we ask that you state objectives, action steps, programs that implement the actions steps (including a description of the program, resources in the FY 1995 estimated budget and the FY 1996 proposed budget, populations served, and constituency involvement in development of the program), and the unmet need. The first chart shows how this might be formatted. The second chart shows a fictitious example of how two prevention entries might be made.

Comments. We think this outline is workable and reflects the discussion we had at the meeting. We know there may be suggestions and questions, and we urge you to provide your feedback on this outline. Please call or fax your comments to Jeff Levi at 632-1090 by February 22nd. A final version of this outline will then be sent to you.

Please feel free to contact us as you undertake your work on this project. We will help in any way we can.

Also, feel free to contact Jeff or me if you feel there are issues that the task force should be addressing at any time in the future.

Thank you again for your commitment to this undertaking.

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GOAL: REDUCE THE NUMBER OF NEW INFECTIONS

[illegible]

THE WHITE HOUSE
WASHINGTON

MEMORANDUM FOR THE PRESIDENT

FROM: Patricia S. Fleming, Director, National AIDS Policy Office

SUBJECT: Update on Status of HIV/AIDS

Summary

In preparation for your July 28 meeting with the new Presidential Advisory Council on HIV and AIDS, the following is a briefing on the status of the epidemic and Federal policies related to the epidemic.

I State of the Epidemic

In mid-June, the nation entered the fifteenth year of the AIDS epidemic. Between 1981 and December 1994, the Centers for Disease Control and Prevention (CDC) report that a total of 441,000 cases of AIDS had been reported in the U.S. and an estimated 271,000 Americans had died as a result of complications related to HIV. In 1994 alone, nearly 81,000 cases of AIDS were reported to the CDC and an estimated 40,000 deaths occurred in that year. The CDC estimates that 40,000 Americans become infected with HIV each year and that between 800,000 and 1.2 million Americans are living with HIV.

The demographics of the epidemic have been shifting throughout the first fourteen years. While the early years of the epidemic were dominated by cases involving gay or bisexual men living in major urban centers (New York, San Francisco, and Los Angeles), it has now been reported in every state of the union. In 1994, the CDC reported that the greatest number of new AIDS cases were reported in the Southeast region.

AIDS is having an enormous impact on our nation's ability to prepare itself for the 21st century. The CDC recently reported that AIDS is now the leading cause of death among all Americans between the ages of 25 and 44. An estimated 52 percent of American workers are in this age group. As a result, it is estimated that, in 1995, AIDS will cause a loss of 1.1 million years of productive life.

While gay and bisexual men continue to represent the largest number of all AIDS cases, in 1994 they comprised less than half (44%) of all new cases, continuing a decline begun in the late 1980s. Among the populations being more heavily impacted are young men between 20 and 24 (53% of cases in 1994), women (18%), and heterosexual injecting drug users (24%). Communities of color are also being severely affected. African-Americans and Hispanics represent 40 percent of new cases in 1994. Most importantly, CDC estimates that more than 50 percent of all new cases are now related directly or indirectly to substance abuse, particularly the use of injectible drugs.

In terms of new infections, young people are comprising a much greater proportion than in the past. The National Cancer Institute estimates that one-half of all new infections occurs among people under age 25; one-quarter of infections occurs in people under 20. While the number of cases among children under 13 remains small (1,017 cases in 1994), that represents an 8 percent increase over 1993. Moreover, with the rising number of cases among women leads researchers to estimate that by the end of this decade, some 80,000 American children will be orphaned by AIDS.

The American epidemic is part of a global pandemic. The World Health Organization (WHO) recently estimated that since 1981, 4.5 million cases of AIDS have occurred around the world. Between June 1994 and June 1995, nearly 184,000 cases were reported, an increase of 19 percent over the previous 12-month period. WHO also estimates that between 18.5 million adults and 1.5 million children are living with HIV. Among the areas with the largest growth rates are the nations of southern and central Africa and the nations of South Asia. In some of these nations, as many as 50 percent of the population are infected.

II The Federal Response

The first twelve years of the Federal response to AIDS were marked by an often indifferent and hostile Executive Branch. The Reagan and Bush administrations frequently rejected the requests by health agencies for additional funding for AIDS research, prevention, and care. The Congress consistently increased the Administration requests.

During the 1992 campaign, you promised a "loud, clear, and consistent war on AIDS." In the first 30 months of your Administration you have delivered on that promise. Among the steps taken are:

- A 40% increase in funding for AIDS research, prevention, and care. That compares with a 3% increase in overall discretionary spending.
- Full funding of the Ryan White CARE Act (including the FY1996 request, funding has increased by 108%).
- Strengthening the Office of AIDS Research at the National Institutes of Health.
- Easing of Social Security disability rules to speed approval of eligibility.
- Creation of the Office of National AIDS Policy at the White House; the Presidential Advisory Council on HIV and AIDS; and the National Task Force on AIDS Drug Development.
- A 46% increase in funding for Housing Opportunities for People with AIDS.

III AIDS Research

There has been a substantial investment in AIDS-related research at the National Institutes of Health (NIH). In part, the size of this investment was necessary because of the fact that there was no existing AIDS research infrastructure at the NIH or at the major academic health centers that conduct much of the government-sponsored research. As a result, there were significant annual increases provided by the Congress in NIH AIDS research funding during the 1980s. Since then, however, the increases have been more in line with overall increases in NIH funding.

Creation of the Office of AIDS Research at NIH has helped to focus research efforts. It has been termed, by some, as a functional equivalent of a "Manhattan Project" for AIDS research. OAR Director Dr. William Paul has published a well-received AIDS research plan which is providing a focused, targeted approach to HIV/AIDS research.

The investment in AIDS research has produced some important advances in terms of understanding HIV, the treatment of opportunistic infections, and the development of drugs to delay the onset of full-blown AIDS. Due in great part to Federally-sponsored research, persons with AIDS are now living twice as long as they did a decade ago. While several AIDS vaccines are in the preliminary stages of research, none is close to approval. There have been several recent advances that have improved the immediate outlook. They include:

- **Basic Research.** Based on a consensus among researchers and affected communities, Dr. Paul has created a greater emphasis on basic research into HIV. One important breakthrough in this area indicated that the body's immune system begins to confront HIV immediately after infection. This indicates that early treatment of HIV infection can have a greater impact on life expectancy.
- **Perinatal Transmission.** The results of AIDS Clinical Trials Group 076 showed that we can diminish the risk of perinatal transmission from 25% to 8% by giving AZT to a pregnant woman early in her pregnancy, during delivery, and to her newborn for six weeks. Not only is this the first proof that we can block HIV transmission, it's the first time a drug has been shown to block transmission of any retroviral disease.
- **Long-Term Non-Progressors.** A small subset of HIV+ people (5-7%) live with no clinical manifestations of their infection. NIH is studying the characteristics of non-progressors to see what factors might contribute to this reaction to see if it is possible to induce the same reaction in others.
- **Promising Therapies.** There are several emerging therapies that show promise. Several versions of protease inhibitors are in the final stages of human testing. These drugs may block replication of HIV and allow the human body to rebuild its damaged immune system. Also, early tests of Interleukin-2 therapy indicate that IL-2 may replenish the human immune system.

IV AIDS Prevention

In the absence of a vaccine or cure, education and prevention are our best hope for controlling the transmission of HIV. Through the CDC, the Federal government spends nearly \$600 million a year in partnership with states, local government, and community-based organizations to develop and disseminate education materials and programs. These efforts have been quite successful in terms of increasing public awareness of AIDS, the methods of HIV transmission, and the means to prevent such transmission. There have been some real "success stories" with prevention, especially among gay men, where changes in behavior were initiated by community organizations and have helped to reduce the incidence of HIV in this population.

However, there has been mixed success at permanently changing behavior associated with HIV transmission (i.e. unprotected intercourse, sharing of contaminated needles and "works"). A major challenge is to find ways to sustain behavioral changes over a lifetime (e.g. consistent use of condoms during intercourse). Effective prevention programs must be ongoing, so that they can reach new generations while reinforcing messages with older groups. These messages must also be targeted so that segments of society will recognize the applicability of the message. And they must be linked to other services -- substance abuse treatment, in particular.

Among the positive developments are:

- Establishment of a community planning process that involves local groups in the design and implementation of prevention programs. This is a "bottom up" approach as opposed to a "top down" approach.
- The Prevention Marketing Initiative, which features public service announcements encouraging sexual abstinence and the correct and consistent use of latex condoms.
- The elimination of restrictive rules on what can and can't be discussed in prevention materials.

V AIDS Treatment and Care

Given our knowledge about the behavior of HIV in the human body, it is critical that people who are infected be entered into a continuum of care as quickly as possible. Early in the epidemic, there was little that physicians could do for patients diagnosed with HIV or AIDS. As researchers discovered treatments to delay the onset of full-blown AIDS and to treat the opportunistic infections associated with HIV, the ability of the health care system to extend the lives of people living with HIV/AIDS improved dramatically. There were two major impediments to getting this care to the people who needed it. First, many physicians and other health care professionals knew little about these new treatment advances. Second, a significant percentage of people with AIDS did not have private health insurance.

A major source of care for people with HIV/AIDS is the Medicaid program. The Health Care Financing Administration (HCFA) estimates that more than 50 percent of people with AIDS receive Medicaid benefits. Among children with AIDS, that figure is 92 percent. Another 20 percent of people living with AIDS have private health insurance. The remaining 30 percent are uninsured.

In 1990, Congress enacted the Ryan White Comprehensive AIDS Resources Emergency (CARE) Act, which authorized funds to provide outpatient care and support services to people living with HIV and AIDS. Under its four titles, the CARE Act provides funds to (1) cities that are heavily affected by AIDS; (2) all states; (3) community-based clinics; and (4) other nonprofit organizations. In 1994, the CARE Act provided care to more than 200,000 uninsured and underinsured people living with HIV or AIDS, paid the prescription drugs bills of 75,000 individuals, covered the cost of counseling and testing for nearly 100,000 people, provided early care for an estimated 85,000 HIV-infected individuals, and paid the medical costs of 15,000 women and children enrolled in AIDS-related clinical drug trials.

Also in 1990, Congress enacted the Housing Opportunities for People with AIDS (HOPWA) program to assist people living with HIV and AIDS retain or obtain affordable housing. In addition to providing people and their families with housing, HOPWA helps to improve the health status of people with AIDS by reducing the need to balance the cost of housing versus the cost of care and prescription drugs. Earlier this year, the House voted to rescind the entire \$186 million HOPWA appropriation for FY1995. Following efforts by the Administration, that figure was reduced to \$30 million in the legislation you vetoed. The current version of the rescissions bill cuts \$15 million in HOPWA funds.

VI The Advisory Council

On June 11, you signed an Executive Order directing the creation of the Presidential Advisory Council on HIV and AIDS. Twenty-three members of the 30-member council were named on June 12. (A list of members is attached).

Advisory Council members are expected to present you with recommendations in the following subject areas: Leadership, Prevention, Research, Care, Medicaid, and Drug Development.

- **Leadership.** The AIDS community and members of the Council are looking for a greater level of visible Presidential leadership. The focus of this criticism is less about the policies you have advocated than about the use of your voice.
- **Research.** While Council members are generally supportive of the funding increases for AIDS research and the strengthening of the Office of AIDS Research, some feel you have not fulfilled your promise of a "Manhattan Project" for AIDS research. Members are also quite concerned by the recent decision by the House Appropriations Committee not to provide a single appropriation to the OAR for FY1996.

- **Prevention.** Council members are generally pleased with the direction of prevention policy, in particular, the community planning process. Some would like to see a more aggressive approach, including more targeted efforts to reach young gay men, support for clean needle exchange programs, and a greater integration of AIDS prevention and substance abuse prevention programs.
- **Care.** Council members are very pleased with the investments in the Ryan White CARE Act but are concerned about the future of HOPWA and the potential for weakening amendments to the CARE Act reauthorization.
- **Medicaid.** Council members are quite alarmed by the proposals in Congress to sharply reduce Medicaid funding and convert that program to a state-run block grant since more than 50 percent of people living with AIDS rely on Medicaid for their health benefits. Managed care programs traditionally have not served the chronically ill well due to a lack of specialists and limits on benefits.
- **Drug Development/Approval.** While drug approval time is at an all-time best, Council members are concerned by the continuing slow pace of AIDS drug development. Of particular concern is the emerging class of drugs known as protease inhibitors. Manufacturers of these drugs will make them available only to a small number of people prior to FDA approval because they do not have the manufacturing capacity to make them available more broadly.

VII Attachments

- Membership of the Presidential Advisory Council on HIV and AIDS.
- Questions and Answers

Questions and Answers

Why haven't you been more vocal and more visible in the fight against AIDS?

I have attempted to use my office to advocate for a greater government response to AIDS while reminding the American people of the importance of this matter and the need for greater compassion for people living with this disease. I would say we've been quite successful in obtaining more funding for AIDS research, prevention, and care and improving the quality of those programs. I do intend to speak out more on this issue and use the power of the "bully pulpit."

What about your promise for a Manhattan Project of AIDS research?

When I made that promise in 1992, I felt that our AIDS research efforts lacked the kind of focus that a Manhattan Project brings. I believe we have accomplished that through the combination of a much-strengthened Office of AIDS Research at NIH, the development of a comprehensive plan by Dr. Paul, and a 26 percent increase in AIDS research funding in two years. I would say this is the equivalent of a "Manhattan Project."

You promised to lift the ban on immigration of HIV-infected individuals yet you signed a bill continuing that policy. Why?

My Administration did attempt to lift the immigration ban. However, the Congress voted overwhelmingly to maintain the prohibition begun under the Reagan Administration. The Justice Department has tried to make sure that waivers are provided for important meetings and events like the Gay Games in New York.

The National AIDS Commission recommended the use of Federal funds for clean needle exchange programs yet your Administration refuses to fund them. Why?

As you know, the Congress has created some stringent rules on the use of Federal dollars for that purpose. So far, we have been unable to show that we can meet those standards. We will continue to study this issue.

Your policies regarding gays and lesbians have been severely criticized. Are your gestures toward AIDS policy a smoke screen for those failures?

Well, first of all, I would have to say that this has been the most inclusive Administration in our nation's history. We've made it clear that we cannot afford to waste anyone's skills and talents. Now we haven't gotten everything we want but I think our successes far outweigh our failures. Regarding AIDS policy, the war on AIDS is everyone's war. And, as I reminded Senator Helms earlier this month, AIDS is not just a gay issue. If we are to win it, we must all engage in it.

Is this Council just window-dressing? What about the recommendations of the last AIDS Commission?

The Council includes experts in all areas of this epidemic who can bring us "real-world" expertise on HIV and AIDS. I believe it is very important for government to listen to the people it serves. As to the previous AIDS Commission, I took those recommendations very seriously and we have worked hard to carry out their proposals. More than half of the 30 recommendations were implemented in the first few months of this Administration. Most of the rest were incorporated into the Health Security Act. I continue to work with the Congress on a package of health care reforms that would address many of these issues.

Why isn't the AIDS Czar a member of the Cabinet?

This is the first time that any President has created an office within the White House to deal with a single disease. It reflects my desire to have an expert on my staff who can keep me up to date on the epidemic and help drive the Administration's response. Patsy Fleming has done a tremendous job and is a very valuable member of my staff. She has my ear and she has access to all members of the Cabinet. We all share a commitment to do everything possible to defeat this disease.

Senator Helms and others say we're spending too much on AIDS compared with what we spend on cancer and heart disease. How do you respond?

I don't think that kind of divisiveness serves anyone's interests. People with AIDS deserve our compassion and they deserve our help. The investment in AIDS research is also an investment in science, including cancer research. We have to continue to make this investment if we are ever to find a cure to AIDS.

What is your position on the proposal to require testing of pregnant women and newborns?

It's remarkable that we now know how to block transmission of the AIDS virus from mothers to infants. The key is to get more women into prenatal care and to get all pregnant women to be tested and to understand the importance of taking AZT if they are positive. The Public Health Service guidelines are an excellent way to accomplish this and I'm very encouraged by the Senate's approval of the Kassebaum Amendment. These guidelines must be implemented aggressively so that they become the standard of care.

The Housing Opportunities for People with AIDS (HOPWA) program seems to be in danger. What will you do to save it?

We recognize that people with AIDS often have a difficult time continuing to pay their rent and many times end up homeless. HOPWA was created to keep people with AIDS in their homes and with their families. This has been a very successful program and we should build on that success. I will continue to fight for funding for this critical program.

You have proposed eliminating HOPWA and folding it into a block grant. How is that different from the Republican plan?

There are two important differences. First, my proposal continues to increase funding for HOPWA and other housing programs for disabled persons. The Republican plan would reduce funding by 25 percent. Second, my proposal gives HOPWA grantees two years to adjust to the new performance partnership grant. The Republican proposal would allow no time to adjust. It is vital that we continue to provide the resources needed for this important program.

The Pentagon continues to make plans to eliminate its AIDS research portfolio. Will you prevent this from happening?

It's important that we make sure that we explore all avenues of research and that we continue the clinical trials that are being conducted at the Department of Defense. We are looking into ways to achieve both of those goals and I believe we will be successful.

Drug manufacturers plan to make protease inhibitors available to only a small number of people with AIDS prior to FDA approval. Can you do something to make these drugs more available?

I would be very reluctant to interfere in that process regarding a specific drug or product. I will ask Dr. Kessler and Dr. Paul to look at ways to avoid this supply problem in the future. The key is that we must continue our investment in research so that more drugs are developed and made available as quickly as possible. The drug approval process is the fastest its ever been and we hope to make it even faster.

The HIV/AIDS Pandemic -- Why Continued Funding is Needed

■ *HIV/AIDS: A Continuing Public Health Crisis*

The pandemic of HIV infection and AIDS continues to grow -- more persons in every geographic area and age group are becoming infected every day. Unlike cancer and heart disease, AIDS is an **expanding** public health threat. Since 1987, AIDS has gone from being the 15th ranked cause of death to the 8th -- it is now the leading cause of death for persons between the ages of 25 and 44. Since the disease was identified less than two decades ago, AIDS has killed over a quarter of a million Americans.

- In the United States, one person dies from AIDS every 8 minutes.
- An estimated 1 in 300 Americans are infected with HIV, the virus that causes AIDS.
- The CDC reports that in 1994 alone there were over 80,000 newly diagnosed cases of AIDS.
- One in four new HIV infections occurs among Americans under the age of 20. One in two new infections occurs among people under 25.
- The World Health Organization (WHO) estimates that by the end of the century, 30 - 40 million people will have been infected with HIV worldwide.

■ *Economic Impact of the Epidemic*

Unlike other leading causes of death, AIDS is a disease that strikes people in the prime of life -- it disproportionately kills the younger people during their most productive years.

- AIDS is now **the leading cause of death** for Americans between the ages of 25 and 44.
- Deaths due to AIDS are disproportionately disruptive to society. Persons aged 25-44 constituted 54% of the U.S. civilian labor force in 1992.
- Premature deaths due to AIDS result in the loss of many productive years of life and deprive young children of their parents. In terms of years of potential life lost (YPLL), in 1994 AIDS ranked fourth among all leading causes of death:

Cancer	1,874 YPLL (in thousands)
Unintentional Injuries	1,796
Heart Diseases	1,324
HIV/AIDS	1,056

■ ***AIDS is not just an urban problem.***

AIDS cases have been reported in all 50 states, the District of Columbia, Puerto Rico, and the American territories. The HIV/AIDS pandemic is spreading in rural areas and the south -- these are areas that to date have been less affected by the pandemic.

- In 1994, 35 percent of new AIDS cases were reported in Southern states.
- While most cases are still reported from urban areas, the rate of reported AIDS cases in non-metropolitan areas is increasing faster than urban areas.
- In six counties of North Carolina, AIDS was reported to be the leading cause of death among residents aged 20-29 years.

■ ***AIDS is spreading rapidly among women and children.***

The proportion of cases among women has increased steadily during the past decade -- and the epidemic in children is closely associated with the epidemic in women.

- In 1994 alone, over 14,000 women were diagnosed with AIDS -- that's one quarter of the AIDS cases reported among women since 1981.
- As of 1993, 21,000 women have died from AIDS.
- Women now comprise 21 % of reported HIV-infection cases.
- In 1994 alone, over 1,000 new pediatric AIDS cases were reported -- an 8% increase from the number reported in 1993.
- An estimated 80,000 American children will have been orphaned by AIDS by the end of this decade.

■ ***Spending for AIDS and Other Public Health Threats***

AIDS is an increasing public health threat. Since its discovery in 1981, AIDS has consistently risen in the rankings as a cause of death, while cancer and heart disease rates have been comparatively stable.

- Direct lifetime medical care after diagnosis for an HIV-infected person costs more than for patients with cancer or heart disease, specifically:

\$ 61,211 for Heart Disease*

\$ 25,000 to 84,000 for Cancer**

\$119,000 for HIV/AIDS***

*for 5 years of care after initial heart attack. Source: *American Journal of Cardiology*, 1990.

**depending on stage diagnosed -- early or late. Source: Swartz & Rollins, *Business and Health*, 1985, 85, 24-6.

***Source: *Journal of the American Medical Association*, July 28, 1993.

- Spending for AIDS research is not out of balance with other diseases. Within the Public Health Service (PHS), research funding for cancer exceeded research on HIV/AIDS. In FY 1995, the PHS is slated to spend:

\$2.0 billion for cancer research,
\$1.5 billion for HIV/AIDS research,
\$805 million for heart disease research.

- Overall HHS spending for research, treatment, prevention, and income supplements is significantly greater for cancer, and heart disease than for AIDS. In FY 1995 HHS is slated to spend:

\$38.0 billion for heart disease
\$17.5 billion for cancer
\$ 6.0 billion for AIDS

■ *AIDS Research -- Collateral Benefits*

The nation's investment in HIV-related research is providing important benefits for understanding and treating other diseases. For example:

- AIDS research has accelerated study of the human immune system. This basic immunologic information is being applied to research to better understand and treat many other diseases, such as cancer and autoimmune diseases, including systemic lupus erythematosus, type I diabetes mellitus, rheumatoid arthritis, and multiple sclerosis. AIDS research also contributes to the prevention of other infectious diseases.
- HIV research involving the blood/brain barrier has led to a better understanding of the mechanisms by which infectious agents spread into the nervous system. This research has valuable implications for research on Alzheimer's disease, dementia, multiple sclerosis, neuropsychological disorders, encephalitis, and meningitis.
- Before the AIDS epidemic, little investment was made in research to treat viral diseases. Studies to develop anti-HIV therapies has led to drug development against many other disease-causing viruses.
- Research on HIV-related wasting has provided important information for research on nutritional disorders, metabolic abnormalities and gastrointestinal dysfunctions.



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MORBIDITY AND MORTALITY WEEKLY REPORT

- 849 First 500,000 AIDS Cases — United States, 1995
- 853 Deaths Associated with a Purported Aphrodisiac — New York City, February 1993–May 1995
- 861 Update: Influenza Activity — United States and England, 1995–96 Season
- 862 Notice to Readers

First 500,000 AIDS Cases — United States, 1995

As of October 31, 1995, a total of 501,310 persons with acquired immunodeficiency syndrome (AIDS) had been reported to CDC by state and territorial health departments; 311,381 (62%) had been reported as having died. The AIDS surveillance case definition was substantially expanded in late 1987 and again in 1993 to reflect increased knowledge of the natural history of human immunodeficiency virus (HIV) and to remain consistent with the clinical management of HIV disease (1,2). This report presents rates of reported AIDS cases for 1994 and describes the temporal changes in the characteristics of persons reported with AIDS during three periods corresponding to changes in the AIDS case definition—1981–1987, 1988–1992, and 1993–October 1995—and how this information can be used to plan local, state, and national prevention programs.*

Of the cumulative AIDS cases, 50,352 (10%) were reported during 1981–1987, 203,217 (41%) during 1988–1992, and 247,741 (49%) during 1993–October 1995. The proportion of AIDS cases among females increased from 8% of cases reported during 1981–1987 to 18% during 1993–October 1995 (Table 1). The proportion of cases among whites decreased from 60% to 43%, and the proportion among blacks and Hispanics increased from 25% to 38% and from 14% to 18%, respectively. During 1994, the rates per 100,000 population for blacks and Hispanics (101 and 51, respectively) were substantially higher than rates for whites (17), American Indians/Alaskan Natives (12), and Asians/Pacific Islanders (6).

The proportion of cases among persons who reported injecting-drug use increased from 17% during 1981–1987 to 27% during 1993–October 1995, and the proportion of cases attributed to heterosexual transmission increased from 3% to 10%. Cases among men who have sex with men decreased from 64% to 45%.

During 1994, the rates per 100,000 population for reported AIDS cases were 48 in the Northeast, 31 in the South, 29 in the West, and 13 in the Midwest.[†] However,

*Single copies of this report will be available free until November 22, 1996, from the CDC National AIDS Clearinghouse, P.O. Box 6003, Rockville, MD 20849-6003; telephone (800) 458-5231 or (301) 217-0023.

[†]Northeast=Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont; Midwest=Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin; South=Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia; West=Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming.

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MMWR

November 24, 1995

AIDS Cases — Continued

TABLE 1. Number and percentage of persons with AIDS, by selected characteristics and period of report — United States, 1981–October 1995

Characteristic	1981–1987		1988–1992		1993–October 1995		Cumulative	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Sex								
Male	46,317	(92.0)	177,807	(87.5)	204,356	(82.5)	428,480	(85.5)
Female	4,035	(8.0)	25,410	(12.5)	43,383	(17.5)	72,828	(14.5)
Age group (yrs)								
0–4	653	(1.3)	2,766	(1.4)	2,013	(0.8)	5,432	(1.1)
5–12	100	(0.2)	669	(0.3)	616	(0.2)	1,385	(0.3)
13–19	199	(0.4)	758	(0.4)	1,343	(0.5)	2,300	(0.5)
20–29	10,531	(20.9)	38,662	(19.0)	41,861	(16.9)	91,054	(18.2)
30–39	23,269	(46.2)	92,493	(45.5)	111,992	(45.3)	227,754	(45.4)
40–49	10,491	(20.8)	47,088	(23.1)	64,990	(26.2)	122,569	(24.4)
50–59	3,890	(7.3)	14,537	(7.2)	18,413	(7.5)	36,640	(7.3)
≥60	1,419	(2.8)	6,244	(3.1)	6,513	(2.6)	14,176	(2.8)
Race/Ethnicity								
White, non-Hispanic	30,104	(59.8)	102,551	(50.5)	105,516	(42.6)	238,171	(47.5)
Black, non-Hispanic	12,794	(25.4)	63,319	(31.2)	94,158	(38.0)	170,271	(34.0)
Hispanic*	7,039	(14.0)	35,213	(17.3)	45,135	(18.2)	87,387	(17.4)
Asian/Pacific Islander	309	(0.6)	1,339	(0.7)	1,809	(0.7)	3,457	(0.7)
American Indian/ Alaskan Native	67	(0.1)	433	(0.2)	783	(0.3)	1,283	(0.3)
HIV-exposure category								
Men who have sex with men	32,246	(64.0)	110,934	(54.8)	111,257	(44.9)	254,437	(50.8)
Injecting-drug use	8,639	(17.2)	49,093	(24.2)	67,708	(27.3)	125,440	(25.0)
Men who have sex with men and inject drugs	4,193	(8.3)	14,252	(7.0)	13,984	(5.6)	32,429	(6.5)
Hemophilia	505	(1.0)	1,744	(0.9)	2,009	(0.8)	4,258	(0.8)
Heterosexual contact	1,248	(2.5)	12,335	(6.1)	24,958	(10.1)	38,541	(7.7)
Transfusion recipients	1,285	(2.6)	3,894	(1.9)	2,521	(1.0)	7,700	(1.6)
Perinatal transmission	608	(1.2)	3,084	(1.5)	2,432	(1.0)	6,124	(1.2)
No risk reported	1,628	(3.2)	7,881	(3.9)	22,872	(9.2)	32,381	(6.4)
Region†								
Northeast	19,544	(38.8)	62,282	(30.6)	74,769	(30.2)	156,595	(31.2)
Midwest	3,770	(7.5)	20,352	(10.0)	24,914	(10.1)	49,036	(9.8)
South	12,960	(25.7)	65,926	(32.4)	86,462	(34.9)	165,348	(33.0)
West	13,550	(26.9)	46,675	(23.0)	53,729	(21.7)	113,954	(22.7)
U.S. territories	516	(1.0)	7,889	(3.9)	7,566	(3.1)	15,971	(3.2)
Vital status								
Living	2,779	(5.5)	32,144	(15.8)	155,006	(62.6)	189,929	(37.9)
Deceased	47,573	(94.5)	171,073	(84.2)	92,735	(37.4)	311,381	(62.1)
Total‡	50,352	(100.0)	203,217	(100.0)	247,741	(100.0)	501,310	(100.0)

*Persons of Hispanic origin may be of any race.

†Northeast=Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont; Midwest=Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin; South=Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia; West=Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming.

‡Includes persons for whom sex, race/ethnicity, or region are missing.

AIDS Cases — Continued

during 1988–1992 and 1993–October 1995, the largest numbers of cases (65,926 and 86,462, respectively) were reported from the South, which also accounted for the largest proportionate increase of reported cases (31%). The proportionate increases in reported cases from 1988–1992 to 1993–October 1995 for the Midwest, Northeast, and West were 22%, 20%, and 15%, respectively.

During 1993–October 1995 in the South and Midwest, higher proportions of cases among adolescents and young adults (aged 13–29 years) occurred in small (50,000–499,999 population) metropolitan statistical areas (MSAs) and non-MSAs (rural areas) (27% and 24%, respectively) compared with 9% in the Northeast and 11% in the West. During this time period, among cases in adolescent and young adult men who have sex with men, 25% of 8481 cases in the South occurred in persons who resided in small MSAs and rural areas, 21% of 2670 in the Midwest, 9% of 3311 in the Northeast, and 9% of 5706 in the West. Among adolescent and young adult injecting-drug users, 30% of 531 cases in the Midwest occurred among persons residing in small MSAs and rural areas, 23% of 2370 in the South, 17% of 930 in the West, and 8% of 3304 in the Northeast. The proportion of cases among adolescents and young adults residing in small MSAs and rural areas that resulted from heterosexual transmission was highest in the South (32% of 2842), followed by the Midwest (22% of 678), the West (18% of 691), and the Northeast (7% of 1745).

During 1993–October 1995, most AIDS cases among adolescent and young adult men who have sex with men occurred among whites in all four regions (Midwest, 57%; West, 56%; South, 49%; and Northeast, 42%). Black adolescent and young adult men who have sex with men accounted for 39% of cases in the South, 37% in the Midwest, 36% in the Northeast, and 14% in the West. These proportions were higher than those for cases among black adolescent and young adult men who have sex with men reported during 1988–1992 (South, 31%; Midwest, 30%; Northeast, 31%; and West, 12%).

Reported by: Div of HIV/AIDS Prevention, National Center for Prevention Svcs, CDC.

Editorial Note: The World Health Organization estimates that 18 million adults and 1.5 million children have been infected with HIV, resulting in approximately 4.5 million AIDS cases worldwide (3). The theme for the 1995 World AIDS Day (December 1) is "Shared Rights, Shared Responsibilities." The findings in this report document both the magnitude and evolving nature of the AIDS epidemic in the United States, and underscore that HIV-prevention programs must be planned and implemented collaboratively by persons with diverse skills, training, and experience.

In addition to describing the overall magnitude of the epidemic—approximately one half million cases, nearly half of which have been reported since 1993—this report highlights changes in the epidemiologic patterns during 1993–October 1995 compared with those during earlier periods. In particular, although men who have sex with men continue to account for the largest proportion of cases, the AIDS epidemic is increasing more rapidly among injecting-drug users and persons infected through heterosexual contact with a partner at risk for or known to have HIV infection or AIDS (4,5). The increase in AIDS cases resulting from heterosexual transmission also is reflected in the increase in cases reported among women. The proportions of AIDS cases reported during 1993–October 1995 that are attributed to these risk behaviors will increase as records of persons who were reported initially without risk are reviewed and the risk is identified (6). Geographic patterns also have changed, as

AIDS Cases — Continued

reflected by increases occurring among persons in the South. Finally, regardless of transmission mode or region, the epidemic continues to affect blacks and Hispanics disproportionately.

Although the AIDS epidemic in the United States was recognized initially in the Northeast and West (7), and rates remain highest in the Northeast, the findings from AIDS surveillance document that the greatest proportionate increases in the HIV epidemic have occurred in the South and Midwest—areas that account for the largest proportion of the total U.S. population. These regional variations, especially in adolescents and young adults, underscore the importance of developing HIV-prevention programs based on local trends in the epidemiology of HIV transmission. In the South and Midwest, more detailed characterization of the epidemiologic patterns in small cities and rural areas is particularly important for developing effective regionwide prevention programs.

The disproportionate impact of the epidemic among racial/ethnic minorities is reflected by rates of reported AIDS cases that are six and three times higher for blacks and Hispanics, respectively, than for whites. Rates for HIV infection and the proportions of men who have sex with men and injecting-drug users with AIDS who are black and Hispanic also vary substantially by region (8). For example, Hispanics account for lower proportions of reported cases of AIDS among adolescents and young adult men who have sex with men in the Midwest and South than in the Northeast and West. Because race and ethnicity are not risk factors for HIV transmission, programs to prevent HIV transmission among racial/ethnic minorities should be based on underlying social, economic, and cultural factors that influence risk behaviors (8).

Because of the regional and local variations in the AIDS epidemic in the United States, HIV-prevention efforts must be directed at the local level. In 1993, a CDC advisory committee review of HIV-prevention programs emphasized the importance of 1) enhancing the capacity of local and state agencies to collect and analyze information relevant to the specific and unique aspects of HIV transmission in their communities, 2) strengthening the behavioral and social science bases of HIV-prevention activities, and 3) ensuring that HIV-prevention strategies and interventions reflect the preferences and needs of the affected communities for whom they are intended (9). As a result, in 1994, CDC initiated the HIV Prevention Community Planning process (10) that has provided resources for collaboration between health departments and planning groups that are representative of the local communities. These resources facilitate HIV-prevention programs that are based on scientific data (including data from HIV/AIDS surveillance, seroprevalence surveys, vital statistics, and behavioral research) and knowledge of the community norms and practices. This approach is consistent with the focus of World AIDS Day and emphasizes the necessity of shared participation in HIV-prevention planning and program implementation.

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AIDS Cases — Continued

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**Deaths Associated with a Purported Aphrodisiac —
New York City, February 1993–May 1995**

During February 1993–May 1995, the New York City Poison Control Center (NYCPCC) was informed about onset of illness in five previously healthy men after they ingested a substance marketed as a topical aphrodisiac; four of the men died. These cases were investigated by the New York City Department of Health, the New York City Department of Environmental Protection, and the Food and Drug Administration (FDA). Four cases were referred to the NYCPCC and one case to the New York City medical examiner's office. The decedents died from cardiac dysrhythmias, and all five patients had measurable levels of digoxin* detected in their serum. Digoxin had not been prescribed for therapeutic purposes for any of these patients, and none had medical conditions associated with endogenous digoxin-like immunoreactive substances. The purported aphrodisiac contains bufadienolides, naturally occurring cardioactive steroids that have digoxin-like effects. This report describes three of the five case reports, summarizes the investigations of the five cases, and underscores the health risks associated with inappropriate use of preparations containing digoxin-like substances.

Case 1

On February 23, 1993, a 26-year-old man ingested one piece of the topical aphrodisiac. Several hours after ingestion, he had onset of vomiting, abdominal pain, and weakness. Sixteen hours after ingestion, he sought medical care at an emergency department (ED). On examination, his blood pressure was 94/60 mm Hg; heart rate, 90 beats per minute (regular); respiratory rate, 16 per minute; and temperature, 98.3 F (36.8 C). Initial laboratory test results included sodium of 135 mEq/L (normal: 135–147 mEq/L), potassium of 8.4 mEq/L (not hemolyzed) (normal: 3.5–5.0 mEq/L), chloride of 102 mEq/L (normal: 95–105 mEq/L), bicarbonate of 18 mEq/L (normal: 22–28 mEq/L), urea nitrogen of 18 mg/dL (normal: 8–18 mg/dL), creatinine of 3.2 mg/dL (normal: 0.6–1.2 mg/dL), and glucose of 164 mg/dL (normal: 70–110 mg/dL). Analysis of arterial blood samples obtained during administration of oxygen revealed a pH of 7.2, pCO₂ of 36 mm Hg, and pO₂ of 519 mm Hg.

Based on the laboratory results, toxic ingestion was diagnosed, and the patient was treated empirically for hypotension and hyperkalemia. His cardiac rhythm deteriorated from normal sinus rhythm to atrial fibrillation to progressive sinus bradycardia.

*A cardiac glycoside obtained from the leaves of *Digitalis lantana*.

HIV/AIDS

Surveillance Report

U.S. HIV and AIDS cases reported through June 1995

Mid-year Edition Vol. 7, No. 1

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Acquired immunodeficiency syndrome (AIDS) is a specific group of diseases or conditions which are indicative of severe immunosuppression related to infection with the human immunodeficiency virus (HIV).

Single copies of the *HIV/AIDS Surveillance Report* are available free from the CDC National AIDS Clearinghouse, P.O. Box 6003, Rockville, MD 20849-6003; telephone 1-800-458-5231 or 1-301-217-0023. Individuals or organizations can be added to the mailing list by writing to MASO/MSB/IDS, CDC, Mailstop A-22, 1600 Clifton Rd., N.E., Atlanta, GA 30333. Internet users may obtain an electronic copy of the *Report* by accessing gopher.niaid.nih.gov. Confidential information, referrals, and educational material on AIDS are available from the CDC National AIDS Hotline: 1-800-342-2437, 1-800-344-7432 (Spanish access), and 1-800-243-7889 (TTY, deaf access).

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*Pending approval by the Department of Health and Human Services.

About this report

Through June 1995, nearly half a million (476,899) persons have been reported with AIDS. The expanded AIDS surveillance case definition (implemented on January 1, 1993) continues to influence the pattern of AIDS diagnosis and reporting. In the first half of 1995, 37,142 AIDS cases were reported. Although this number exceeds the 23,896 cases reported in the first half of 1992, before the case definition was expanded, it is less than the 61,887 and 40,457 cases reported in the first halves of 1993 and 1994, respectively. Trends in reporting of AIDS cases are expected to continue to stabilize gradually over the next several reporting periods as the surge in cases caused by the expanded definition continues to wane.

Analysis of the absolute numbers of cases reported each year, as presented in this report, continues to provide valuable information on the magnitude of the epidemic in affected communities. The data provide an important profile of young (13 to 24 years) men and women with HIV infection and AIDS, and demonstrate the need for prevention strategies appropriate for these age groups (see Tables 7 and 20). They also profile the characteristics of children with HIV and AIDS, in whom nearly all recent HIV infections occurred perinatally, and emphasize that, to prevent HIV in children, prevention programs need to assist women in reducing their risk of acquiring HIV infection by reducing high risk drug-injection or sexual activities (see Tables 6 and 19). These data will assist states in monitoring the impact of current recommendations to reduce HIV transmission to children through counseling, voluntary testing, and prenatal care services for women.

The expansion of the case definition artifactually distorted the AIDS epidemic curve. Fluctuation in the number of reported cases in recent years has complicated the interpretation of trends in the absolute number of reported cases. However, comparing proportions and relative rates over time permits trends to be monitored. For example, in the two most recent 12-month periods, about 10 percent of persons with AIDS were residents of small metropolitan areas (50,000 to 500,000 population), and about 6 percent were residents of non-metropolitan areas (see Table 2). These percentages are consistent with those reported for 1992 (10 percent and 6 percent, respectively), before the case definition was expanded. They not only reflect the emergence of AIDS outside large metropol-

itan areas (500,000 or more population), but also illustrate that the epidemic remains disproportionately concentrated in large metropolitan areas, where AIDS incidence rates are consistently 2 to 3 times higher than in small metropolitan areas, and about 5 times higher than in non-metropolitan areas.

To monitor trends in the incidence of AIDS-defining opportunistic illnesses (AIDS-OIs), CDC is using analytic methods that adjust for the case definition expansion by using comparable definitions over time. The estimated number of persons with AIDS-OIs diagnosed in 1994 (64,300) increased approximately 6 percent over the estimated number in 1993 (see Table 13). In addition, previously reported trends continued: the South and the Northeast accounted for the majority of the estimated number of persons with AIDS-OIs, and blacks and Hispanics accounted for a growing proportion of persons with AIDS-OIs (see Table 14). Although men who have sex with men accounted for the largest proportion of AIDS-OIs, the rate of growth has slowed; persons infected through injecting drug-use and their heterosexual partners accounted for an increasing proportion of persons with AIDS-OIs (see Table 15).

AIDS surveillance data can detect recent shifts in the epidemic: because AIDS develops in a substantial number of HIV-infected persons within a year or two of infection, their characteristics are soon reflected in the surveillance data. For example, emerging trends among women, black and Hispanic minorities, persons in moderate- and small-sized metropolitan statistical areas and in the rural South, persons infected through heterosexual contact, minority homosexual/bisexual men, and young men who have sex with men have all been detected through AIDS surveillance. In addition, timely data from 25 states on characteristics of adults/adolescents with HIV infection (not AIDS) have documented the impact of the epidemic among sexually active and drug-using adolescents at early stages of HIV disease and have highlighted the need for appropriate prevention interventions in these populations (see Table 20).

National population-based HIV/AIDS surveillance data can be used to guide allocation of resources for HIV/AIDS prevention and control. State and local health departments provide surveillance information to assist prevention planning in local communities. Together with data from seroprevalence surveys, behavioral surveys, and vital statistics, HIV/AIDS sur-

veillance data can assist communities in developing HIV needs assessments, health care planning, and community profiles for implementing and evaluating prevention interventions.

Suggested Reading

CDC. AIDS among racial/ethnic minorities—United States, 1993. *MMWR* 1994;43:644-47,653-55.

CDC. Update: trends in AIDS diagnosis and reporting under the expanded surveillance definition for adolescents and adults—United States, 1993. *MMWR* 1994;43:826-31.

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Table 1. AIDS cases and annual rates per 100,000 population, by state, reported July 1993 through June 1994, July 1994 through June 1995;¹ and cumulative totals, by state and age group, through June 1995, United States

State of residence	July 1993– June 1994		July 1994– June 1995		Cumulative totals		
	No.	Rate	No.	Rate	Adults/ adolescents	Children < 13 years old	Total
Alabama	556	13.3	566	13.4	3,266	52	3,318
Alaska	74	12.4	79	13.0	301	4	305
Arizona	645	16.4	559	13.7	4,047	19	4,066
Arkansas	289	11.9	288	11.7	1,725	25	1,750
California	14,388	46.1	10,989	35.0	82,937	460	83,397
Colorado	880	24.7	718	19.6	4,914	26	4,940
Connecticut	1,303	39.8	1,066	32.5	6,321	140	6,461
Delaware	263	37.7	313	44.3	1,338	11	1,349
District of Columbia	1,575	272.0	1,220	214.0	7,593	115	7,708
Florida	7,750	56.5	9,377	67.2	47,076	1,062	48,138
Georgia	2,240	32.5	2,284	32.4	13,203	140	13,343
Hawaii	318	27.3	263	22.3	1,667	13	1,680
Idaho	55	5.0	57	5.0	303	2	305
Illinois	2,748	23.5	2,785	23.7	15,306	171	15,477
Indiana	723	12.7	524	9.1	3,538	28	3,566
Iowa	99	3.5	145	5.1	794	8	802
Kansas	266	10.5	284	11.1	1,508	9	1,517
Kentucky	300	7.9	311	8.1	1,671	13	1,684
Louisiana	1,226	28.6	1,124	26.0	6,995	92	7,087
Maine	137	11.1	139	11.2	644	6	650
Maryland	2,235	45.1	2,951	58.9	11,613	224	11,837
Massachusetts	2,024	33.6	1,396	23.1	9,874	163	10,037
Michigan	1,080	11.4	1,071	11.3	6,728	75	6,803
Minnesota	392	8.7	413	9.0	2,529	17	2,546
Mississippi	411	15.6	414	15.5	2,156	37	2,193
Missouri	815	15.6	696	13.2	5,934	41	5,975
Montana	30	3.6	24	2.8	176	2	178
Nebraska	106	6.6	111	6.8	639	7	646
Nevada	444	32.1	413	28.3	2,368	20	2,388
New Hampshire	90	8.0	116	10.2	560	7	567
New Jersey	5,220	66.4	4,764	60.3	26,562	600	27,162
New Mexico	163	10.1	228	13.8	1,175	4	1,179
New York	15,122	83.3	12,578	69.2	86,318	1,704	88,022
North Carolina	1,295	18.6	1,015	14.4	5,828	81	5,909
North Dakota	27	4.2	7	1.1	64	-	64
Ohio	1,359	12.3	1,188	10.7	7,044	82	7,126
Oklahoma	346	10.7	266	8.2	2,301	17	2,318
Oregon	577	19.0	506	16.4	3,151	13	3,164
Pennsylvania	2,815	23.4	2,678	22.2	13,822	207	14,029
Rhode Island	277	27.7	291	29.2	1,324	15	1,339
South Carolina	1,170	32.2	995	27.2	4,817	58	4,875
South Dakota	17	2.4	20	2.8	91	4	95
Tennessee	851	16.7	883	17.1	4,222	37	4,259
Texas	5,841	32.4	5,153	28.0	32,732	270	33,002
Utah	136	7.3	153	8.0	1,074	20	1,094
Vermont	81	14.1	32	5.5	243	3	246
Virginia	1,369	21.1	1,150	17.6	6,829	125	6,954
Washington	1,182	22.5	933	17.5	6,394	22	6,416
West Virginia	78	4.3	114	6.3	536	6	542
Wisconsin	401	7.9	366	7.2	2,323	23	2,346
Wyoming	20	4.3	13	2.7	121	-	121
Subtotal	81,809	31.7	74,029	28.4	454,695	6,280	460,975
Guam	1	0.7	-	-	14	-	14
Pacific Islands, U.S.	-	-	-	-	2	-	2
Puerto Rico	2,616	72.5	2,582	71.0	14,937	320	15,257
Virgin Islands, U.S.	38	36.8	62	59.7	234	9	243
Total²	84,577	32.3	76,802	29.1	470,288	6,611	476,899

¹See Technical Notes for a discussion of the impact of the 1993 AIDS surveillance case definition for adults and adolescents (implemented January 1, 1993) on the number of cases reported in the two most recent 12-month reporting periods.

²Totals include 408 persons whose state of residence is unknown.

Table 2. AIDS cases and annual rates per 100,000 population, by metropolitan area with 500,000 or more population, reported July 1993 through June 1994, July 1994 through June 1995;¹ and cumulative totals, by area and age group, through June 1995, United States

Metropolitan area of residence	July 1993– June 1994		July 1994– June 1995		Cumulative totals		
	No.	Rate	No.	Rate	Adults/ adolescents	Children <13 years old	Total
Akron, Ohio	62	9.2	47	6.9	311	-	311
Albany-Schenectady, N.Y.	146	16.7	169	19.3	938	20	958
Albuquerque, N.Mex.	79	12.5	108	16.7	649	2	651
Allentown, Pa.	98	16.1	94	15.4	450	5	455
Ann Arbor, Mich.	38	7.5	36	7.0	246	5	251
Atlanta, Ga.	1,499	46.4	1,600	48.0	9,537	74	9,611
Austin, Tex.	528	56.6	388	40.3	2,486	16	2,502
Bakersfield, Calif.	129	21.5	76	12.5	516	3	519
Baltimore, Md.	1,478	60.5	2,058	83.7	7,590	161	7,751
Baton Rouge, La.	175	31.6	168	30.1	785	13	798
Bergen-Passaic, N.J.	788	60.7	614	47.1	3,488	59	3,547
Birmingham, Ala.	193	22.3	158	18.1	1,020	14	1,034
Boston, Mass.	1,754	30.8	1,217	21.2	8,777	143	8,920
Buffalo, N.Y.	104	8.7	107	9.0	954	10	964
Charleston, S.C.	187	35.6	152	29.1	913	10	923
Charlotte, N.C.	260	21.1	220	17.5	1,191	12	1,203
Chicago, Ill.	2,381	31.3	2,479	32.3	13,406	152	13,558
Cincinnati, Ohio	225	14.3	220	13.9	1,151	12	1,163
Cleveland, Ohio	343	15.4	474	21.3	2,101	32	2,133
Columbus, Ohio	360	25.5	191	13.4	1,504	8	1,512
Dallas, Tex.	1,171	41.2	1,422	49.1	8,124	34	8,158
Dayton, Ohio	106	11.1	52	5.4	615	8	623
Denver, Colo.	676	38.4	569	31.7	4,000	18	4,018
Detroit, Mich.	659	15.3	778	18.1	4,690	55	4,745
El Paso, Tex.	82	12.7	116	17.4	482	2	484
Fort Lauderdale, Fla.	1,130	83.7	1,609	116.3	7,466	173	7,639
Fort Worth, Tex.	321	22.4	550	37.6	2,092	21	2,113
Fresno, Calif.	155	18.8	123	14.7	729	8	737
Gary, Ind.	74	12.0	97	15.6	401	2	403
Grand Rapids, Mich.	85	8.7	69	7.0	463	3	466
Greensboro, N.C.	169	15.5	206	18.6	976	12	988
Greenville, S.C.	232	26.9	143	16.4	823	2	825
Harrisburg, Pa.	106	17.5	89	14.6	483	5	488
Hartford, Conn.	587	52.4	393	35.2	2,158	36	2,194
Honolulu, Hawaii	224	25.9	191	21.8	1,237	10	1,247
Houston, Tex.	2,082	58.0	1,337	36.6	11,904	104	12,008
Indianapolis, Ind.	413	28.6	216	14.8	1,721	11	1,732
Jacksonville, Fla.	347	36.1	478	49.2	2,738	61	2,799
Jersey City, N.J.	777	140.6	887	160.6	4,321	99	4,420
Kansas City, Mo.	352	21.6	304	18.5	2,770	11	2,781
Knoxville, Tenn.	106	17.1	89	14.1	401	4	405
Las Vegas, Nev.	343	33.9	337	31.3	1,850	19	1,869
Little Rock, Ark.	98	18.4	96	17.9	643	9	652
Los Angeles, Calif.	4,786	52.4	3,979	43.5	28,850	188	29,038
Louisville, Ky.	130	13.3	142	14.5	737	8	745
Memphis, Tenn.	308	29.6	334	31.6	1,521	12	1,533
Miami, Fla.	2,924	146.0	2,980	147.2	14,835	373	15,208
Middlesex, N.J.	361	34.2	392	36.7	2,163	60	2,223
Milwaukee, Wis.	218	15.0	212	14.6	1,263	14	1,277
Minneapolis-Saint Paul, Minn.	334	12.6	369	13.7	2,235	14	2,249
Mobile, Ala.	86	17.0	104	20.3	665	9	674
Monmouth-Ocean City, N.J.	335	32.8	351	33.9	1,865	48	1,913
Nashville, Tenn.	241	23.1	289	27.0	1,310	14	1,324
Nassau-Suffolk, N.Y.	573	21.7	552	20.8	4,119	75	4,194
New Haven, Conn.	612	37.6	580	35.7	3,650	98	3,748
New Orleans, La.	701	53.8	612	46.8	4,106	50	4,156
New York, N.Y.	13,431	156.7	10,780	125.6	74,312	1,547	75,859
Newark, N.J.	2,136	110.8	1,741	90.0	10,621	262	10,883
Norfolk, Va.	371	24.5	392	25.6	1,658	43	1,701
Oakland, Calif.	968	44.6	745	34.1	5,615	32	5,647

Table 2. AIDS cases and annual rates per 100,000 population, by metropolitan area with 500,000 or more population, reported July 1993 through June 1994, July 1994 through June 1995:¹ and cumulative totals, by area and age group, through June 1995, United States — Continued

Metropolitan area of residence	July 1993– June 1994		July 1994– June 1995		Cumulative totals		
	No.	Rate	No.	Rate	Adults/ adolescents	Children <13 years old	Total
Oklahoma City, Okla.	141	14.2	100	9.9	1,055	2	1,057
Omaha, Nebr.	70	10.6	77	11.6	454	2	456
Orange County, Calif.	569	22.6	543	21.4	3,775	24	3,799
Orlando, Fla.	430	32.2	747	54.9	3,320	57	3,377
Philadelphia, Pa.	2,258	45.7	2,039	41.2	10,699	173	10,872
Phoenix, Ariz.	431	18.0	393	15.9	2,904	11	2,915
Pittsburgh, Pa.	269	11.2	329	13.7	1,599	10	1,609
Portland, Oreg.	443	26.9	398	23.7	2,650	8	2,658
Providence, R.I.	261	28.6	273	29.9	1,242	14	1,256
Raleigh-Durham, N.C.	266	28.4	186	19.3	1,205	19	1,224
Richmond, Va.	258	28.5	227	24.8	1,430	19	1,449
Riverside-San Bernardino, Calif.	976	34.0	830	28.6	4,252	41	4,293
Rochester, N.Y.	193	17.7	218	20.0	1,124	8	1,132
Sacramento, Calif.	434	30.3	356	24.7	2,142	21	2,163
Saint Louis, Mo.	442	17.5	382	15.1	2,927	26	2,953
Salt Lake City, Utah	119	10.3	126	10.7	942	14	956
San Antonio, Tex.	636	45.2	384	26.7	2,438	22	2,460
San Diego, Calif.	1,221	46.7	952	36.2	6,758	39	6,797
San Francisco, Calif.	3,433	209.6	2,163	131.4	21,795	33	21,828
San Jose, Calif.	479	31.0	291	18.7	2,146	11	2,157
San Juan, P.R.	1,553	82.0	1,542	80.6	9,351	209	9,560
Sarasota, Fla.	183	35.8	170	32.8	876	18	894
Scranton, Pa.	36	5.6	49	7.7	269	3	272
Seattle, Wash.	770	35.7	658	30.2	4,673	13	4,686
Springfield, Mass.	265	44.3	185	31.1	967	19	986
Stockton, Calif.	135	26.4	48	9.3	450	12	462
Syracuse, N.Y.	96	12.7	120	15.9	697	7	704
Tacoma, Wash.	127	20.1	82	12.8	511	7	518
Tampa-Saint Petersburg, Fla.	778	36.4	830	38.5	5,116	73	5,189
Toledo, Ohio	52	8.5	47	7.7	351	7	358
Tucson, Ariz.	165	23.2	118	16.1	859	6	865
Tulsa, Okla.	117	15.8	81	10.9	702	6	708
Ventura, Calif.	79	11.4	72	10.2	509	2	511
Washington, D.C.	2,742	62.1	2,160	48.3	13,426	200	13,626
West Palm Beach, Fla.	586	62.9	864	90.5	4,203	152	4,355
Wichita, Kans.	72	14.3	98	19.3	428	2	430
Wilmington, Del.	219	41.0	256	47.5	1,043	9	1,052
Youngstown, Ohio	33	5.5	35	5.8	209	-	209
Metropolitan areas with 500,000 or more population	70,974	44.0	63,710	39.1	398,022	5,604	403,626
<i>Central counties</i>	<i>69,653</i>	<i>47.1</i>	<i>62,408</i>	<i>41.9</i>	<i>390,951</i>	<i>5,501</i>	<i>396,452</i>
<i>Outlying counties</i>	<i>1,321</i>	<i>9.6</i>	<i>1,302</i>	<i>9.3</i>	<i>7,071</i>	<i>103</i>	<i>7,174</i>
Metropolitan areas with 50,000 to 500,000 population	8,400	17.7	7,905	16.5	45,419	623	46,042
<i>Central counties</i>	<i>7,891</i>	<i>18.7</i>	<i>7,402</i>	<i>17.4</i>	<i>42,662</i>	<i>570</i>	<i>43,232</i>
<i>Outlying counties</i>	<i>509</i>	<i>9.9</i>	<i>503</i>	<i>9.6</i>	<i>2,757</i>	<i>53</i>	<i>2,810</i>
Non-metropolitan areas	4,699	8.9	4,617	8.6	24,740	369	25,109
Total²	84,577	32.3	76,802	29.1	470,288	6,611	476,899

¹See Technical Notes for a discussion of the impact of the 1993 AIDS surveillance case definition for adults and adolescents (implemented January 1, 1993) on the number of cases reported in the two most recent 12-month reporting periods.

²Totals include 2,122 persons whose area of residence is unknown.

Table 3. AIDS cases by age group, exposure category, and sex, reported July 1993 through June 1994, July 1994 through June 1995;¹ and cumulative totals, by age group and exposure category, through June 1995, United States

Adult/adolescent exposure category	Males				Females				Totals ²		
	July 1993–June 1994		July 1994–June 1995		July 1993–June 1994		July 1994–June 1995		July 1993–June 1994		Cumulative total ³
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	
Men who have sex with men	38,504	(55)	32,448	(52)	–	–	–	–	38,504	(46)	244,235 (52)
Injecting drug use	17,468	(25)	14,728	(24)	6,343	(45)	5,421	(39)	23,811	(28)	118,694 (25)
Men who have sex with men and inject drugs	4,765	(7)	3,609	(6)	–	–	–	–	4,765	(6)	31,024 (7)
Hemophilia/coagulation disorder	583	(1)	430	(1)	19	(0)	23	(0)	602	(1)	3,872 (1)
Heterosexual contact:	2,914	(4)	2,974	(5)	5,685	(40)	5,204	(38)	8,600	(10)	35,683 (8)
Sex with injecting drug user	1,004		903		2,299		1,893		3,303		17,118
Sex with bisexual male	–		–		441		346		441		1,999
Sex with person with hemophilia	3		6		61		57		64		299
Sex with transfusion recipient with HIV infection	61		65		82		57		143		692
Sex with HIV-infected person, risk not specified	1,846		2,000		2,802		2,851		4,649		15,575
Receipt of blood transfusion, blood components, or tissue ⁴	468	(1)	382	(1)	361	(3)	305	(2)	829	(1)	7,128 (2)
Other/risk not reported or identified ⁵	4,745	(7)	7,414	(12)	1,734	(12)	2,885	(21)	6,479	(8)	29,652 (6)
Adult/adolescent subtotal	69,447	(100)	61,985	(100)	14,142	(100)	13,838	(100)	83,590	(100)	470,288 (100)
Pediatric (<13 years old) exposure category											
Hemophilia/coagulation disorder	16	(3)	11	(2)	1	(0)	–	–	17	(2)	226 (3)
Mother with/at risk for HIV infection: ⁵	443	(92)	419	(88)	478	(95)	462	(92)	921	(93)	5,925 (90)
Injecting drug use	153		120		160		136		313		2,471
Sex with injecting drug user	74		70		71		69		145		1,107
Sex with bisexual male	5		10		5		10		10		120
Sex with person with hemophilia	1		1		–		1		1		24
Sex with transfusion recipient with HIV infection	3		1		1		3		4		27
Sex with HIV-infected person, risk not specified	70		91		85		89		155		676
Receipt of blood transfusion, blood components, or tissue	12		2		10		5		22		140
Has HIV infection, risk not specified	125		124		146		149		271		1,360
Receipt of blood transfusion, blood components, or tissue	17	(4)	23	(5)	13	(3)	14	(3)	30	(3)	359 (5)
Other/risk not reported or identified ⁵	6	(1)	24	(5)	13	(3)	24	(5)	19	(2)	101 (2)
Pediatric subtotal	482	(100)	477	(100)	505	(100)	500	(100)	987	(100)	6,611 (100)
Total	69,929		62,462		14,647		14,338		84,577		476,899

¹See Technical Notes for a discussion of the impact of the 1993 AIDS surveillance case definition for adults and adolescents (implemented January 1, 1993) on the number of cases reported in the two most recent 12-month reporting periods.

²Includes 4 persons whose sex is unknown.

³Includes 7 persons reported with AIDS who are infected with human immunodeficiency virus type 2 (HIV-2). See *MMWR* 1995;44:603–06.

⁴Thirty-three adults/adolescents and 2 children developed AIDS after receiving blood screened negative for HIV antibody. Ten additional adults developed AIDS after receiving tissue, organs, or artificial insemination from HIV-infected donors. Three of the 10 received tissue, organs, or artificial insemination from a donor who was negative for HIV antibody at the time of donation. See *N Engl J Med* 1992;326:726–32.

⁵See Table 11 and Figure 6 for a discussion of the "other" exposure category. "Other" also includes 25 persons who acquired HIV infection perinatally but were diagnosed with AIDS after age 13. These 25 persons are tabulated under the adult/adolescent, not pediatric, exposure category.

Table 4. Male adult/adolescent AIDS cases by exposure category and race/ethnicity, reported July 1994 through June 1995, and cumulative totals, through June 1995, United States

Exposure category	White, not Hispanic				Black, not Hispanic				Hispanic			
	July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Men who have sex with men	19,837	(71)	162,549	(77)	7,543	(34)	48,167	(40)	4,568	(40)	30,303	(45)
Injecting drug use	2,943	(11)	17,915	(8)	7,652	(35)	44,054	(36)	4,049	(36)	25,742	(38)
Men who have sex with men and inject drugs	1,840	(7)	16,651	(8)	1,219	(6)	9,388	(8)	498	(4)	4,691	(7)
Hemophilia/coagulation disorder	323	(1)	3,008	(1)	54	(0)	365	(0)	41	(0)	304	(0)
Heterosexual contact:	584	(2)	2,663	(1)	1,667	(8)	6,653	(5)	700	(6)	2,647	(4)
<i>Sex with injecting drug user</i>	185		1,164		519		3,032		193		931	
<i>Sex with person with hemophilia</i>	4		16		2		4		–		6	
<i>Sex with transfusion recipient with HIV infection</i>	30		110		18		90		16		66	
<i>Sex with HIV-infected person, risk not specified</i>	365		1,373		1,128		3,527		491		1,644	
Receipt of blood transfusion, blood components, or tissue	208	(1)	2,797	(1)	119	(1)	829	(1)	43	(0)	450	(1)
Risk not reported or identified ¹	2,127	(8)	6,273	(3)	3,744	(17)	11,561	(10)	1,426	(13)	3,914	(6)
Total	27,862	(100)	211,856	(100)	21,998	(100)	121,017	(100)	11,325	(100)	68,051	(100)

Exposure category	Asian/Pacific Islander				American Indian/Alaska Native				Cumulative totals ²			
	July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Men who have sex with men	347	(72)	2,263	(78)	106	(54)	618	(61)	32,448	(52)	244,235	(60)
Injecting drug use	26	(5)	132	(5)	39	(20)	135	(13)	14,728	(24)	88,121	(22)
Men who have sex with men and inject drugs	16	(3)	92	(3)	33	(17)	175	(17)	3,609	(6)	31,024	(8)
Hemophilia/coagulation disorder	8	(2)	46	(2)	2	(1)	24	(2)	430	(1)	3,755	(1)
Heterosexual contact:	16	(3)	57	(2)	3	(2)	17	(2)	2,974	(5)	12,049	(3)
<i>Sex with injecting drug user</i>	3		17		2		8		903		5,154	
<i>Sex with person with hemophilia</i>	–		–		–		–		6		26	
<i>Sex with transfusion recipient with HIV infection</i>	1		4		–		1		65		272	
<i>Sex with HIV-infected person, risk not specified</i>	12		36		1		8		2,000		6,597	
Receipt of blood transfusion, blood components, or tissue	9	(2)	89	(3)	2	(1)	6	(1)	382	(1)	4,183	(1)
Risk not reported or identified	61	(13)	223	(8)	13	(7)	35	(3)	7,414	(12)	22,095	(5)
Total	483	(100)	2,902	(100)	198	(100)	1,010	(100)	61,985	(100)	405,462	(100)

¹See Figure 6.

²Includes 626 men whose race/ethnicity is unknown.

Table 5. Female adult/adolescent AIDS cases by exposure category and race/ethnicity, reported July 1994 through June 1995, and cumulative totals, through June 1995, United States

Exposure category	White, not Hispanic				Black, not Hispanic				Hispanic			
	July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Injecting drug use	1,238	(40)	6,739	(43)	3,119	(40)	17,601	(50)	1,030	(37)	6,043	(45)
Hemophilia/coagulation disorder	15	(0)	78	(1)	5	(0)	25	(0)	3	(0)	13	(0)
Heterosexual contact:	1,167	(38)	5,786	(37)	2,664	(34)	11,767	(33)	1,330	(47)	5,846	(44)
<i>Sex with injecting drug user</i>	455		2,639		892		5,891		531		3,341	
<i>Sex with bisexual male</i>	142		934		127		717		68		297	
<i>Sex with person with hemophilia</i>	41		211		10		37		5		20	
<i>Sex with transfusion recipient with HIV infection</i>	26		229		20		105		8		69	
<i>Sex with HIV-infected person, risk not specified</i>	503		1,773		1,615		5,017		718		2,119	
Receipt of blood transfusion, blood components, or tissue	117	(4)	1,596	(10)	125	(2)	834	(2)	55	(2)	436	(3)
Risk not reported or identified ¹	535	(17)	1,371	(9)	1,934	(25)	5,145	(15)	391	(14)	955	(7)
Total	3,072	(100)	15,570	(100)	7,847	(100)	35,372	(100)	2,809	(100)	13,293	(100)

Exposure category	Asian/Pacific Islander				American Indian/Alaska Native				Cumulative totals ²			
	July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Injecting drug use	13	(22)	59	(18)	15	(47)	84	(49)	5,421	(39)	30,573	(47)
Hemophilia/coagulation disorder	–	–	1	(0)	–	–	–	–	23	(0)	117	(0)
Heterosexual contact:	24	(40)	144	(44)	14	(44)	63	(36)	5,204	(38)	23,633	(36)
<i>Sex with injecting drug user</i>	7		43		7		36		1,893		11,964	
<i>Sex with bisexual male</i>	5		41		4		8		346		1,999	
<i>Sex with person with hemophilia</i>	1		3		–		2		57		273	
<i>Sex with transfusion recipient with HIV infection</i>	2		15		–		–		57		420	
<i>Sex with HIV-infected person, risk not specified</i>	9		42		3		17		2,851		8,977	
Receipt of blood transfusion, blood components, or tissue	8	(13)	68	(21)	–	–	10	(6)	305	(2)	2,945	(5)
Risk not reported or identified	15	(25)	53	(16)	3	(9)	16	(9)	2,885	(21)	7,554	(12)
Total	60	(100)	325	(100)	32	(100)	173	(100)	13,838	(100)	64,822	(100)

¹See Figure 6.

²Includes 89 women whose race/ethnicity is unknown.

Table 6. Pediatric AIDS cases by exposure category and race/ethnicity, reported July 1994 through June 1995, and cumulative totals, through June 1995, United States

Exposure category	White, not Hispanic				Black, not Hispanic				Hispanic			
	July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Hemophilia/coagulation disorder	9	(6)	156	(13)	1	(0)	32	(1)	1	(0)	34	(2)
Mother with/at risk for HIV infection:	115	(80)	868	(71)	528	(92)	3,578	(95)	228	(92)	1,424	(91)
<i>Injecting drug use</i>	32		373		149		1,470		73		609	
<i>Sex with injecting drug user</i>	20		162		70		541		48		395	
<i>Sex with bisexual male</i>	5		44		8		41		7		33	
<i>Sex with person with hemophilia</i>	1		15		—		—5		1		4	
<i>Sex with transfusion recipient with HIV infection</i>	1		10		1		9		2		8	
<i>Sex with HIV-infected person, risk not specified</i>	24		87		111		440		42		138	
<i>Receipt of blood transfusion, blood components, or tissue</i>	1		39		4		73		2		27	
<i>Has HIV infection, risk not specified</i>	31		138		185		999		53		210	
Receipt of blood transfusion, blood components, or tissue	16	(11)	178	(15)	8	(1)	80	(2)	12	(5)	91	(6)
Risk not reported or identified ¹	4	(3)	14	(1)	36	(6)	68	(2)	6	(2)	17	(1)
Total	144	(100)	1,216	(100)	573	(100)	3,758	(100)	247	(100)	1,566	(100)

Exposure category	Asian/Pacific Islander		American Indian/Alaska Native		Cumulative totals ²			
	July 1994– June 1995		July 1994– June 1995		July 1994– June 1995		Cumulative total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Hemophilia/coagulation disorder	—	—	3	(8)	—	—	11	(1)
Mother with/at risk for HIV infection:	5	(63)	24	(63)	2	(100)	18	(95)
<i>Injecting drug use</i>	—		4		1		256	
<i>Sex with injecting drug user</i>	1		3		—		139	
<i>Sex with bisexual male</i>	—		2		—		20	
<i>Sex with person with hemophilia</i>	—		—		—		2	
<i>Sex with transfusion recipient with HIV infection</i>	—		—		—		4	
<i>Sex with HIV-infected person, risk not specified</i>	2		6		—		180	
<i>Receipt of blood transfusion, blood components, or tissue</i>	—		1		—		7	
<i>Has HIV infection, risk not specified</i>	2		8		1		273	
Receipt of blood transfusion, blood components, or tissue	1	(13)	9	(24)	—	—	37	(4)
Risk not reported or identified	2	(25)	2	(5)	—	—	48	(5)
Total	8	(100)	38	(100)	2	(100)	977	(100)

¹See Figure 6, footnote 1.

²Includes 14 children whose race/ethnicity is unknown.

Table 7. AIDS cases in adolescents and adults under age 25, by sex and exposure category, reported July 1993 through June 1994, July 1994 through June 1995;¹ and cumulative totals through June 1995, United States

Male exposure category	13-19 years old						20-24 years old					
	July 1993– June 1994		July 1994– June 1995		Cumulative total		July 1993– June 1994		July 1994– June 1995		Cumulative total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Men who have sex with men	75	(29)	82	(32)	471	(33)	1,250	(60)	1,029	(60)	8,613	(63)
Injecting drug use	15	(6)	16	(6)	92	(6)	275	(13)	207	(12)	1,727	(13)
Men who have sex with men and inject drugs	10	(4)	10	(4)	68	(5)	178	(9)	112	(7)	1,486	(11)
Hemophilia/coagulation disorder	112	(43)	89	(35)	613	(43)	85	(4)	55	(3)	501	(4)
Heterosexual contact:	10	(4)	10	(4)	36	(3)	95	(5)	108	(6)	456	(3)
<i>Sex with injecting drug user</i>	3		1		13		26		37		196	
<i>Sex with person with hemophilia</i>	–		1		1		–		–		1	
<i>Sex with transfusion recipient with HIV infection</i>	–		–		–		2		2		11	
<i>Sex with HIV-infected person, risk not specified</i>	7		8		22		67		69		248	
Receipt of blood transfusion, blood components, or tissue	15	(6)	11	(4)	60	(4)	17	(1)	10	(1)	99	(1)
Risk not reported or identified ²	21	(8)	39	(15)	97	(7)	171	(8)	200	(12)	717	(5)
Male subtotal	258	(100)	257	(100)	1,437	(100)	2,071	(100)	1,721	(100)	13,599	(100)
Female exposure category												
Injecting drug use	18	(11)	14	(7)	122	(16)	223	(27)	183	(22)	1,351	(33)
Hemophilia/coagulation disorder	2	(1)	3	(2)	9	(1)	2	(0)	2	(0)	12	(0)
Heterosexual contact:	93	(55)	89	(48)	397	(53)	455	(54)	423	(51)	2,093	(50)
<i>Sex with injecting drug user</i>	32		27		186		189		129		1,058	
<i>Sex with bisexual male</i>	5		6		22		31		23		165	
<i>Sex with person with hemophilia</i>	1		3		10		13		6		41	
<i>Sex with transfusion recipient with HIV infection</i>	–		–		1		2		3		12	
<i>Sex with HIV-infected person, risk not specified</i>	55		53		178		220		262		817	
Receipt of blood transfusion, blood components, or tissue	7	(4)	13	(7)	57	(8)	12	(1)	10	(1)	98	(2)
Risk not reported or identified	49	(29)	68	(36)	162	(22)	149	(18)	209	(25)	592	(14)
Female subtotal	169	(100)	187	(100)	747	(100)	841	(100)	827	(100)	4,146	(100)
Total	427		444		2,184		2,912		2,548		17,745	

¹See Technical Notes for a discussion of the impact of the 1993 AIDS surveillance case definition for adults and adolescents (implemented January 1, 1993) on the number of cases reported in the two most recent 12-month reporting periods.

²See Figure 6.

Table 8. AIDS cases by sex, age at diagnosis, and race/ethnicity, reported through June 1995, United States

Male Age at diagnosis (years)	White, not Hispanic		Black, not Hispanic		Hispanic		Asian/Pacific Islander		American Indian/ Alaska Native		Total ¹	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Under 5	401	(0)	1,593	(1)	630	(1)	15	(1)	9	(1)	2,651	(1)
5-12	288	(0)	270	(0)	193	(0)	8	(0)	1	(0)	761	(0)
13-19	649	(0)	468	(0)	288	(0)	18	(1)	13	(1)	1,437	(0)
20-24	6,054	(3)	4,641	(4)	2,735	(4)	99	(3)	48	(5)	13,599	(3)
25-29	29,889	(14)	16,854	(14)	10,851	(16)	384	(13)	210	(21)	58,268	(14)
30-34	49,941	(23)	27,096	(22)	16,750	(24)	646	(22)	272	(27)	94,836	(23)
35-39	47,371	(22)	28,321	(23)	15,311	(22)	630	(22)	199	(20)	91,986	(22)
40-44	34,274	(16)	20,518	(17)	10,332	(15)	509	(17)	142	(14)	65,883	(16)
45-49	20,271	(10)	10,877	(9)	5,608	(8)	281	(10)	63	(6)	37,156	(9)
50-54	10,900	(5)	5,863	(5)	2,923	(4)	154	(5)	30	(3)	19,899	(5)
55-59	6,082	(3)	3,236	(3)	1,677	(2)	90	(3)	15	(1)	11,128	(3)
60-64	3,514	(2)	1,746	(1)	908	(1)	42	(1)	11	(1)	6,230	(2)
65 or older	2,911	(1)	1,397	(1)	668	(1)	49	(2)	7	(1)	5,040	(1)
Male subtotal	212,545	(100)	122,880	(100)	68,874	(100)	2,925	(100)	1,020	(100)	408,874	(100)
Female												
Age at diagnosis (years)												
Under 5	406	(3)	1,606	(4)	596	(4)	9	(3)	9	(5)	2,634	(4)
5-12	121	(1)	289	(1)	147	(1)	6	(2)	-	-	565	(1)
13-19	140	(1)	482	(1)	119	(1)	4	(1)	1	(1)	747	(1)
20-24	980	(6)	2,217	(6)	910	(6)	16	(5)	18	(10)	4,146	(6)
25-29	2,825	(18)	5,885	(16)	2,488	(18)	36	(11)	36	(20)	11,280	(17)
30-34	3,695	(23)	8,692	(23)	3,412	(24)	70	(21)	44	(24)	15,936	(23)
35-39	3,043	(19)	8,140	(22)	2,766	(20)	61	(18)	35	(19)	14,075	(21)
40-44	1,850	(11)	5,085	(14)	1,663	(12)	50	(15)	19	(10)	8,676	(13)
45-49	953	(6)	2,208	(6)	852	(6)	28	(8)	8	(4)	4,054	(6)
50-54	565	(4)	1,166	(3)	479	(3)	16	(5)	4	(2)	2,233	(3)
55-59	445	(3)	660	(2)	303	(2)	10	(3)	4	(2)	1,424	(2)
60-64	326	(2)	422	(1)	151	(1)	16	(5)	3	(2)	918	(1)
65 or older	748	(5)	415	(1)	150	(1)	18	(5)	1	(1)	1,333	(2)
Female subtotal	16,097	(100)	37,267	(100)	14,036	(100)	340	(100)	182	(100)	68,021	(100)
Total²	228,644		160,148		82,910		3,265		1,202		476,899	

¹Includes 630 males, 99 females, and 1 person with unknown sex whose race/ethnicity is unknown.

²Includes 4 persons whose sex is unknown.

Table 9. AIDS cases, case-fatality rates,¹ and deaths, by half-year and age group, through June 1995, United States

Half-year	Adults/adolescents			Children <13 years old		
	Cases diagnosed during interval	Case-fatality rate	Deaths occurring during interval	Cases diagnosed during interval	Case-fatality rate	Deaths occurring during interval
Before 1981	86	90.7	30	8	75.0	1
1981 Jan.-June	104	90.4	37	10	80.0	2
July-Dec.	203	92.1	83	6	83.3	6
1982 Jan.-June	428	93.2	151	15	93.3	10
July-Dec.	725	91.6	295	16	87.5	4
1983 Jan.-June	1,343	94.2	525	32	100.0	14
July-Dec.	1,700	94.2	945	44	90.9	16
1984 Jan.-June	2,667	93.6	1,423	52	88.5	26
July-Dec.	3,494	93.7	2,015	63	87.3	24
1985 Jan.-June	5,120	92.7	2,869	108	81.5	47
July-Dec.	6,529	93.1	3,973	137	85.4	72
1986 Jan.-June	8,647	92.1	5,185	143	83.2	68
July-Dec.	10,210	92.3	6,696	195	77.9	97
1987 Jan.-June	13,476	91.1	7,798	228	78.1	121
July-Dec.	14,860	89.4	8,233	269	73.6	171
1988 Jan.-June	17,283	87.5	9,671	262	68.3	137
July-Dec.	17,769	87.3	11,032	348	65.5	179
1989 Jan.-June	20,799	84.1	12,694	368	64.4	173
July-Dec.	21,131	82.8	14,592	345	67.5	194
1990 Jan.-June	23,901	80.0	14,995	386	60.6	193
July-Dec.	23,403	77.7	15,952	402	54.0	199
1991 Jan.-June	27,836	73.7	16,993	400	52.0	174
July-Dec.	29,924	69.3	18,861	389	48.1	218
1992 Jan.-June	36,048	61.3	19,247	473	44.4	190
July-Dec.	38,962	54.4	20,416	425	47.3	219
1993 Jan.-June	40,147	41.3	20,571	413	37.8	244
July-Dec.	32,818	34.0	21,503	396	36.9	254
1994 Jan.-June	32,090	24.2	22,091	345	26.7	271
July-Dec.	25,577	15.8	21,475	243	20.6	215
1995 Jan.-June	13,008	7.8	11,112	90	8.9	112
Total²	470,288	62.1	291,815	6,611	55.3	3,658

¹Case-fatality rates are calculated for each half-year by date of diagnosis. Each 6-month case-fatality rate is the number of deaths ever reported among cases diagnosed in that period (regardless of the year of death), divided by the number of total cases diagnosed in that period, multiplied by 100. For example, during the interval January through June 1982, AIDS was diagnosed in 428 adults/adolescents. Through June 1995, 399 of these 428 were reported as dead. Therefore, the case-fatality rate is 93.2 (399 divided by 428, multiplied by 100). The case-fatality rates shown here may be underestimates because of incomplete reporting of deaths. Reported deaths are not necessarily caused by HIV-related disease.

²Death totals include 352 adults/adolescents and 7 children known to have died, but whose dates of death are unknown.

1994 32,090 + 25,577 + 345 + 243 = 58,255

Table 10. AIDS cases by year of diagnosis and definition category, diagnosed through June 1995, United States

Definition category	Period of diagnosis											
	Before July 1991		July 1991–June 1992		July 1992–June 1993		July 1993–June 1994		July 1994–June 1995		Cumulative total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Pre-1987 definition	163,750	(73)	34,781	(52)	30,933	(39)	19,976	(30)	9,831	(25)	259,271	(54)
1987 definition	52,050	(23)	18,514	(28)	17,522	(22)	11,591	(18)	6,084	(16)	105,761	(22)
1993 definition ¹	9,751	(4)	13,539	(20)	31,492	(39)	34,082	(52)	23,003	(59)	111,867	(23)
<i>Pulmonary tuberculosis</i>	1,616		1,276		1,891		1,480		528		6,791	
<i>Recurrent pneumonia</i>	380		370		926		914		439		3,029	
<i>Invasive cervical cancer</i>	68		51		98		115		43		375	
<i>Severe HIV-related immunosuppression</i> ²	7,720		11,867		28,609		31,603		22,002		101,801	
Total	225,551	(100)	66,834	(100)	79,947	(100)	65,649	(100)	38,918	(100)	476,899	(100)

¹Persons who meet only the 1993 AIDS case definition and whose date of diagnosis is before January 1993 were diagnosed retrospectively. The sum of diagnoses listed for the four conditions under the 1993 definition do not equal the 1993 definition total because some persons have more than one diagnosis from the added conditions of pulmonary tuberculosis, recurrent pneumonia, and invasive cervical cancer.

²Defined as CD4⁺ T-lymphocyte count of less than 200 cells/μL or a CD4⁺ percentage less than 14 in persons with laboratory confirmation of HIV infection.

Table 11. Health care workers with documented and possible occupationally acquired AIDS/HIV infection, by occupation, reported through June 1995, United States¹

Occupation	Documented occupational transmission ²	Possible occupational transmission ³
	No.	No.
Dental worker, including dentist	—	6
Embalmer/morgue technician	—	2
Emergency medical technician/paramedic	—	9
Health aide/attendant	1	11
Housekeeper/maintenance worker	1	7
Laboratory technician, clinical	15	14
Laboratory technician, nonclinical	3	0
Nurse	16	23
Physician, nonsurgical	6	10
Physician, surgical	—	4
Respiratory therapist	1	2
Technician, dialysis	1	2
Technician, surgical	2	1
Technician/therapist, other than those listed above	—	4
Other health care occupations	—	2
Total	46	97

¹Health care workers are defined as those persons, including students and trainees, who have worked in a health care, clinical, or HIV laboratory setting at any time since 1978. See *MMWR* 1992;41:823-25.

²Health care workers who had documented HIV seroconversion after occupational exposure or had other laboratory evidence of occupational infection: 40 had percutaneous exposure, 4 had mucocutaneous exposure, 1 had both percutaneous and mucocutaneous exposures, and 1 had an unknown route of exposure. Forty-one exposures were to blood from an HIV-infected person, 1 to visibly bloody fluid, 1 to an unspecified fluid, and 3 to concentrated virus in a laboratory. Twenty of these health care workers developed AIDS.

³These health care workers have been investigated and are without identifiable behavioral or transfusion risks; each reported percutaneous or mucocutaneous occupational exposures to blood or body fluids, or laboratory solutions containing HIV, but HIV seroconversion specifically resulting from an occupational exposure was not documented.

Table 12. Adult/adolescent AIDS cases by single and multiple exposure categories, reported through June 1995, United States

Exposure category	AIDS cases	
	No.	(%)
Single mode of exposure		
Men who have sex with men	235,025	(50)
Injecting drug use	97,574	(21)
Hemophilia/coagulation disorder	3,024	(1)
Heterosexual contact	34,597	(7)
Receipt of transfusion ¹	7,118	(2)
Receipt of transplant of tissues/organs or artificial insemination ²	10	(0)
Other ³	52	(0)
Single mode of exposure subtotal	377,400	(80)
Multiple modes of exposure		
Men who have sex with men; injecting drug use	27,164	(6)
Men who have sex with men; hemophilia/coagulation disorder	118	(0)
Men who have sex with men; heterosexual contact	5,814	(1)
Men who have sex with men; receipt of transfusion/transplant	3,009	(1)
Injecting drug use; hemophilia/coagulation disorder	155	(0)
Injecting drug use; heterosexual contact	18,841	(4)
Injecting drug use; receipt of transfusion/transplant	1,384	(0)
Hemophilia/coagulation disorder; heterosexual contact	55	(0)
Hemophilia/coagulation disorder; receipt of transfusion/transplant	766	(0)
Heterosexual contact; receipt of transfusion/transplant	1,086	(0)
Men who have sex with men; injecting drug use; hemophilia/coagulation disorder	34	(0)
Men who have sex with men; injecting drug use; heterosexual contact	3,170	(1)
Men who have sex with men; injecting drug use; receipt of transfusion/transplant	509	(0)
Men who have sex with men; hemophilia/coagulation disorder; heterosexual contact	12	(0)
Men who have sex with men; hemophilia/coagulation disorder; receipt of transfusion/transplant	30	(0)
Men who have sex with men; heterosexual contact; receipt of transfusion/transplant	223	(0)
Injecting drug use; hemophilia/coagulation disorder; heterosexual contact	36	(0)
Injecting drug use; hemophilia/coagulation disorder; receipt of transfusion/transplant	29	(0)
Injecting drug use; heterosexual contact; receipt of transfusion/transplant	660	(0)
Hemophilia/coagulation disorder; heterosexual contact; receipt of transfusion/transplant	27	(0)
Men who have sex with men; injecting drug use; hemophilia/coagulation disorder; heterosexual contact;	7	(0)
Men who have sex with men; injecting drug use; hemophilia/coagulation disorder; receipt of transfusion/transplant	13	(0)
Men who have sex with men; injecting drug use; heterosexual contact; receipt of transfusion/transplant	125	(0)
Men who have sex with men; hemophilia/coagulation disorder; heterosexual contact; receipt of transfusion/transplant	4	(0)
Injecting drug use; hemophilia/coagulation disorder; heterosexual contact; receipt of transfusion/transplant	15	(0)
Men who have sex with men; injecting drug use; hemophilia/coagulation disorder; heterosexual contact; receipt of transfusion/transplant	2	(0)
Multiple modes of exposure subtotal	63,288	(13)
Risk not reported or identified⁴	29,600	(6)
Total	470,288	(100)

¹Includes 33 adult/adolescents who developed AIDS after receiving blood screened negative for HIV antibody.

²Ten adults developed AIDS after receiving tissue, organs, or artificial insemination from HIV-infected donors. Three of the 10 received tissue or organs from a donor who was negative for HIV antibody at the time of donation. See *N Engl J Med* 1992;326:726-32.

³See Table 11 and Figure 6 for a discussion of the "other" exposure category. "Other" also includes 25 persons who acquired HIV infection perinatally, but were diagnosed with AIDS after age 13.

⁴See Figure 6.

Figure 1. Male adult/adolescent AIDS annual rates per 100,000 population, for cases reported July 1994 through June 1995, United States

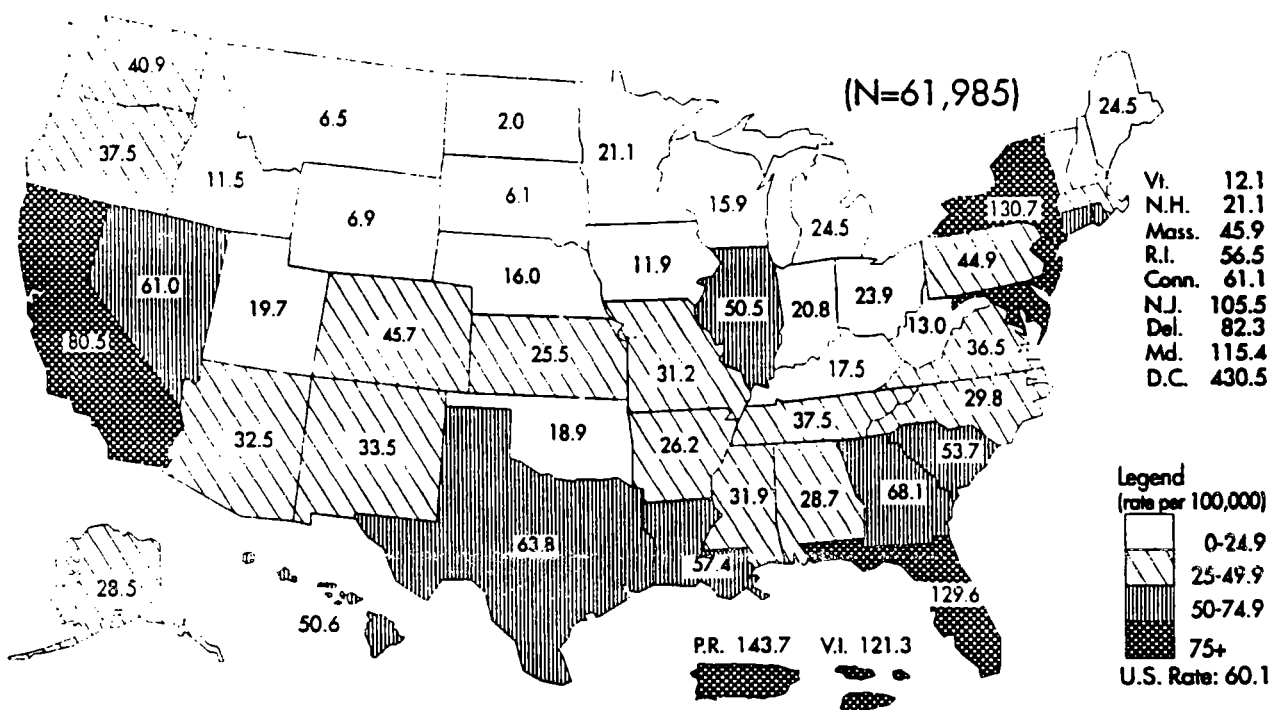


Figure 2. Female adult/adolescent AIDS annual rates per 100,000 population, for cases reported July 1994 through June 1995, United States

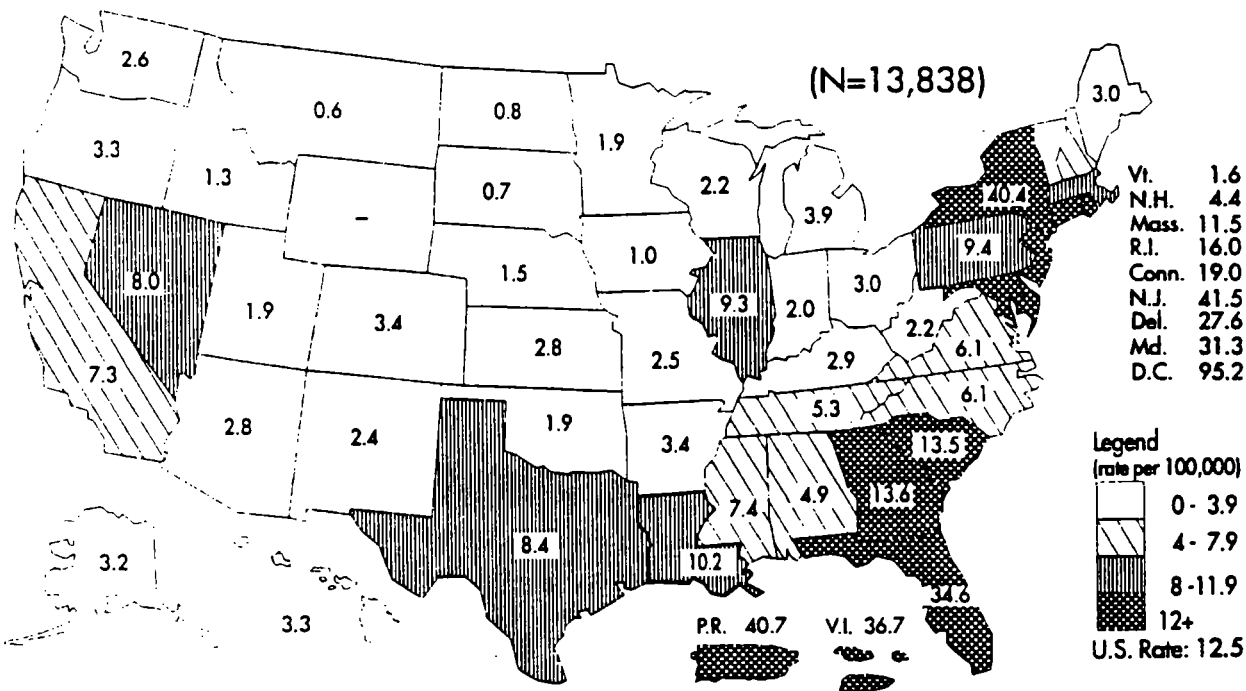


Figure 3. Male adult/adolescent AIDS cases reported July 1994 through June 1995, United States

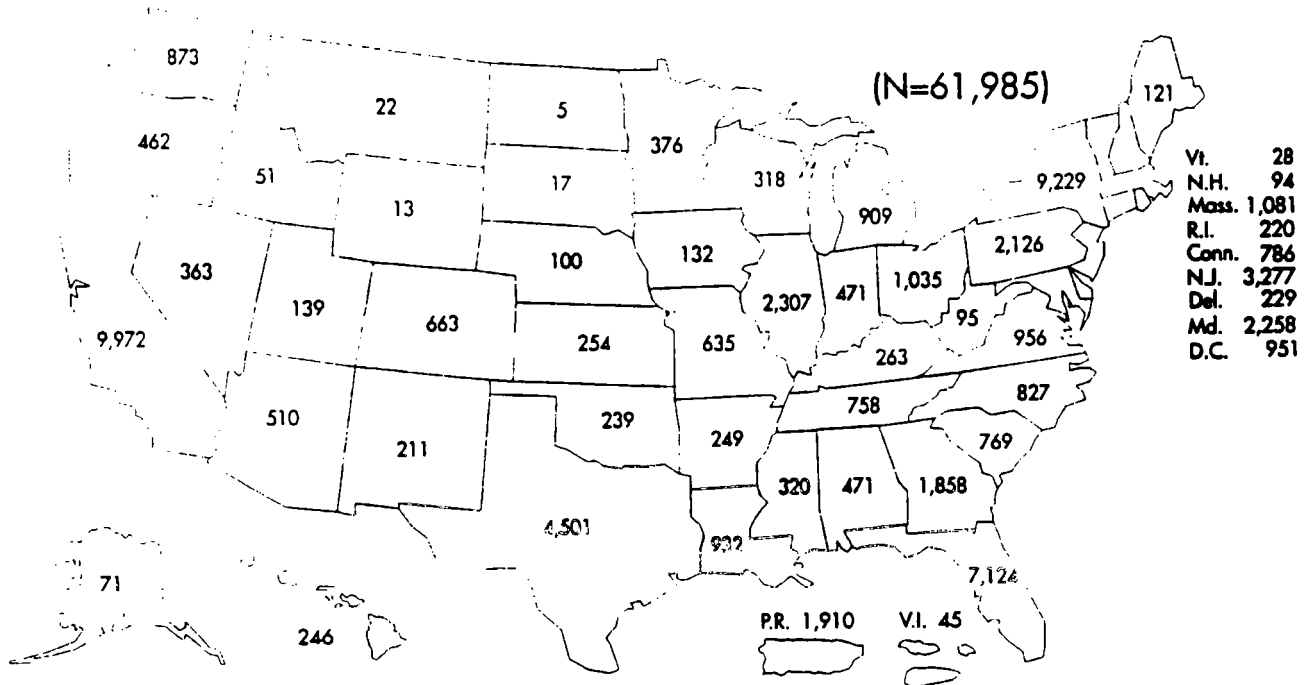


Figure 4. Female adult/adolescent AIDS cases reported July 1994 through June 1995, United States

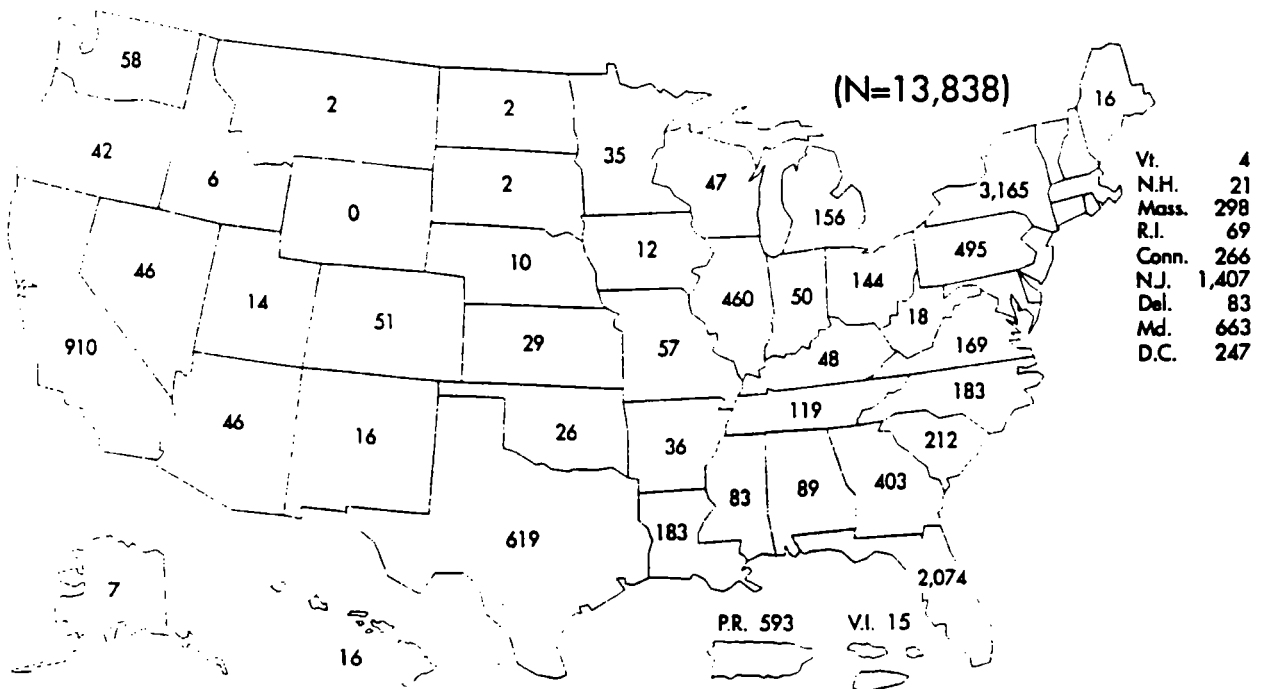


Figure 5. Pediatric AIDS cases reported July 1994 through June 1995, United States

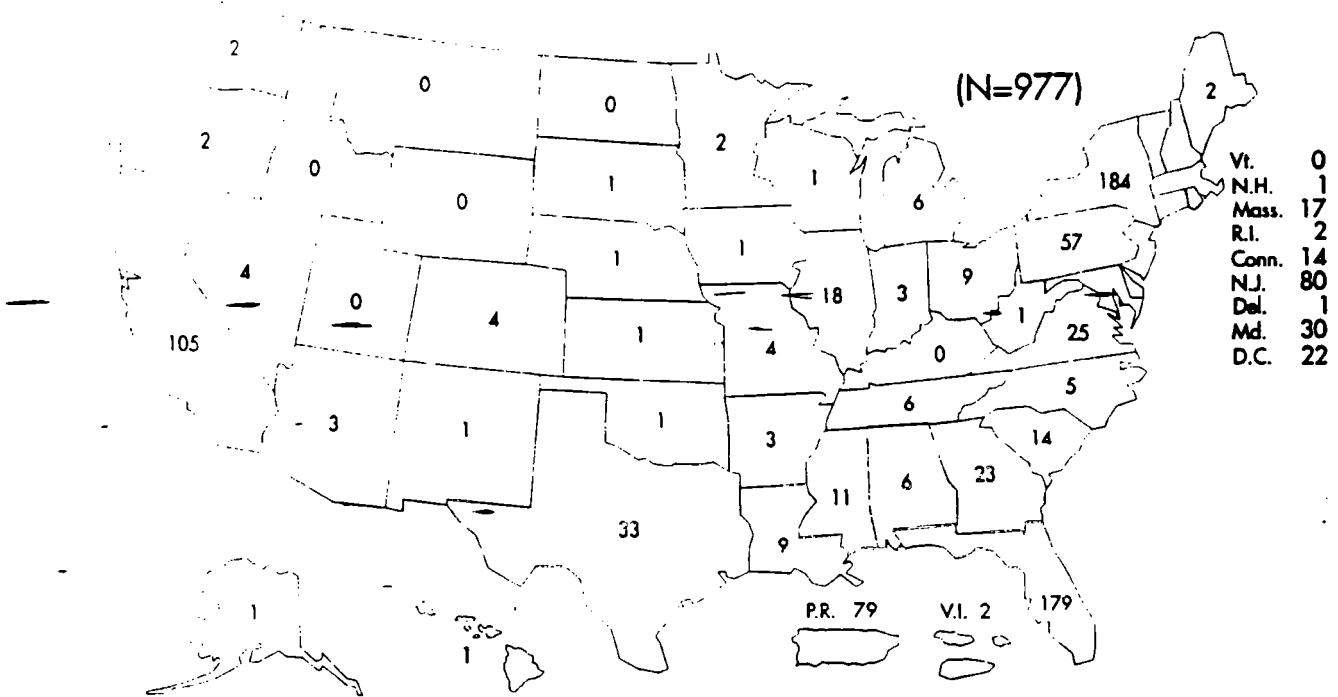
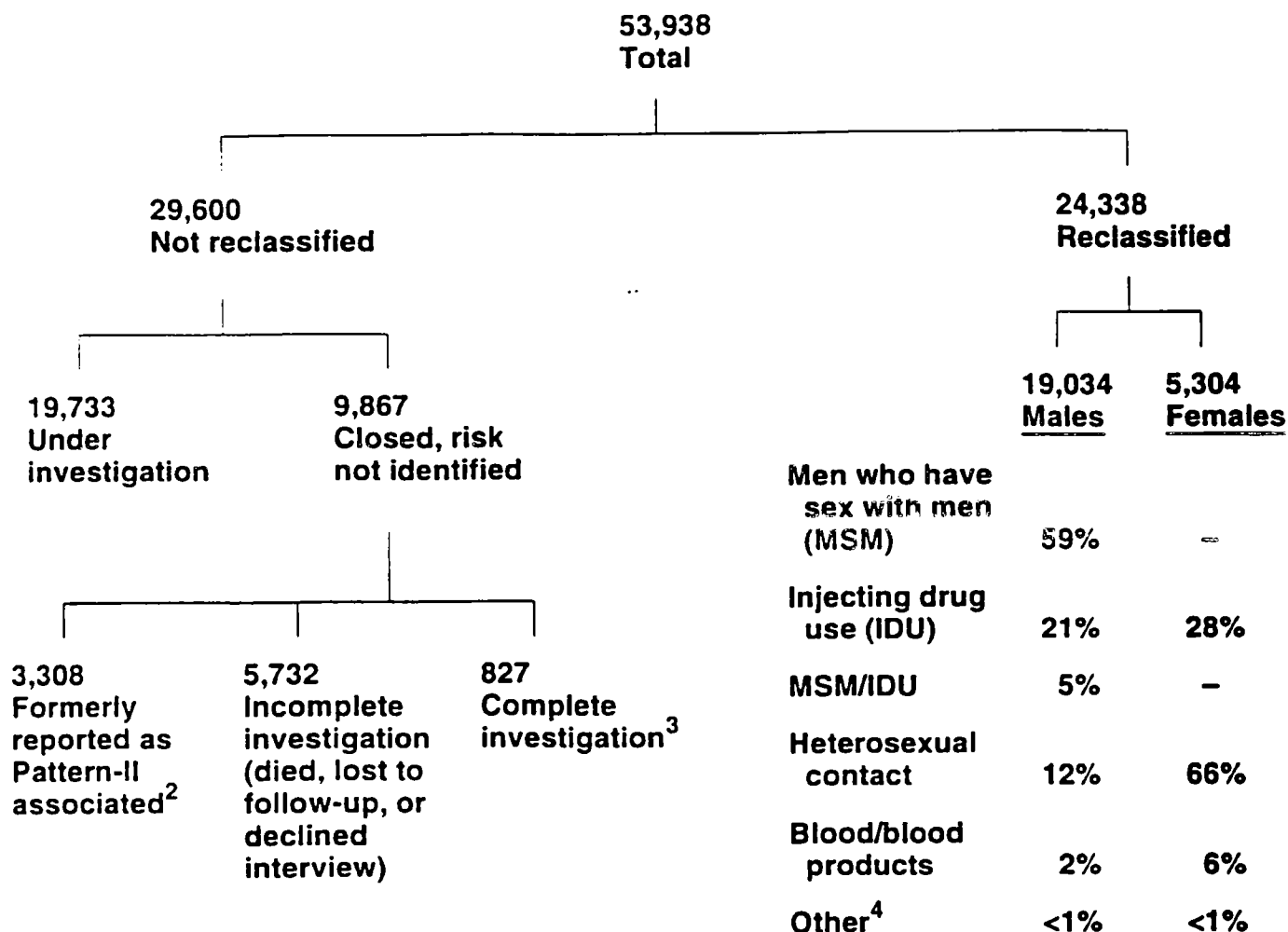


Figure 6. Investigations of adult/adolescent AIDS cases ever classified as risk not reported or identified, through June 1995, United States¹



¹Excludes 101 children under 13 years of age classified as "other/risk not reported or identified" in Table 3: 100 whose risk is not identified and 1 who was exposed to HIV-infected blood in a household setting, as supported by seroconversion, epidemiologic, and/or laboratory evidence (see *MMWR* 1992;41:228-31). An additional 303 children who were initially reported without risk information have been reclassified after investigation.

²Cases associated with persons born in Pattern-II countries are no longer classified as heterosexual transmission. See Technical Notes.

³Investigations of these persons included patient interviews. Based on available information, these persons could not be reclassified into an exposure category. This group includes persons possibly infected through heterosexual contact with a partner who is not known to be HIV infected or at high risk for HIV infection; persons who may choose not to disclose high-risk information; and persons with possible occupational exposure. These 827 persons report heterosexual contact, sexually transmitted disease infections, non-injecting drug use, hepatitis infections, and occupational exposures to blood or body fluids.

⁴Fifty-two adult/adolescents are included in the "other" exposure category listed here and in Table 3, and were exposed to HIV-infected blood, body fluids, or concentrated virus in health care, laboratory, or household settings, as supported by seroconversion, epidemiologic, and/or laboratory evidence. See Table 11, *MMWR* 1993;42:329-31, and *MMWR* 1993;42:948-51. One person was infected following intentional self-inoculation of blood from an HIV-infected person. Twenty-five persons acquired HIV infection perinatally and were diagnosed with AIDS after age 13.

Table 13. Estimated AIDS-opportunistic illness incidence, by region of residence and year of diagnosis, 1990 through 1994, United States¹

Region of residence ²	Year of diagnosis				
	1990	1991	1992	1993	1994
Northeast	13,900	15,500	17,000	18,600	19,100
Midwest	4,600	5,500	6,300	6,300	6,500
South	15,000	17,400	20,400	21,000	23,500
West	10,600	12,200	13,000	12,500	13,200
Territories	1,700	2,100	2,100	2,200	2,000
Total³	45,800	52,500	58,800	60,600	64,300

¹Estimates are adjusted for delays in the reporting of AIDS cases, but not for incomplete reporting of cases. Estimates are rounded to the nearest 100. Opportunistic illness refers to AIDS-defining opportunistic illnesses included in the 1993 AIDS surveillance case definition. See Technical Notes.

²See Technical Notes for a list of states or dependencies and possessions which comprise each region of residence.

³The sum of the regional estimates may not equal the total annual estimates because of rounding.

Table 14. Estimated AIDS-opportunistic illness incidence, by race/ethnicity and year of diagnosis, 1990 through 1994, United States¹

Race/ethnicity	Year of diagnosis				
	1990	1991	1992	1993	1994
White, not Hispanic	22,600	25,200	26,700	25,700	26,400
Black, not Hispanic	14,600	17,400	21,000	23,000	25,300
Hispanic	8,000	9,400	10,400	11,100	11,900
Asian/Pacific Islander	300	360	420	460	480
American Indian/Alaska Native	110	140	160	170	200
Total²	45,800	52,500	58,800	60,600	64,300

¹Estimates are adjusted for delays in the reporting of AIDS cases, but not for incomplete reporting of cases. Estimates of less than 200, 200 to 499, 500 to 999, and 1,000 or more are rounded to the nearest 10, 20, 50, and 100, respectively. See Technical Notes.

²The sum of race/ethnicity estimates may not equal the total annual estimates because of rounding. Totals include estimates of persons whose race/ethnicity is unknown.

Table 15. Estimated AIDS-opportunistic illness incidence, by age group, sex, exposure category, and year of diagnosis, 1990 through 1994, United States ¹

Male adult/adolescent exposure category	Year of diagnosis				
	1990	1991	1992	1993	1994
Men who have sex with men	25,200	28,300	30,000	29,600	31,300
Injecting drug use	8,700	10,100	12,000	12,700	13,400
Men who have sex with men and inject drugs	3,200	3,500	3,800	3,600	3,500
Hemophilia/coagulation disorder	340	380	440	440	420
Heterosexual contact	1,100	1,500	2,100	2,600	3,100
Receipt of blood transfusion, blood components, or tissue	440	460	440	380	440
Risk not reported or identified	360	380	440	400	280
Male subtotal	39,300	44,700	49,200	49,700	52,400
Female adult/adolescent exposure category					
Injecting drug use	3,000	3,600	4,300	4,600	4,900
Hemophilia/coagulation disorder	10	20	10	20	20
Heterosexual contact	2,200	2,900	3,800	4,800	5,700
Receipt of blood transfusion, blood components, or tissue	320	320	320	340	400
Risk not reported or identified	120	190	200	150	110
Female subtotal	5,700	7,000	8,600	9,900	11,100
Pediatric (<13 years old) exposure category²	800	830	990	970	850
Total³	45,800	52,500	58,800	60,600	64,300

¹ Estimates are adjusted for delays in the reporting of AIDS cases and anticipated redistribution of cases initially reported with no identified risk, but not for incomplete reporting of cases. Adult/adolescent and total estimates of less than 200, 200 to 499, 500 to 999, and 1,000 or more are rounded to the nearest 10, 20, 50, and 100, respectively. Pediatric estimates are rounded to the nearest 10. Opportunistic illness refers to AIDS-defining opportunistic illnesses included in the 1993 AIDS surveillance case definition. See Technical Notes.

² Estimates are based on cases diagnosed using the 1987 definition, adjusted for reporting delays. The 1993 AIDS surveillance case definition affected only adult/adolescent cases, not pediatric cases.

³ The sum of the exposure category estimates may not equal the subtotal and total annual estimates because of rounding.

Table 16. HIV infection cases (not AIDS) by state, reported July 1994 through June 1995; and cumulative totals, by state and age group, through June 1995; from states with confidential HIV infection reporting

State of residence (Date HIV reporting initiated)	July 1994– June 1995	Cumulative totals		
		Adults/ adolescents	Children <13 years old	Total
Alabama (Jan. 1988)	559	3,764	31	3,795
Arizona (Jan. 1987)	366	3,087	29	3,116
Arkansas (July 1989)	316	1,298	20	1,318
Colorado (Nov. 1985)	461	5,248	26	5,274
Connecticut (July 1992) ¹	22	–	93	93
Idaho (June 1986)	50	343	3	346
Indiana (July 1988)	411	2,563	23	2,586
Louisiana (Feb. 1993)	1,161	3,714	42	3,756
Michigan (April 1992)	1,277	2,679	73	2,752
Minnesota (Oct. 1985)	309	2,093	22	2,115
Mississippi (Aug. 1988)	604	2,893	35	2,928
Missouri (Oct. 1987)	656	3,289	36	3,325
Nevada (Feb. 1992)	417	1,944	20	1,964
New Jersey (Jan. 1992)	4,259	10,221	306	10,527
North Carolina (Feb. 1990)	1,427	5,659	46	5,705
North Dakota (Jan. 1988)	7	59	–	59
Ohio (June 1990)	575	2,992	26	3,018
Oklahoma (June 1988)	176	1,540	9	1,549
South Carolina (Feb. 1986)	736	5,444	73	5,517
South Dakota (Jan. 1988)	21	148	5	153
Tennessee (Jan. 1992)	1,075	2,989	37	3,026
Texas (Feb. 1994) ¹	145	–	189	189
Utah (April 1989)	89	775	5	780
Virginia (July 1989)	1,000	5,623	57	5,680
West Virginia (Jan. 1989)	96	359	2	361
Wisconsin (Nov. 1985)	252	1,845	23	1,868
Wyoming (June 1989)	9	57	–	57
Subtotal	16,476	70,626	1,231	71,857
Persons reported from states with confidential HIV reporting who were residents of other states ²	490	1,694	26	1,720
Total	16,966	72,320	1,257	73,577

¹Connecticut and Texas have confidential HIV infection reporting for pediatric cases only.

²Includes 347 persons reported from states with confidential HIV infection reporting, but whose state of residence is unknown. See Technical Notes.

Table 17. Male adult/adolescent HIV infection cases (not AIDS) by exposure category and race/ethnicity, reported July 1994 through June 1995, and cumulative totals through June 1995, from states with confidential HIV infection reporting¹

Exposure category	White, not Hispanic				Black, not Hispanic				Hispanic			
	July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Men who have sex with men	2,615	(57)	15,135	(60)	1,715	(28)	7,883	(31)	265	(29)	1,132	(35)
Injecting drug use	559	(12)	2,274	(9)	1,403	(23)	5,646	(22)	306	(33)	964	(30)
Men who have sex with men and inject drugs	283	(6)	2,103	(8)	210	(3)	1,272	(5)	27	(3)	203	(6)
Hemophilia/coagulation disorder	48	(1)	308	(1)	10	(0)	72	(0)	1	(0)	8	(0)
Heterosexual contact:	117	(3)	598	(2)	472	(8)	2,064	(8)	46	(5)	163	(5)
<i>Sex with an injecting drug user</i>	36		179		139		558		14		61	
<i>Sex with person with hemophilia</i>	–		4		2		5		–		–	
<i>Sex with transfusion recipient with HIV infection</i>	–		16		7		30		–		2	
<i>Sex with HIV-infected person, risk not specified</i>	81		399		324		1,471		32		100	
Receipt of blood transfusion, blood components, or tissue	17	(0)	168	(1)	33	(1)	141	(1)	2	(0)	18	(1)
Risk not reported or identified ²	942	(21)	4,642	(18)	2,226	(37)	8,247	(33)	281	(30)	749	(23)
Total	4,581	(100)	25,228	(100)	6,069	(100)	25,325	(100)	928	(100)	3,237	(100)

Exposure category	Asian/Pacific Islander				American Indian/Alaska Native				Cumulative totals ³			
	July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Men who have sex with men	16	(47)	74	(50)	17	(38)	150	(49)	4,675	(39)	24,611	(44)
Injecting drug use	3	(9)	14	(10)	10	(22)	51	(17)	2,296	(19)	9,028	(16)
Men who have sex with men and inject drugs	1	(3)	3	(2)	6	(13)	47	(15)	529	(4)	3,655	(7)
Hemophilia/coagulation disorder	–	–	3	(2)	–	–	4	(1)	61	(1)	400	(1)
Heterosexual contact:	1	(3)	6	(4)	2	(4)	10	(3)	644	(5)	2,869	(5)
<i>Sex with an injecting drug user</i>	1		3		1		2		193		811	
<i>Sex with person with hemophilia</i>	–		–		–		–		2		9	
<i>Sex with transfusion recipient with HIV infection</i>	–		–		–		–		7		48	
<i>Sex with HIV-infected person, risk not specified</i>	–		3		1		8		442		2,001	
Receipt of blood transfusion, blood components, or tissue	1	(3)	3	(2)	–	–	3	(1)	53	(0)	339	(1)
Risk not reported or identified	12	(35)	44	(30)	10	(22)	44	(14)	3,637	(31)	14,761	(27)
Total	34	(100)	147	(100)	45	(100)	309	(100)	11,895	(100)	55,663	(100)

¹See Table 16 for states with confidential HIV infection reporting.

²For HIV infection cases (not AIDS), "risk not reported or identified" refers primarily to persons whose mode of exposure was not reported and who have not been followed up to determine their mode of exposure, and to a smaller number of persons who are not reported with one of the exposures listed above after follow-up. See Technical Notes.

³Includes 1,417 men whose race/ethnicity is unknown.

Table 18. Female adult/adolescent HIV infection cases (not AIDS) by exposure category and race/ethnicity, reported July 1994 through June 1995, and cumulative totals through June 1995, from states with confidential HIV infection reporting¹

Exposure category	White, not Hispanic				Black, not Hispanic				Hispanic			
	July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Injecting drug use	291	(28)	1,286	(30)	691	(22)	2,693	(25)	97	(26)	290	(29)
Hemophilia/coagulation disorder	1	(0)	7	(0)	1	(0)	7	(0)	–	–	–	–
Heterosexual contact:	346	(34)	1,595	(38)	891	(28)	3,660	(33)	113	(30)	382	(38)
<i>Sex with an injecting drug user</i>	120		614		276		1,188		49		178	
<i>Sex with a bisexual male</i>	39		207		72		295		5		17	
<i>Sex with person with hemophilia</i>	11		45		3		24		–		5	
<i>Sex with transfusion recipient with HIV-infection</i>	4		23		6		27		–		3	
<i>Sex with HIV-infected person, risk not specified</i>	172		706		534		2,126		59		179	
Receipt of blood transfusion, blood components, or tissue	8	(1)	102	(2)	53	(2)	188	(2)	2	(1)	18	(2)
Risk not reported or identified ²	381	(37)	1,238	(29)	1,507	(48)	4,425	(40)	159	(43)	308	(31)
Total	1,027	(100)	4,229	(100)	3,143	(100)	10,973	(100)	371	(100)	998	(100)

Exposure category	Asian/Pacific Islander				American Indian/Alaska Native				Cumulative totals ³			
	July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Injecting drug use	2	(13)	6	(14)	7	(30)	40	(40)	1,094	(24)	4,340	(26)
Hemophilia/coagulation disorder	–	–	–	–	–	–	–	–	2	(0)	14	(0)
Heterosexual contact:	4	(27)	15	(35)	6	(26)	34	(34)	1,365	(29)	5,718	(34)
<i>Sex with an injecting drug user</i>	1		6		5		22		451		2,015	
<i>Sex with a bisexual male</i>	–		–		–		6		117		527	
<i>Sex with person with hemophilia</i>	–		–		–		–		14		74	
<i>Sex with transfusion recipient with HIV infection</i>	–		–		–		–		10		53	
<i>Sex with HIV-infected person, risk not specified</i>	3		9		1		6		773		3,049	
Receipt of blood transfusion, blood components, or tissue	–	–	1	(2)	1	(4)	1	(1)	64	(1)	316	(2)
Risk not reported or identified	9	(60)	21	(49)	9	(39)	26	(26)	2,120	(46)	6,253	(38)
Total	15	(100)	43	(100)	23	(100)	101	(100)	4,645	(100)	16,642	(100)

¹See Table 16 for states with confidential HIV infection reporting.

²For HIV infection cases (not AIDS), "risk not reported or identified" refers primarily to persons whose mode of exposure was not reported and who have not been followed up to determine their mode of exposure, and to a smaller number of persons who are not reported with one of the exposures listed above after follow-up. See Technical Notes.

³Includes 298 women whose race/ethnicity is unknown.

Table 19. Pediatric HIV infection cases (not AIDS) by exposure category and race/ethnicity, reported July 1994 through June 1995, and cumulative totals through June 1995, from states with confidential HIV infection reporting¹

Exposure category	White, not Hispanic				Black, not Hispanic				Hispanic			
	July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Hemophilia/coagulation disorder	10	(9)	68	(21)	3	(1)	22	(3)	4	(7)	9	(6)
Mother with/at risk for HIV infection:	91	(85)	221	(68)	225	(91)	646	(89)	45	(80)	137	(84)
<i>Injecting drug use</i>	19		50		65		165		15		35	
<i>Sex with injecting drug user</i>	17		31		26		64		10		19	
<i>Sex with bisexual male</i>	1		2		5		9		–		1	
<i>Sex with person with hemophilia</i>	–		–		1		2		–		–	
<i>Sex with transfusion recipient with HIV infection</i>	3		4		–		1		–		–	
<i>Sex with HIV-infected person, risk not specified</i>	15		29		36		78		5		14	
<i>Receipt of blood transfusion, blood components, or tissue</i>	2		3		3		5		1		2	
<i>Has HIV infection, risk not specified</i>	34		102		89		322		14		66	
Receipt of blood transfusion, blood components, or tissue	1	(1)	18	(6)	2	(1)	5	(1)	3	(5)	5	(3)
Risk not reported or identified ²	5	(5)	19	(6)	18	(7)	49	(7)	4	(7)	12	(7)
Total	107	(100)	326	(100)	248	(100)	722	(100)	56	(100)	163	(100)

Exposure category	Asian/Pacific Islander				American Indian/Alaska Native				Cumulative totals ³			
	July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Hemophilia/coagulation disorder	–	–	1	(20)	–	–	2	(17)	18	(4)	105	(8)
Mother with/at risk for HIV infection:	–	–	1	(20)	2	(100)	8	(67)	370	(87)	1,026	(82)
<i>Injecting drug use</i>	–	–	–	–	–	–	3		103		257	
<i>Sex with injecting drug user</i>	–	–	–	–	2		2		55		116	
<i>Sex with bisexual male</i>	–	–	1		–	–	–		6		13	
<i>Sex with person with hemophilia</i>	–	–	–	–	–	–	1		1		3	
<i>Sex with transfusion recipient with HIV infection</i>	–	–	–	–	–	–	–		3		5	
<i>Sex with HIV-infected person, risk not specified</i>	–	–	–	–	–	–	–		56		121	
<i>Receipt of blood transfusion, blood components, or tissue</i>	–	–	–	–	–	–	–		6		10	
<i>Has HIV infection, risk not specified</i>	–	–	–	–	–	–	2		140		501	
Receipt of blood transfusion, blood components, or tissue	–	–	–	–	–	–	–	–	8	(2)	30	(2)
Risk not reported or identified	–	–	3	(60)	–	–	2	(17)	27	(6)	96	(8)
Total	–	–	5	(100)	2	(100)	12	(100)	423	(100)	1,257	(100)

¹See Table 16 for states with confidential HIV infection reporting.

²For HIV infection cases (not AIDS), "risk not reported or identified" refers primarily to persons whose mode of exposure was not reported and who have not been followed up to determine their mode of exposure, and to a smaller number of persons who are not reported with one of the exposures listed above after follow-up. See Technical Notes.

³Includes 29 children whose race/ethnicity is unknown.

Table 20. HIV infection cases (not AIDS) in adolescents and adults under age 25, by sex and exposure category, reported July 1994 through June 1995, and cumulative totals through June 1995, from states with confidential HIV infection reporting¹

Male exposure category	13-19 years old				20-24 years old			
	July 1994– June 1995		Cumulative total		July 1994– June 1995		Cumulative total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Men who have sex with men	108	(46)	583	(43)	728	(53)	4,235	(53)
Injecting drug use	5	(2)	70	(5)	77	(6)	478	(6)
Men who have sex with men and inject drugs	7	(3)	82	(6)	59	(4)	530	(7)
Hemophilia/coagulation disorder	14	(6)	93	(7)	14	(1)	89	(1)
Heterosexual contact:	9	(4)	90	(7)	84	(6)	428	(5)
<i>Sex with an injecting drug user</i>		1		17		24		93
<i>Sex with person with hemophilia</i>		1		2		–		1
<i>Sex with transfusion recipient with HIV infection</i>		–		1		1		4
<i>Sex with HIV-infected person, risk not specified</i>		7		70		59		330
Receipt of blood transfusion, blood components, or tissue	–	–	11	(1)	4	(0)	38	(0)
Risk not reported or identified ²	91	(39)	434	(32)	401	(29)	2,179	(27)
Male subtotal	234	(100)	1,363	(100)	1,367	(100)	7,977	(100)
Female exposure category								
Injecting drug use	11	(4)	99	(8)	83	(12)	436	(15)
Hemophilia/coagulation disorder	–	–	–	–	–	–	1	(0)
Heterosexual contact:	121	(40)	549	(43)	209	(30)	1,158	(39)
<i>Sex with an injecting drug user</i>		23		138		50		349
<i>Sex with a bisexual male</i>		6		41		22		128
<i>Sex with person with hemophilia</i>		2		10		7		26
<i>Sex with transfusion recipient with HIV infection</i>		2		4		2		11
<i>Sex with HIV-infected person, risk not specified</i>		88		356		128		644
Receipt of blood transfusion, blood components, or tissue	3	(1)	11	(1)	6	(1)	28	(1)
Risk not reported or identified	168	(55)	605	(48)	403	(57)	1,337	(45)
Female subtotal	303	(100)	1,264	(100)	701	(100)	2,960	(100)
Total³	537		2,628		2,070		10,940	

¹ See Table 16 for states with confidential HIV infection reporting.

² For HIV infection cases (not AIDS), "risk not reported or identified" refers primarily to persons whose mode of exposure was not reported and who have not been followed up to determine their mode of exposure, and to a smaller number of persons who are not reported with one of the exposures listed above after follow-up. See Technical Notes.

³ Includes 4 persons whose sex is unknown.

Table 21. HIV infection cases (not AIDS), by sex, age at diagnosis, and race/ethnicity, reported through June 1995, from states with confidential HIV infection reporting¹

Male Age at diagnosis (years)	White, not Hispanic		Black, not Hispanic		Hispanic		Asian/ Pacific Islander		American Indian/ Alaska Native		Total ²	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Under 5	116	(0)	321	(1)	63	(2)	2	(1)	3	(1)	511	(1)
5-12	74	(0)	59	(0)	19	(1)	—	—	2	(1)	161	(0)
13-19	558	(2)	712	(3)	51	(2)	4	(3)	8	(3)	1,363	(2)
20-24	3,744	(15)	3,546	(14)	415	(13)	26	(17)	59	(19)	7,977	(14)
25-29	6,579	(26)	5,477	(21)	833	(25)	41	(28)	95	(30)	13,353	(24)
30-34	6,041	(24)	5,703	(22)	813	(24)	31	(21)	69	(22)	12,998	(23)
35-39	3,975	(16)	4,759	(19)	571	(17)	18	(12)	40	(13)	9,807	(17)
40-44	2,199	(9)	2,831	(11)	322	(10)	14	(9)	22	(7)	5,521	(10)
45-49	1,100	(4)	1,180	(5)	137	(4)	7	(5)	8	(3)	2,516	(4)
50-54	546	(2)	607	(2)	46	(1)	3	(2)	5	(2)	1,243	(2)
55-59	239	(1)	254	(1)	21	(1)	2	(1)	2	(1)	532	(1)
60-64	131	(1)	133	(1)	17	(1)	—	—	1	(0)	287	(1)
65 or older	116	(0)	123	(0)	11	(0)	1	(1)	—	—	266	(0)
Male subtotal	25,418	(100)	25,705	(100)	3,319	(100)	149	(100)	314	(100)	56,335	(100)
Female												
Age at diagnosis (years)												
Under 5	115	(3)	291	(3)	65	(6)	2	(4)	6	(6)	491	(3)
5-12	21	(0)	51	(0)	16	(1)	1	(2)	1	(1)	93	(1)
13-19	252	(6)	930	(8)	52	(5)	1	(2)	10	(9)	1,264	(7)
20-24	816	(19)	1,924	(17)	149	(14)	10	(22)	19	(18)	2,960	(17)
25-29	1,047	(24)	2,462	(22)	271	(25)	16	(35)	18	(17)	3,888	(23)
30-34	931	(21)	2,406	(21)	255	(24)	9	(20)	20	(19)	3,689	(21)
35-39	590	(14)	1,678	(15)	122	(11)	1	(2)	22	(20)	2,452	(14)
40-44	264	(6)	883	(8)	80	(7)	3	(7)	9	(8)	1,264	(7)
45-49	158	(4)	332	(3)	35	(3)	2	(4)	2	(2)	546	(3)
50-54	53	(1)	148	(1)	15	(1)	1	(2)	1	(1)	222	(1)
55-59	45	(1)	100	(1)	13	(1)	—	—	—	—	160	(1)
60-64	22	(1)	50	(0)	5	(0)	—	—	—	—	79	(0)
65 or older	51	(1)	60	(1)	1	(0)	—	—	—	—	118	(1)
Female subtotal	4,365	(100)	11,315	(100)	1,079	(100)	46	(100)	108	(100)	17,226	(100)
Total³	29,784		37,022		4,398		195		423		73,577	

¹See Table 16 for states with confidential HIV infection reporting.

²Includes 1,430 males and 313 females whose race/ethnicity is unknown.

³Includes 16 persons whose sex is unknown.

Table 22. Persons reported to be living with HIV infection (not AIDS) and with AIDS, by state and age group, reported through June 1995¹

State of residence (Date HIV reporting initiated)	Living with HIV (not AIDS) ²			Living with AIDS ³			Cumulative totals		
	Adults/ adolescents	Children <13 years old	Total	Adults/ adolescents	Children <13 years old	Total	Adults/ adolescents	Children <13 years old	Total
Alabama (Jan. 1988)	3,673	31	3,704	1,431	18	1,449	5,104	49	5,153
Alaska	—	—	—	140	1	141	140	1	141
Arizona (Jan. 1987)	2,768	25	2,793	1,343	8	1,351	4,111	33	4,144
Arkansas (July 1989)	1,279	20	1,299	849	15	864	2,128	35	2,163
California	—	—	—	28,622	169	28,791	28,622	169	28,791
Colorado (Nov. 1985)	5,107	26	5,133	2,010	8	2,018	7,117	34	7,151
Connecticut (July 1992) ⁴	—	86	86	3,016	75	3,091	3,016	161	3,177
Delaware	—	—	—	585	4	589	585	4	589
District of Columbia	—	—	—	3,086	62	3,148	3,086	62	3,148
Florida	—	—	—	19,202	495	19,697	19,202	495	19,697
Georgia	—	—	—	5,688	71	5,759	5,688	71	5,759
Hawaii	—	—	—	583	4	587	583	4	587
Idaho (June 1986)	275	3	278	120	—	120	395	3	398
Illinois	—	—	—	5,805	86	5,891	5,805	86	5,891
Indiana (July 1988)	2,475	22	2,497	1,477	14	1,491	3,952	36	3,988
Iowa	—	—	—	345	4	349	345	4	349
Kansas	—	—	—	559	3	572	569	3	572
Kentucky	—	—	—	578	8	586	578	8	586
Louisiana (Feb. 1993)	3,585	40	3,625	2,820	45	2,865	6,405	85	6,490
Maine	—	—	—	308	5	313	308	5	313
Maryland	—	—	—	4,889	131	5,020	4,889	131	5,020
Massachusetts	—	—	—	3,623	63	3,686	3,623	63	3,686
Michigan (April 1992)	2,382	62	2,444	2,706	28	2,734	5,088	90	5,178
Minnesota (Oct. 1985)	1,985	20	2,005	1,022	11	1,033	3,007	31	3,038
Mississippi (Aug. 1988)	2,820	35	2,855	882	19	901	3,702	54	3,756
Missouri (Oct. 1987)	3,203	36	3,239	2,580	15	2,595	5,783	51	5,834
Montana	—	—	—	63	1	64	63	1	64
Nebraska	—	—	—	247	3	250	247	3	250
Nevada (Feb. 1992)	1,849	19	1,868	996	11	1,007	2,845	30	2,875
New Hampshire	—	—	—	273	3	276	273	3	276
New Jersey (Jan. 1992)	9,224	295	9,519	9,102	242	9,344	18,326	537	18,863
New Mexico	—	—	—	466	2	468	466	2	468
New York	—	—	—	26,240	671	26,911	26,240	671	26,911
North Carolina (Feb. 1990)	5,374	45	5,419	2,363	42	2,405	7,737	87	7,824
North Dakota (Jan. 1988)	52	—	52	26	—	26	78	—	78
Ohio (June 1990)	1,911	13	1,924	2,496	30	2,526	4,407	43	4,450
Oklahoma (June 1988)	1,493	9	1,502	946	5	951	2,439	14	2,453
Oregon	—	—	—	1,260	4	1,264	1,260	4	1,264
Pennsylvania	—	—	—	5,725	115	5,840	5,725	115	5,840
Rhode Island	—	—	—	575	5	580	575	5	580
South Carolina (Feb. 1986)	5,189	71	5,260	2,248	23	2,271	7,437	94	7,531
South Dakota (Jan. 1988)	132	5	137	36	2	38	168	7	175
Tennessee (Jan. 1992)	2,918	37	2,955	2,044	14	2,058	4,962	51	5,013
Texas (Feb. 1994) ⁴	—	181	181	13,174	129	13,303	13,174	310	13,484
Utah (April 1989)	760	5	765	458	6	464	1,218	11	1,229
Vermont	—	—	—	102	1	103	102	1	103
Virginia (July 1989)	5,453	55	5,508	2,623	70	2,693	8,076	125	8,201
Washington	—	—	—	2,618	11	2,629	2,618	11	2,629
West Virginia (Jan. 1989)	331	2	333	208	2	210	539	4	543
Wisconsin (Nov. 1985)	1,752	22	1,774	1,024	9	1,033	2,776	31	2,807
Wyoming (June 1989)	56	—	56	46	—	46	102	—	102
Subtotal	66,046	1,165	67,211	169,638	2,763	172,401	235,684	3,928	239,612
Guam	—	—	—	4	—	4	4	—	4
Pacific Islands, U.S.	—	—	—	—	—	—	—	—	—
Puerto Rico	—	—	—	5,851	153	6,004	5,851	153	6,004
Virgin Islands, U.S.	—	—	—	134	7	141	134	7	141
Total	66,046	1,165	67,211	175,627	2,923	178,550	241,673	4,088	245,761

¹Persons reported with vital status "alive" as of the last update.

²Includes only persons reported from states with confidential HIV reporting. Excludes 1,553 adults/adolescents and 26 children reported from states with confidential HIV infection reporting whose state of residence is unknown or are residents of other states.

³Includes 225 adults/adolescents and 2 children whose state of residence is unknown

⁴Connecticut and Texas have confidential HIV infection reporting for pediatric cases only.

Surveillance of AIDS

All 50 states, the District of Columbia, U.S. dependencies and possessions, and independent nations in free association with the United States¹ report AIDS cases to CDC using a uniform surveillance case definition and case report form. The original definition was modified in 1985 (*MMWR* 1985;34:373-75) and 1987 (*MMWR* 1987;36[suppl no. 1S]:1S-15S). The case definition for adults and adolescents was modified again in 1993 (*MMWR* 1992;41[no. RR-17]:1-19; see also *MMWR* 1995;44:160-61,64-7). The revisions incorporated a broader range of AIDS-indicator diseases and conditions and used HIV diagnostic tests to improve the sensitivity and specificity of the definition. The laboratory and diagnostic criteria for the 1987 pediatric case definition (*MMWR* 1987;36:225-30,235) were updated in 1994 (*MMWR* 1994;43[no. RR-12]:1-19).

For persons with laboratory-confirmed HIV infection, the 1987 revision incorporated HIV encephalopathy, wasting syndrome, and other indicator diseases that are diagnosed presumptively (i.e., without confirmatory laboratory evidence of the opportunistic disease). In addition to the 23 clinical conditions in the 1987 definition, the 1993 case definition for adults and adolescents includes HIV-infected persons with CD4⁺ T-lymphocyte counts of less than 200 cells/ μ L or a CD4⁺ percentage of less than 14, and persons diagnosed with pulmonary tuberculosis, recurrent pneumonia, and invasive cervical cancer. All conditions added to the 1993 definition require laboratory confirmation of HIV infection. Persons who meet the criteria for more than one definition category are classified hierarchically in the following order: pre-1987, 1987, and 1993. Persons in the 1993 definition category meet only the 1993 definition.

The pediatric case definition incorporates the revised 1994 pediatric classification system for evidence of HIV infection. Children with their first positive results on Western blot or HIV detection tests before October 1994 were categorized based on the 1987 classification system. Those tested during or after October 1994 are categorized under the revised 1994 pediatric classification system. For children of any

age with an AIDS-defining condition that requires evidence of HIV infection, a single positive HIV-detection test (i.e., HIV culture, HIV PCR, or HIV antigen [p24]) is sufficient for a reportable AIDS diagnosis if the diagnosis is confirmed by a clinician. The 1994 pediatric definitions for HIV encephalopathy and HIV wasting syndrome reflect increased knowledge of these conditions in children, and replace the 1987 definitions.

Although completeness of reporting of diagnosed AIDS cases to state and local health departments varies by geographic region and patient population, studies conducted by state and local health departments indicate that reporting of AIDS cases in most areas of the United States is more than 85 percent complete (*J Acquir Immune Def Syndr*, 1992;5:257-64 and *Am J Public Health* 1992;82:1495-99). In addition, multiple routes of exposure, opportunistic diseases diagnosed after the initial AIDS case report was submitted to CDC, and vital status may not be determined or reported for all cases.

Included in this report are persons known to be infected with human immunodeficiency virus type 2 (HIV-2). See *MMWR* 1995;44:603-06.

Surveillance of HIV infection (not AIDS)

Through December 31, 1994, 25 states had laws or regulations requiring confidential reporting by name of all persons with confirmed HIV infection, in addition to reporting of persons with AIDS. Two other states, Connecticut and Texas, required reporting by name of HIV infection only for children less than 13 years of age. These states initiated reporting at various times after the development of serum HIV-antibody tests in 1985. Before 1991, surveillance of HIV infection was not standardized and reporting of HIV infections was based primarily on passive surveillance. Consequently, many cases reported before 1991 do not have complete information. Since then, CDC has assisted states in conducting active surveillance of HIV infection using standardized report forms and software. However, collection of demographic and risk information still varies greatly among states.

HIV infection data should be interpreted with caution. HIV surveillance reports are not representative of all persons with HIV infection. Because many HIV-reporting states also offer anonymous HIV testing, confidential HIV infection reports are not representative of all persons being tested in these areas. Furthermore, many factors may influence testing pat-

¹ Included among the dependencies, possessions, and independent nations are Puerto Rico, the U.S. Virgin Islands, Guam, American Samoa, the Republic of Palau, the Republic of the Marshall Islands, the Commonwealth of the Northern Mariana Islands, and the Federated States of Micronesia. The latter 5 comprise the category "Pacific Islands, U.S." listed in Tables 1 and 22.

terns, including the extent that testing is targeted or routinely offered to specific groups and the availability and access to medical care and testing services. These data provide a minimum estimate of the number of persons known to be HIV infected in states with confidential HIV infection reporting.

For this report, persons greater than 18 months of age were considered HIV infected if they had at least one positive Western blot or positive detection test (culture, antigen, or other detection test) or had a diagnosis of HIV infection documented by a physician. Before October 1994, children less than 15 months of age were considered HIV infected if they met the definition stated in the 1987 pediatric classification system for HIV infection (*MMWR* 1987;36:225-30,235). Beginning October 1994, children less than 18 months of age are considered HIV infected if they meet the definition stated in the 1994 pediatric classification system for HIV infection (*MMWR* 1994;43[no. RR-12]:1-10). This report also includes children who were diagnosed as HIV infected by a physician. Although many states monitor reports of children born to infected mothers, only those with documented diagnosis of HIV infection are included in this report.

Because states initiated reporting on different dates, the length of time reporting has been in place will influence the number of HIV infection cases reported. For example, data presented for a given annual period may include cases reported during only a portion of the year. Prior to statewide HIV reporting, some states collected reports of HIV infection in selected populations. Therefore, these states have reports prior to initiation of statewide confidential reporting.

Over time, persons with HIV infection will be diagnosed and reported with AIDS. HIV infection cases later reported with AIDS are deleted from the HIV infection tables and added to the AIDS tables. Persons with HIV infection may be tested at any point in the clinical spectrum of disease, therefore the time between diagnosis of HIV infection and AIDS will vary. In addition, because surveillance practices differ, reporting and updating of clinical and vital status of cases vary among states.

Included in this report are persons known to be infected with human immunodeficiency virus type 2 (HIV-2). See *MMWR* 1995;44:603-06.

Tabulation and presentation of HIV infection and AIDS data

Data in this report are provisional. Each issue of this report includes information received by CDC

through the last day of the reporting period. AIDS data are tabulated by date of report to CDC unless otherwise noted. Data for U.S. dependencies and possessions and for associated independent nations are included in the totals.

Age group tabulations are based on the person's age at first documented positive HIV-antibody test result for HIV infection cases, and age at diagnosis of AIDS for AIDS cases. Adult/adolescent cases include persons 13 years of age and older; pediatric cases include children under 13 years of age. Age group tabulations for AIDS cases in Table 14 (year-end edition only) are based on age at death.

Tabulations of persons living with HIV and AIDS (Table 22), include persons whose vital status was "alive" as of the last update; persons whose vital status is missing or unknown are not included. Caution should be used in interpreting these data because states vary in the frequency with which they review the vital status of persons reported with HIV infection and AIDS. In addition, some cases may be lost to follow-up.

Table 12 (year-end edition only) tabulates AIDS-indicator conditions reported during the last year. These data are known to underreport AIDS-indicator conditions and should be interpreted with caution. Reported conditions overrepresent initial AIDS-indicator illness because follow-up for subsequent indicator diseases is resource intensive and has not been systematic or standardized in most health departments. The 1993 AIDS surveillance case definition for adults and adolescents added reporting of HIV-infected persons with severe HIV-related immunosuppression (CD^+ T-lymphocyte count of less than 200 μ L or less than 14 percent). Since implementation of the 1993 definition, approximately half of all cases were reported based only on immunologic criteria; consequently, reporting of AIDS cases based on AIDS-defining opportunistic infections has decreased (see *AIDS* 1994;8:1489-93).

Table 2 lists AIDS case counts for each metropolitan area with 500,000 or more population. AIDS case counts for metropolitan areas with 50,000 to 500,000 population are reported as a combined subtotal. On December 31, 1992, the Office of Management and Budget announced new Metropolitan Statistical Area (MSA) definitions, which reflect changes in the U.S. population as determined by the 1990 census. These definitions were updated most recently on July 1, 1994. The cities and counties which compose each metropolitan area listed in Table 2 are provided in the publication "Metropolitan Areas as of June 30, 1995" (available by calling the National Technical Informa-

tion Service, 1-703-487-4650, and ordering accession no. PB95-208880). Standards for defining central and outlying counties of metropolitan areas were published in the *Federal Register* (see *FR* 1990;55:12154-60).

The metropolitan areas definitions are the MSAs for all areas except the 6 New England states. For these states, the New England County Metropolitan Areas (NECMA) are used. Metropolitan areas are named for a central city in the MSA or NECMA, may include several cities and counties, and may cross state boundaries. For example, AIDS cases and annual rates presented for the District of Columbia in Table 1 include only persons residing within the geographic boundaries of the District. AIDS cases and annual rates for Washington, D.C., in Table 2 include persons residing within the several counties in the metropolitan area, including counties in Maryland, Virginia, and West Virginia. State or metropolitan area data tabulations are based on the person's residence at first positive HIV-antibody test result for HIV infection cases and residence at diagnosis of the first AIDS-indicator condition(s) for AIDS cases.

Estimated AIDS-opportunistic illness

In 1993, the AIDS surveillance case definition was expanded to include a laboratory measure of severe immunosuppression ($CD4^+$ T-lymphocyte count of less than 200 cells/ μ L or a percent of total lymphocytes less than 14) and three additional clinical conditions (pulmonary tuberculosis, recurrent pneumonia, and invasive cervical cancer). Before 1993, the surveillance definition included only opportunistic illnesses, and trends in the incidence of AIDS were evaluated by examining the number of AIDS opportunistic illnesses (AIDS-OIs) diagnosed per year or quarter (adjusted for reporting delays). Because most HIV-infected persons become severely immunosuppressed before the onset of AIDS-OIs, the addition of the $CD4^+$ criteria has temporarily distorted observed trends in AIDS incidence. To examine trends over time, an additional adjustment is required to estimate when an AIDS-OI will develop in persons who were reported based on the $CD4^+$ criteria. CDC has developed a procedure to estimate the incidence of AIDS-OIs among persons reported with AIDS based on the $CD4^+$ criteria. Estimates of trends in AIDS-OIs are displayed in Tables 13, 14, and 15.

The estimated AIDS-OI incidence is the sum of incidence in two groups. The first group is persons reported to AIDS surveillance with AIDS-OIs. Inci-

dence in this group is estimated by adjusting reported cases for delays in case reporting.

The second group is persons reported with AIDS based on a $CD4^+$ count or percent. Most of these persons will eventually have an AIDS-OI diagnosed. CDC has estimated the number of persons who had or will have an AIDS-OI diagnosed after the date of the reported $CD4^+$ count or percent, by month of AIDS-OI diagnosis. To do this, CDC used data from the Adult Spectrum of Disease Project (see *JAMA* 1992;267:1798-1805) to estimate the probability distribution of the time interval between a $CD4^+$ count in a particular range (e.g., 0 to 29 cells/ μ L, 30 to 59 cells/ μ L, etc.) and the diagnosis of an AIDS-OI. This probability distribution is the proportion of persons with a $CD4^+$ count in a given range who will have an AIDS-OI diagnosed 1 month, 2 months, etc., after the reported $CD4^+$ count. The expected number of persons with an AIDS-OI diagnosed in each later month among persons whose $CD4^+$ count was in a particular range during a given month is the product of the number of these persons and the proportion expected to have an AIDS-OI diagnosed in this later month. The estimate of the number of AIDS-OI diagnoses in a particular month among persons reported with AIDS based on the $CD4^+$ criteria is the sum, over all combinations of $CD4^+$ ranges and previous months, of the number of persons expected to be diagnosed with an AIDS-OI in the month for which the estimate is made.

There is uncertainty in these estimates of AIDS-OI incidence. Some uncertainty is the result of the need to adjust for delays in reporting of AIDS cases. There is additional uncertainty because some persons reported with AIDS based on the $CD4^+$ criteria die before an AIDS-OI is diagnosed and hence should not contribute to the AIDS-OI incidence estimate. Other persons reported with AIDS based on the $CD4^+$ criteria have an unreported AIDS-OI diagnosis by the date of the $CD4^+$ determination; the estimation procedure counts their contribution to AIDS-OI incidence later than it should. However, preliminary analyses show that these two sources of bias change estimated AIDS-OI incidence by only a few percentage points.

Reporting delays were estimated by a maximum likelihood statistical procedure, taking into account possible differences in reporting delays among exposure, geographic, racial/ethnic, age, and sex categories, but assuming that reporting delays within these groups have not changed over time (see *Lecture Notes in Biomathematics* 1989;83:58-88).

The regions of residence included in Table 13 are defined as follows. Northeast: Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New

York, Pennsylvania, Rhode Island, and Vermont; Midwest: Indiana, Illinois, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin; South: Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia; West: Alaska, Arizona, California, Colorado, Idaho, Hawaii, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming; Territories: Guam, Puerto Rico, the U.S. Virgin Islands, and the U.S. Pacific Islands listed on page 30.

Exposure categories

For surveillance purposes, HIV infection cases and AIDS cases are counted only once in a hierarchy of exposure categories. Persons with more than one reported mode of exposure to HIV are classified in the exposure category listed first in the hierarchy, except for men with both a history of sexual contact with other men and injecting drug use. They make up a separate exposure category.

"Men who have sex with men" cases include men who report sexual contact with other men (i.e., homosexual contact) and men who report sexual contact with both men and women (i.e., bisexual contact). "Heterosexual contact" cases are in persons who report specific heterosexual contact with a person with, or at increased risk for, HIV infection (e.g., an injecting drug user).

Adults/adolescents born, or who had sex with someone born, in a country where heterosexual transmission was believed to be the predominant mode of HIV transmission (formerly classified as Pattern-II countries by the World Health Organization) are no longer classified as having heterosexually acquired AIDS. Similar to case reports for other persons who are reported without behavioral or transfusion risks for HIV, these reports are now classified (in the absence of other risk information which would classify them into another exposure category) as "no risk reported or identified" (see *MMWR* 1994;43:155-60). Children whose mother was born, or whose mother had sex with someone born, in a Pattern-II country are now classified (in the absence of other risk information which would classify them into another exposure category) as "Mother with/at risk for HIV infection: has HIV infection, risk not specified."

"No risk reported or identified" cases are in persons with no reported history of exposure to HIV through

any of the routes listed in the hierarchy of exposure categories. Risk not identified cases include persons who are currently under investigation by local health department officials; persons whose exposure history is incomplete because they died, declined to be interviewed, or were lost to follow-up; and persons who were interviewed or for whom other follow-up information was available and no exposure mode was identified. Persons who have an exposure mode identified at the time of follow-up are reclassified into the appropriate exposure category. In general, investigations and follow up for modes of exposure by state health departments are conducted routinely for persons reported with AIDS and as resources allow for those reported with HIV infection. Therefore, the percentage of HIV infected persons with risk not reported or identified is substantially higher than for those reported with AIDS. As HIV infected persons with risk not reported or identified are diagnosed and reported with AIDS, they are assigned higher priority for follow-up to determine the mode(s) of exposure.

Rates

Rates are calculated on a 12-month basis per 100,000 population for AIDS cases only. Rates are not calculated for HIV infection reports because case counts for HIV infection are believed to be less complete than AIDS case counts. Population denominators for computing AIDS rates for the 50 states and the District of Columbia are based on official post-census estimates from the U.S. Bureau of Census. Denominators for U.S. dependencies and possessions are linear extrapolations of official 1980 and 1990 census counts. Each 12-month rate is the number of cases reported during the 12-month period, divided by the 1994 or 1995 population, multiplied by 100,000. The denominators for computing race-specific rates (Table 10, year-end edition only) are based on 1990 census projections published in U.S. Bureau of Census publication P25-1104, "Population Projections of the United States, by Age, Sex, Race, and Hispanic Origin: 1993 to 2050." Race-specific rates are the number of cases reported for a particular racial/ethnic group during the preceding 12-month period divided by the projected population for that race/ethnicity, multiplied by 100,000.

Case-fatality rates are calculated for each half-year by date of diagnosis of AIDS. Each 6-month case-fatality rate is the number of deaths ever reported among cases diagnosed in that period (regardless of the year of death), divided by the num-

ber of total cases diagnosed in that period, multiplied by 100. Reported deaths are not necessarily caused by HIV-related disease. Caution should be used in interpreting case-fatality rates because reporting of deaths is incomplete (see *Am J Public Health* 1992; 82:1500-05 and *Am J Public Health* 1990; 80: 1080-86).

Reporting delays

Reporting delays (time between diagnosis of HIV infection or AIDS and report to CDC) vary widely among exposure, geographic, racial/ethnic, age and sex categories, and have been as long as several years for some AIDS cases. About 50 percent of all AIDS cases were reported to CDC within 3 months of diagnosis, with about 20 percent being reported more than one year after diagnosis. Reporting delay for HIV infection cases is being evaluated.

**OFFICE OF NATIONAL AIDS POLICY
EXECUTIVE OFFICE OF THE PRESIDENT**

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FACSIMILE COVER SHEET

TO: Eva Seiler

FAX NUMBER: 404-639-8153

FROM: Jane Sanville

DATE: 1.18.96

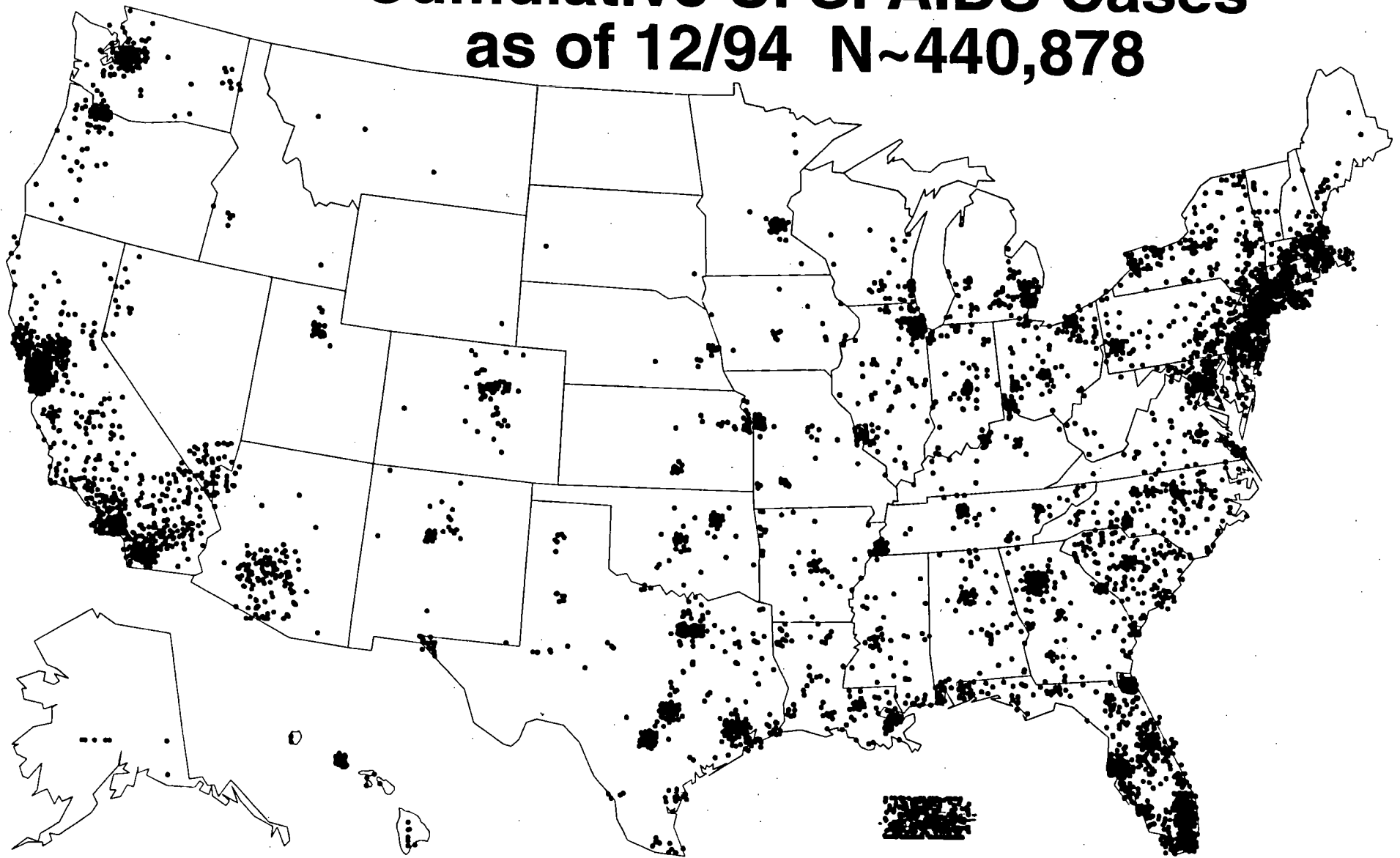
PAGES INCLUDING COVER SHEET: 6

COMMENTS:

Thank you! Here are the charts...

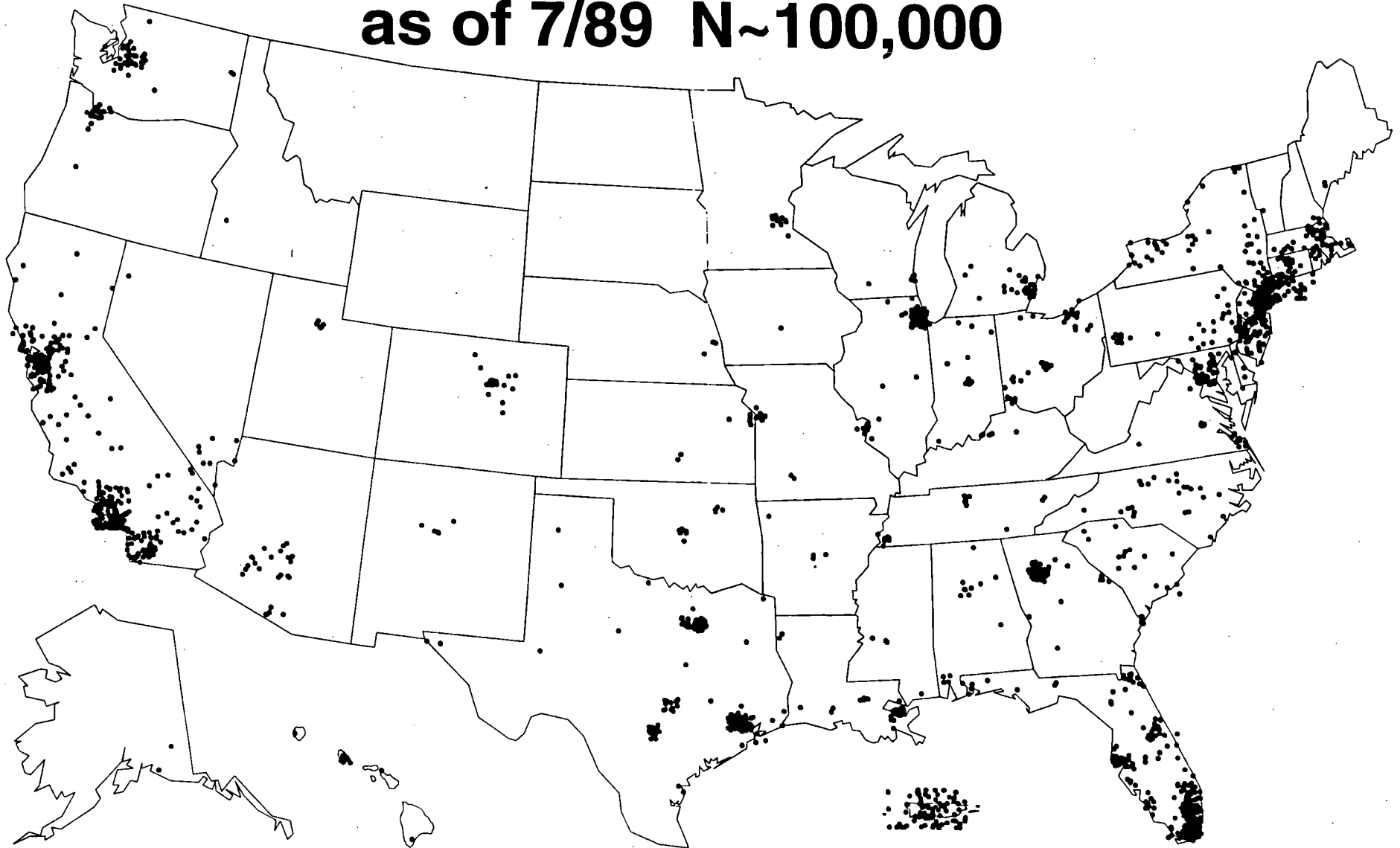
FIGURE
CHART #2

Cumulative U. S. AIDS Cases as of 12/94 N~440,878



Each point = 30 cases

Cumulative U.S. AIDS Cases as of 7/89 N~100,000



Each point = 30 cases

Cumulative U. S. AIDS Cases as of 5/85 N~10,000



Each point = 30 cases

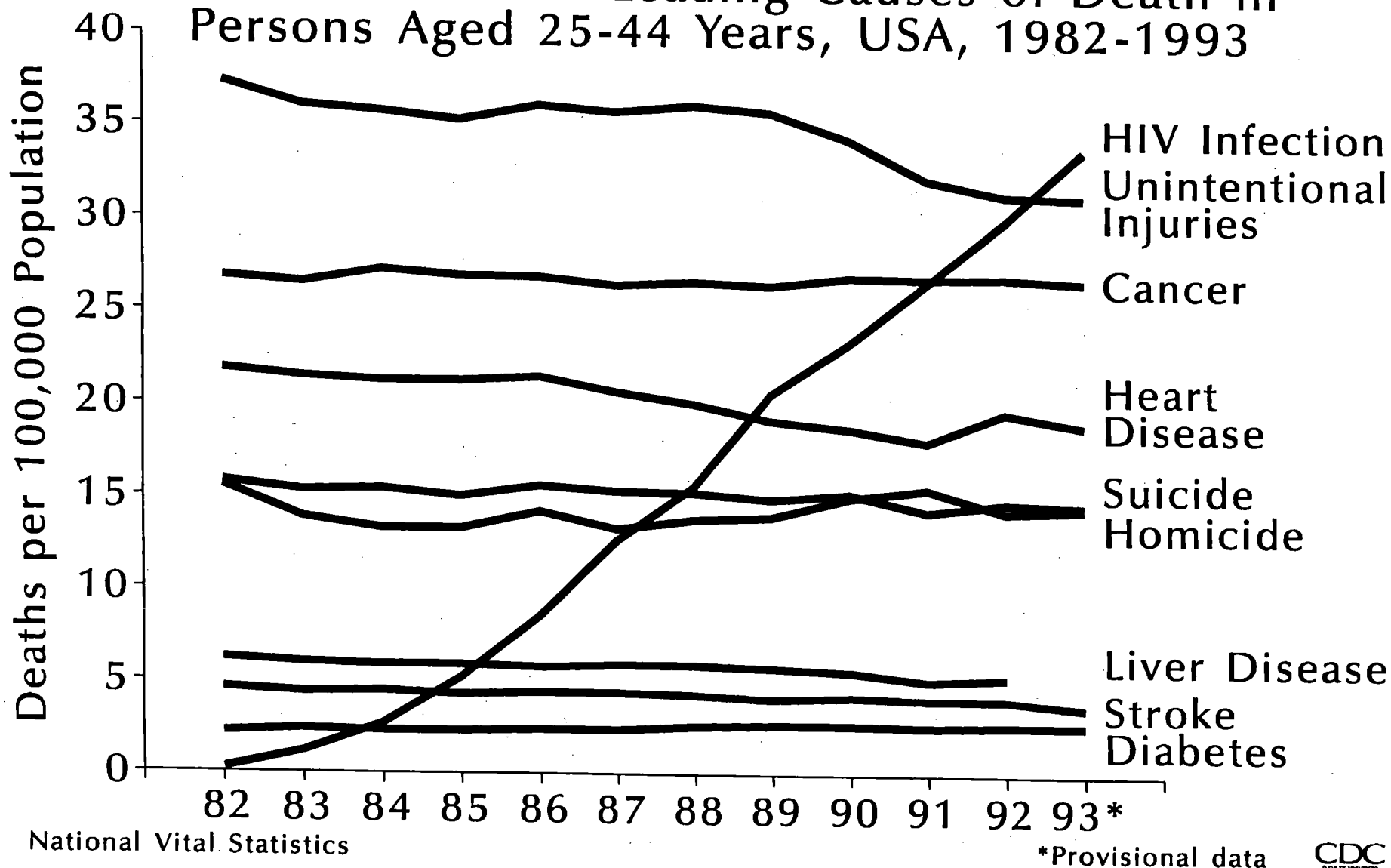
Cumulative U.S. AIDS Cases as of 2/83 N~1,000



Each point = 30 cases

Figure
CHART #1

Death Rates from Leading Causes of Death in Persons Aged 25-44 Years, USA, 1982-1993





Facsimile Transmission

National Center for HIV, STD, and TB Prevention

Corporate Square

Atlanta, Georgia

TO:

Jane Sanville

FROM:

Eva Margolies Seiler

Name

Name

Address

Office of the DirectorNCHSTP11 2116 E-07Building/Room/Mailstop(202) 632-1090

Telephone No.

(404) 639-8008

Telephone No.

(404) 639-8600 / 8153

Facsimile Telephone No.

(202) 632-1096

Facsimile Telephone No.

DATE: 1/19/96NUMBER OF PAGES (Including cover): 8SUBJECT: HIV/TB ConnectionMESSAGE: We don't have much "canned" material on the connection between HIV & TB. I've faxed you acouple of sentences from the TB Division & an article about the risk of TB among IV drug users infected w/ HIV. Please call me to discuss.

CONNECTION BETWEEN HIV AND TB

HIV infection is the strongest known risk factor for the development of TB disease in persons with TB infection. For example, studies suggest that the risk of developing TB disease is 7% to 10% each year for persons who are infected with both *M. tuberculosis* and HIV, whereas it is 10% over a lifetime for persons infected only with *M. tuberculosis*.

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A PROSPECTIVE STUDY OF THE RISK OF TUBERCULOSIS AMONG INTRAVENOUS DRUG USERS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION

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Abstract To determine the risk of active tuberculosis associated with human immunodeficiency virus (HIV) infection, we prospectively studied 520 intravenous drug users enrolled in a methadone-maintenance program. Tuberculin skin testing and testing for HIV antibody were performed in all subjects.

Forty-nine of 217 HIV-seropositive subjects (23 percent) and 62 of 303 HIV-seronegative subjects (20 percent) had a positive response to skin testing with purified protein derivative (PPD) tuberculin before entry into the study. The rates of conversion from a negative to a positive PPD test were similar for seropositive subjects (15 of 131; 11 percent) and seronegative subjects (26 of 202; 13 percent) who were retested during the follow-up period (mean, 22 months). Active tuberculosis developed in eight of the HIV-seropositive subjects (4 percent) and none of the seronegative subjects during the study

period ($P < 0.002$). Seven of the eight cases of tuberculosis occurred in HIV-seropositive subjects with a prior positive PPD test (7.9 cases per 100 person-years, as compared with 0.3 case per 100 person-years among seropositive subjects without a prior positive PPD test; rate ratio, 24.0; $P < 0.0001$).

We conclude that, although the prevalence and incidence of tuberculous infection were similar for both HIV-seropositive and HIV-seronegative intravenous drug users, the risk of active tuberculosis was elevated only for seropositive subjects. These data also suggest that in HIV-infected persons tuberculosis most often results from the reactivation of latent tuberculous infection; our results lend support to recommendations for the aggressive use of chemoprophylaxis against tuberculosis in patients with HIV infection and a positive PPD test. (*N Engl J Med* 1989; 320:545-50.)

EPIDEMIOLOGIC surveillance data in the United States have suggested an important association between tuberculosis and the acquired immunodeficiency syndrome (AIDS). Increasing rates of tuberculosis have been noted in areas with high concentrations of AIDS cases, and comparisons of tuberculosis registries and AIDS registries in several regions have indicated considerable overlap.¹⁻³ Hospital-based studies have suggested that 10 percent or more of patients with AIDS may also have tuberculosis; the risk of tuberculosis is particularly high among nonwhites and among intravenous drug users.^{1,2,6-10} Seroprevalence studies of patients with tuberculosis in regions with high numbers of AIDS cases have found an increased prevalence of antibody to human immunodeficiency virus (HIV) among such patients.^{6,11,12}

The clinical importance of tuberculosis in the spectrum of AIDS-related disease is reflected in the revised case definition for AIDS of the Centers for Disease Control (CDC); this definition now includes extrapulmonary tuberculosis as an AIDS-qualifying diagnosis in HIV-infected patients (i.e., the equivalent of a diagnosis of AIDS).¹³

Despite the suggestive epidemiologic and clinical evidence linking tuberculosis and AIDS, however, few prospective studies have examined the incidence of tuberculosis in HIV-infected populations.¹⁴ Most studies have been either cross-sectional or retrospective, starting with identified patients with AIDS and determining the prevalence of tuberculosis among such patients.^{2,6-10} Such approaches do not permit an analysis of the risk of tuberculosis among HIV-infected persons — an issue that has important implications for both clinical management and public health. In addition, existing studies have been unable to address directly whether tuberculosis in patients with AIDS is more likely to result from the reactivation of latent infection or from primary tuberculous infection.¹⁻⁴

To estimate the risk of tuberculosis among HIV-infected persons and to assess the likelihood of reactivation as compared with primary infection as a cause

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of tuberculosis in this group of patients, it is necessary to study prospectively a defined population, in which both serologic status with respect to HIV and the results of previous tests for tuberculous infection are known. This report describes a two-year prospective study of tuberculosis among 520 HIV-seropositive and HIV-seronegative intravenous drug users in a New York City methadone-maintenance treatment program for whom complete base-line tuberculosis-screening information was available.

METHODS

Beginning in June 1985, current and former intravenous drug users enrolled in a long-term methadone-maintenance program in the Bronx, New York, were recruited for participation in a seroprevalence survey and a subsequent longitudinal study of HIV infection. After giving informed consent, the subjects took part in standardized interviews in which they were asked about sociodemographic and behavioral variables. A medical history, including a history of tuberculosis infection, was elicited, and a limited physical examination was performed. A serum sample was obtained for HIV antibody testing by enzyme immunoassay (Abbott Laboratories, North Chicago), with confirmation by Western blot testing. Specimens were considered positive if antibodies to both one core antigen (p24) and one envelope antigen (gp41 or gp120) were present on Western blot testing. Follow-up visits, with repeat interviews, examinations, and serologic testing, were scheduled every six months.

On admission to the methadone program and at yearly intervals thereafter, as part of mandatory routine physical examinations, all patients were given tuberculin skin tests (Mantoux tests), in which 0.1 ml of 5-tuberculin-unit purified protein derivative (PPD) (Aplisol, Parke-Davis, Morris Plains, N.J.) was injected intradermally. Patients known to have had positive PPD tests in the past were not retested. Induration ≥ 10 mm in diameter at 48 to 72 hours was considered a positive response. Since mid-1987, in order to investigate the possibility of cutaneous anergy in patients with negative PPD tests, all patients have also undergone delayed hypersensitivity skin testing with a seven-antigen multiple-puncture skin-test device (Multitest CMI, Merieux Institute, Miami) at the time of the injection of PPD. Anergy was defined as the absence of induration ≥ 2 mm in diameter in response to any of the seven skin-test antigens at 48 hours. The skin tests were administered and the results were interpreted by trained nurses in the methadone program; the clinical follow-up was conducted by the program's medical staff. Any patients in whom active tuberculosis was suspected were referred for admission to the hospital affiliated with the program.

From June 1985 through January 1988, information was actively sought on all hospitalizations, diagnoses of AIDS, diagnoses of tuberculosis, and deaths among the study subjects. Hospitalizations were identified through a weekly review of logbooks that recorded all hospital admissions among patients in the treatment program, a process facilitated by the requirement that all hospitals verify patients' methadone dosages with the treatment program before inpatient administration of methadone can be authorized.¹ All diagnoses of tuberculosis or AIDS were confirmed through a review of hospital records. Active tuberculosis was defined as a culture positive for *Mycobacterium tuberculosis* from pulmonary or extrapulmonary specimens, in addition to the corresponding clinical manifestations; diagnoses of AIDS were confirmed with use of the standard CDC case-definition criteria.^{13,15} The subjects' history of tuberculosis infections and their prior PPD status were determined by a review of the methadone program clinic's charts; for patients with a history of positive PPD tests, the source of that information (i.e., documented test results or the patient's own report) was noted. Conversions from negative to positive PPD status, defined as newly positive PPD tests (induration ≥ 10 mm in diameter) in patients with documented prior negative tests, were identified by a review of the clinic's charts and the program's centralized registries of all skin-test results.

For purposes of analysis, the patients were divided into HIV-

seropositive and HIV-seronegative groups and were compared with respect to the following variables: history of tuberculosis and PPD status before entry into the study, frequency of newly positive PPD tests after entry into the study, and frequency of active tuberculosis after entry into the study, for patients with and without prior positive PPD tests. For the subgroup of patients who had undergone multiple-antigen skin testing since mid-1987, the prevalence of anergy among HIV-seropositive and HIV-seronegative subjects was determined and compared.

Because of the known association between race or ethnic group and tuberculosis in the United States¹⁶ and because of the earlier observation from our sample that nonwhites tend to be overrepresented among HIV-seropositive subjects,¹⁷ the rates of tuberculosis were also calculated and compared for each serologic group stratified by race or ethnic group.

The cumulative incidence of conversion from negative to positive PPD status and that of active tuberculosis was calculated for both seropositive and seronegative subjects. Associations for two-by-two tables were tested with use of Fisher's exact test. To account for the varying length of follow-up, denominators expressed in person-time were used to calculate the incidence of tuberculosis for both groups, along with the corresponding rate ratios, which were calculated only for tables with cells containing values other than zero. Exact statistical tests of data on person-time were computed on the basis of the hypergeometric distribution.¹⁸ All statistical associations were assessed with use of two-tailed t-tests, with an alpha-error cutoff value of 0.05 for statistical significance.

RESULTS

Of the 1274 patients enrolled in the methadone program from June 1985 through December 1987, 660 (52 percent) participated in the study of HIV seroprevalence and the subsequent longitudinal study. The participants and nonparticipants did not differ materially with respect to age, sex, or race or ethnic background. Of the 660 study subjects, 520 (79 percent) had complete clinical records, documenting their history of tuberculosis and PPD status, available for review; 217 (42 percent) were HIV-seropositive and 303 (58 percent) were seronegative at base line. Of the subjects who were initially seronegative for HIV, 10 were found to have seroconverted by the end of the study period; in this analysis, they have been retained in the seronegative group. The demographic characteristics of the sample are shown in Table 1.

The overall study period extended from June 1985 to January 1988. The mean length of follow-up for seropositive subjects was 21 months (range, 3 to 30), and for seronegative subjects, 23 months (range, 4 to 30; P not significant). One hundred fifty-six seropositive subjects (72 percent) remained in the methadone program and were followed for the entire period, as were 239 seronegative subjects (79 percent; P not significant).

Forty-nine of the 217 seropositive subjects (23 percent) and 62 of the 303 seronegative subjects (20 percent) had had a positive PPD test before entering the study (P not significant). Of these, 42 of the 49 seropositive subjects (86 percent) and 54 of the 62 seronegative subjects (87 percent) had positive PPD results documented in the clinic's medical charts. For the remainder in both groups, the positive PPD test was indicated only by the patient's report. Two seropositive subjects (1 percent) and five seronegative subjects (2 percent) had confirmed histories of active tuberculosis before their entry into the study. Among

Table 1. Demographic Characteristics, History of Tuberculosis, and PPD Status of HIV-Seropositive and HIV-Seronegative Intravenous Drug Users before and after Entry into the Study.*

CHARACTERISTIC	HIV- POSITIVE (N = 217)	HIV- NEGATIVE (N = 303)
Mean age — yr (range)	34 (21–63)	34 (20–57)
no. (percent)		
Sex		
Male	120 (55)	157 (52)
Female	97 (45)	146 (48)
Race or ethnic group		
White	22 (10)	97 (32)†
Black	66 (30)	68 (22)
Hispanic	129 (59)	138 (46)
TB history before entry		
History of treated TB	2 (1)	5 (2)
PPD-positive without disease	49 (23)	62 (20)
PPD-negative	166 (76)	236 (78)
no./no. tested (%)		
Positive PPD test after entry‡	15/131 (11)	26/202 (13)

*PPD denotes the purified protein derivative tuberculin skin test (Mantoux test), HIV the human immunodeficiency virus, and TB tuberculosis. Percentages may not total 100 because of rounding.

†P<0.001 for whites as compared with nonwhites; the P value is not significant for all other comparisons.

‡Newly positive PPD tests among formerly PPD-negative patients who were retested as part of their routine annual physical examinations in the methadone program during the study period.

formerly PPD-negative patients who underwent routine yearly PPD testing after entering the study, 15 of the 131 seropositive subjects (11 percent) and 26 of the 202 seronegative subjects (13 percent) we tested were positive on repeat PPD skin testing during the study period (P not significant; Table 1). Those who became positive on the PPD test did not differ in age from those who remained PPD-negative. The median length of time from the last negative PPD test to the first positive PPD test in those who converted was 16 months (range, 12 to 36).

Although the rates of prior active tuberculosis, prior positive PPD tests, and newly positive PPD tests did not differ between the groups, HIV-seropositive subjects were at significantly increased risk of acquiring active tuberculosis during the study period (Table 2). The cumulative incidence of active tuberculosis we observed (excluding the two seropositive and five seronegative patients who had been treated for active tuberculosis before they entered the study) was 8 of 215 (4 percent) among seropositive subjects (2.1 per 100 person-years); none of the 298 seronegative subjects had active tuberculosis during the follow-up period (P<0.002). Among seropositive subjects with prior positive PPD tests, active tuberculosis developed in 7 of 49 (14 percent; 7.9 per 100 person-years), as compared with none of 62 seronegative subjects with prior positive PPD tests. Thus, of the eight seropositive subjects in whom active tuberculosis was diagnosed during the study period, seven (88 percent) were known to have had latent tuberculous infection at the time of entry into the study; for these seven, the

median length of time from the positive PPD test to the development of clinical disease was four years (range, one to seven). The one patient with tuberculosis who had no known prior positive PPD test had been found to be anergic and had oral candidiasis at the time of the last negative PPD test (nine months before the onset of tuberculosis). Among the patients without prior positive PPD tests, only 1 of 166 seropositive patients (0.3 per 100 person-years) and none of 236 seronegative subjects had active tuberculosis (P not significant). The rate ratio for active tuberculosis was 24.0 for seropositive subjects with prior positive PPD tests, as compared with seropositive subjects with no prior positive test (P<0.0001).

Stratification by race and ethnic group indicated that blacks were more likely than whites or Hispanics to have a history of tuberculosis or a prior positive PPD test, and five of the eight cases of tuberculosis occurred among blacks. Active tuberculosis developed only among blacks who were HIV-seropositive, however (Table 3).

Of the subjects with prior positive PPD tests, 13 of 49 seropositive subjects (27 percent) and 13 of 62 seronegative subjects (21 percent) had received isoniazid prophylaxis before entering the study (P not significant). None of these patients had active tuberculosis during the study period, and none of the patients who acquired active tuberculosis received isoniazid either before or after entering the study. Of the 85 patients (36 seropositive, 49 seronegative) with prior positive PPD tests who had not received isoniazid before entering the study, 22 (26 percent) had refused such treatment, and 23 (27 percent) had been deemed ineligible for treatment because of alcohol abuse or clinically important liver disease; the remaining 40 (47 percent) either had not been offered isoniazid because of their longstanding PPD-positive status or had insufficient data in their clinic records to indicate why isoniazid had not been given.

Six of the eight cases of tuberculosis among seropositive subjects (75 percent) were pulmonary; two

Table 2. Incidence of Active Tuberculosis during the Study Period, According to HIV Status and Prior PPD Status.*

GROUP	HIV- POSITIVE	HIV- NEGATIVE	P VALUE
no./no. tested (%)			
All study subjects†			
New cases of active TB	8/215 (4)	0/298 (0)	<0.002
Cases/100 person-years	2.1	0	<0.001‡
Prior positive PPD test			
New cases of active TB	7/49 (14)	0/62 (0)	<0.005
Cases/100 person-years	7.9‡	0	<0.005§
No prior positive PPD test			
New cases of active TB	1/166 (0.6)	0/236 (0)	NS
Cases/100 person-years	0.3§	0	NS

*HIV denotes the human immunodeficiency virus, PPD the purified protein derivative tuberculin skin test, TB tuberculosis, and NS not significant.

†Two HIV-positive and five HIV-negative subjects with a history of active tuberculosis treated before entry into the study have been excluded.

‡Total person-years for HIV-positive subjects, 389.8; for HIV-negative subjects, 582.2.

§Rate ratio, 24.0; P<0.0001.

¶Total person-years for HIV-positive subjects, 88.1; for HIV-negative subjects, 119.6.

Table 3. PPD and Tuberculosis Status of Whites, Blacks, and Hispanics, According to HIV Serologic Status.*

RACE OR ETHNIC GROUP	HIV-POSITIVE (N = 217)	HIV-NEGATIVE (N = 303)
	no. (%)	
Whites		
No.	22	97
History of TB or prior positive PPD test	3 (14)	17 (18)
Newly positive PPD test	2 (9)	7 (7)
Active TB	1 (5)	0 (0)
Blacks		
No.	66	68
History of TB or prior positive PPD test	24 (36)	21 (31)
Newly positive PPD test	4 (6)	7 (10)
Active TB	5 (8)	0 (0)†
Hispanics		
No.	129	138
History of TB or prior positive PPD test	24 (19)	29 (21)
Newly positive PPD test	9 (7)	12 (9)
Active TB	2 (2)	0 (0)

*PPD denotes the purified protein derivative tuberculin skin test, HIV the human immunodeficiency virus, and TB tuberculosis.

†P<0.05; the P value is not significant for all other comparisons.

(25 percent) were extrapulmonary (one case each of meningitis and peritonitis). Of the six patients with pulmonary tuberculosis, all presented with fever and cough, three had night sweats, and two had weight loss. Only three of the six patients had sputum smears that were positive for acid-fast bacilli, though all had sputum cultures that ultimately grew *M. tuberculosis*. Chest roentgenograms for these six patients showed the following distribution of pulmonary infiltrates: unilateral apical (n = 1), unilateral upper-lobe (n = 2, of whom one had hilar adenopathy and a small pleural effusion), right middle-lobe (n = 1), bilateral upper-lobe (n = 1), and bilateral lower-lobe (n = 1).

Two cases of tuberculosis occurred three to six months after the patients had been diagnosed as having AIDS. One of the extrapulmonary cases (that of peritonitis) was a third patient's first AIDS-qualifying diagnosis and was fatal. Five of the eight cases of tuberculosis (63 percent) occurred in HIV-seropositive patients who did not have AIDS; two had oral candidiasis and three had no HIV-related symptoms when tuberculosis was diagnosed. Of the three patients without HIV-related symptoms, two subsequently acquired oral candidiasis; one was later diagnosed as having AIDS, as was one of the two patients who initially had oral candidiasis. All these events occurred between 3 and 18 months after the diagnosis of tuberculosis was made.

The results of multiple-antigen delayed-hypersensitivity skin tests (Multitest CMI) were available for 64 HIV-seropositive and 102 HIV-seronegative patients who were tested as part of their routine yearly physical examinations in the methadone program. Seventeen of the 64 seropositive patients (27 percent) were anergic, as compared with 3 of 102 seronegative patients (3 percent; P<0.001). Of the anergic seroposi-

tive subjects, nine (53 percent) had clinical evidence of symptomatic HIV-related disease: AIDS (n = 4), oral candidiasis (n = 4), or herpes zoster (n = 1). Of the other eight (47 percent) without specific HIV-related disease, two had chronic renal failure, three had had episodes of bacterial pneumonia but were otherwise healthy, and three were asymptomatic. Of the three anergic seronegative patients, two were clinically healthy, and one had chronic nonhealing leg ulcers.

DISCUSSION

This prospective study of tuberculosis among intravenous drug users with known HIV antibody status and known PPD status permits both an estimate of the frequency of active tuberculosis among seropositive as compared with seronegative drug users and an assessment of the likelihood that tuberculosis in HIV-infected persons is due to reactivation rather than primary tuberculous infection. Although the study population was made up of intravenous drug users, the results may be applicable to the larger population of HIV-infected persons who are also infected with *M. tuberculosis*.

A high frequency of prior positive PPD tests was found among both seropositive and seronegative subjects in our study, comparable to the 20 to 25 percent prevalence reported among drug users in other series both before and after the beginning of the AIDS epidemic.^{19,20} High rates of PPD conversion, from 10 to 13 percent over nearly two years of mean follow-up, were also observed in both HIV-serologic groups in this study. This finding suggests that drug users may be at high risk for new tuberculous infection in an environment where active tuberculosis is increasingly common. We were not able to measure the extent of any possible booster effect, whereby serial PPD testing may produce a positive result,²¹ on the observed rates of PPD conversion in our study. However, we surmise that this effect was not extensive; our patient population was relatively young, and the time elapsed from the last negative to the first positive PPD test was ≥ 12 months in all the subjects who converted from negative to positive PPD status. The booster effect has been observed most frequently in older age groups and is believed to occur more commonly in persons rechallenged less than 12 months after the previous test.^{21,22} It would be interesting to carry out two-step tuberculin testing in populations such as this in order to address this question.

Although HIV-seropositive and HIV-seronegative subjects in our study did not differ with respect to the frequency of prior or newly positive PPD tests, a striking difference was observed in the incidence of active tuberculosis. In our study, new cases of active tuberculosis were observed only among seropositive subjects. This difference remained after the subjects were stratified by race or ethnic group and suggests that, although the rates of latent tuberculous infection are high for all drug users in this population, infection with HIV is an important risk factor for active tuber-

culosis. This finding is similar to the results of another study of tuberculosis and HIV infection among intravenous drug users in New York City, although data on the patients' PPD status were not available in that report.^{2,14} The two studies are not strictly comparable because of differences in methods of case finding and in study design; nonetheless, the rate of active tuberculosis among seropositive subjects in our study was 2 to 3 times as high as the rates observed among participants in different methadone programs in New York City in 1973, before the AIDS epidemic,¹⁹ and more than 10 times as high as the yearly age-specific and race-specific rates reported for New York City for 1980 through 1986.^{2,23}

Although several reports have suggested that tuberculosis in HIV-infected persons probably results from the reactivation of latent tuberculous infection,^{2,3,8} earlier studies have not addressed this issue directly. In the present study, seven of the eight patients who had active tuberculosis had had prior positive PPD tests, and the remaining patient had been anergic at the time of the only documented PPD test. These findings suggest that tuberculosis in HIV-infected persons most commonly indicates the reactivation of latent tuberculous infection in the context of HIV-induced immunosuppression. The observed rate of active tuberculosis among seropositive patients with prior positive PPD tests in this study — 14 percent over approximately two years (or 7.9 cases per 100 person-years) — exceeds the standard estimated lifetime risk of approximately 10 percent for the reactivation of latent tuberculous infection in persons with positive PPD tests.¹

This finding underscores the potential importance of aggressive therapeutic interventions such as isoniazid prophylaxis in HIV-infected persons with latent tuberculous infection.^{1,24-26} Although this study was not designed to evaluate the effectiveness of isoniazid prophylaxis in HIV-infected persons with positive PPD tests, and although the results are not statistically significant, it is noteworthy that none of 13 HIV-seropositive subjects with positive PPD tests who received isoniazid had active tuberculosis during the study period, as compared with 7 of the 36 who did not receive prophylaxis. After the initiation of this study, the methadone program in which the study was conducted developed systematic protocols for identifying and treating HIV-infected patients with positive PPD tests. Isoniazid is now administered along with these patients' daily methadone doses, to ensure compliance, and the rate of acceptance of treatment among such patients has exceeded 75 percent (unpublished data); this experience suggests that these treatment strategies might be effective in other populations of methadone-maintained patients at high risk for both HIV infection and tuberculosis.

Several studies of tuberculosis among HIV-infected patients have found atypical presentations of pulmonary tuberculosis, with a low incidence of cavitary disease, variable roentgenographic findings, and a low yield on sputum smears for acid-fast bacilli.^{7,9,11,27}

Similarly, among our patients, only one had an apical infiltrate and none had cavitary lesions, and smears were negative in three of six cases. Other studies have also noted a temporal clustering of the diagnoses of AIDS and tuberculosis, with tuberculosis often preceding AIDS by several months.^{2,4,6,9,10} In our study, three of the eight cases of tuberculosis followed or constituted the diagnosis of AIDS, and five cases occurred in seropositive patients without AIDS; four of these five patients subsequently acquired either AIDS or oral candidiasis during the study period. Whether tuberculosis in such patients is merely a marker for worsening immunosuppression or actually contributes to the deterioration of immune status through the activation of CD4 cells and the subsequent enhanced replication of HIV²⁸ remains to be determined.

The observation that 27 percent of seropositive subjects were anergic on multiple-antigen skin testing suggests that there may have been some degree of underdetection of latent tuberculous infection among HIV-seropositive subjects. Even applying the observed PPD-positive rates to the estimated one quarter of seropositive subjects likely to be anergic would not appreciably alter the results we obtained, however. The fact that almost half the anergic seropositive subjects we tested had no clinical evidence of advanced HIV-specific disease suggests the importance of testing for anergy at the time of PPD testing in intravenous drug users who are at risk for HIV infection. Given the high levels of probable latent tuberculous infection and the limited usefulness of clinical criteria for predicting the existence of anergy among such patients, anergy testing is critical as an aid in the interpretation of negative PPD tests.

In addition to its clinical implications for patient care, the increased risk of tuberculosis in HIV-seropositive patients suggests that an additional risk of the horizontal transmission of tuberculosis to household members, health care workers, and other nonintimate contacts may exist. The aggressive identification and treatment of HIV-infected intravenous drug users with latent tuberculous infection is therefore of both clinical and public health importance. Finally, the results of this study of intravenous drug users in New York City may portend a similarly increased risk of tuberculosis among non-drug-using populations in other geographic areas, such as central Africa and parts of the Caribbean, where high prevalences of HIV and tuberculous infection may coexist.

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A RANDOMIZED TRIAL OF INTENSIVE INSULIN THERAPY IN NEWLY DIAGNOSED INSULIN-DEPENDENT DIABETES MELLITUS

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Abstract A period of early, intensive insulin treatment is thought to improve subsequent beta-cell function in insulin-dependent diabetes mellitus (IDDM). To study this hypothesis, we randomly assigned adolescents with newly diagnosed IDDM to receive either conventional treatment ($n = 14$) (NPH insulin, 1 U per kilogram of body weight per day, in two divided doses) or an experimental treatment ($n = 12$) (a two-week hospitalization with maintenance of blood glucose levels between 3.3 and 4.4 mmol per liter by continuous insulin infusion delivered by an external artificial pancreas [Biostat]).

During the two-week intervention, the experimental-therapy group received four times more insulin than the conventionally treated group, and their endogenous insulin secretion was more completely suppressed, as evi-

denced by a urinary C-peptide excretion rate one seventh that of the conventionally treated group. After the first two weeks, both groups were treated similarly and received similar amounts of insulin. At one year, the mean ($\pm$ SEM) plasma level of C peptide was significantly higher after mixed-meal stimulation in the experimental-therapy group than in the conventionally treated group (0.51 ± 0.07 vs. 0.27 ± 0.06 ; $P < 0.01$). The experimental-therapy group also had better metabolic control, as evidenced by lower glycohemoglobin values (7.2 ± 0.7 vs. 10.8 ± 1.2 percent; $P < 0.01$).

We conclude that suppression of endogenous insulin by intensive, continuous insulin treatment during the first two weeks after the diagnosis of IDDM may improve beta-cell function during the subsequent year. (*N Engl J Med* 1989; 320:550-4.)

INSULIN-DEPENDENT diabetes mellitus (IDDM) is thought to be due to an autoimmune process that destroys the beta cells.¹ The sequence of events

leading to the total destruction of beta cells is unknown. Attempts at preserving the beta cells in patients with newly diagnosed IDDM have been largely unsuccessful. Several groups have attempted to preserve beta-cell function through the use of intensive insulin therapy during the first two to four weeks after the diagnosis of IDDM. Madsbad et al.² used multiple subcutaneous injections, whereas Perlman et al.³ used a continuous intravenous infusion of insulin (an "open-loop" system). Both groups were able to show improved beta-cell function, as evidenced by C-pep-

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Draft

The National Task Force on AIDS Drug Development



*A Status Report in Response to the
Task Force Recommendations*

November 20, 1995

draft

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The National Task Force on AIDS Drug Development

Status Report in Response to the Task Force Recommendations

Preface

This report was prepared by the Department of Health and Human Services (DHHS) to summarize the current status of the Department's responses to the recommendations of the National Task Force on AIDS Drug Development.

The Task Force was chartered on November 22, 1993 by Secretary Donna E. Shalala to advise DHHS and other relevant Administration organizations "in the establishment of a national strategy in all aspects of the development of treatments for human immunodeficiency virus (HIV) infection and HIV-related diseases (and) with identifying creative options to enhance the development and evaluation of useful treatments".

The Task Force has issued 45 specific recommendations concerning barriers to the most rapid possible development of HIV/AIDS treatments. As indicated in this status report, many of these proposals have been successfully implemented or are underway now, while a number of recent recommendations remain under evaluation within the relevant Federal agencies.

In addition to Assistant Secretary for Health Dr. Philip R. Lee, the Chair of the Task Force, other members appointed by the Secretary include the Director of the National Institutes of Health, the Commissioner of Food and Drugs, and representatives of industry, academia and AIDS-affected communities.

The Department is deeply grateful for the contributions and commitment of the members of the Task Force over the course of the two year charter, which expires on November 22, 1995. The deliberations have contributed greatly to a sense of unified purpose among all participants in this critically important work, and to a better understanding of the complex forces which come to bear on HIV/AIDS drug discovery and development. The Department is committed to following through on all the Task Force recommendations until there have been satisfactory responses to each.

Moreover, the Department recognizes that until safe and effective therapies for this terrible pandemic disease have been discovered, this work will not be complete. In order to build on the efforts the Task Force has begun, a series of well-planned workshops will be convened as necessary to examine critical problems or opportunities in AIDS drug and vaccine development affecting multiple Federal agencies and both the public and private sectors. By establishing a high-level mechanism to plan dynamic, targeted workshops involving government, industry, academia and community representatives, the Department will maximize available resources to more effectively explore every opportunity to accelerate the discovery of new, promising drugs and vaccines, and move them through the development pipeline.

The National Task Force on AIDS Drug Development

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The National Task Force on AIDS Drug Development

January 1995 Recommendations and DHHS Responses

Drug Discovery

The National Task Force on AIDS Drug Development recommends that the Federal Government continue to expand support for biomedical research to identify new targets for drug development and to develop assays of biologically relevant activity of such target molecules. Specifically, the Task Force recommends:

***Recommendation A.1:* The National Institutes of Health (NIH) Office of AIDS Research (OAR) should conduct a thorough review of the NIH AIDS drug discovery and screening programs, eliminate those components that are not effective, and adequately fund those that are.**

DHHS Response: The NIH Revitalization Act of 1993 mandated the OAR to evaluate the NIH-funded AIDS research program in order to delineate future directions and goals. Last December, Dr. Charles Carpenter, Chair of the AIDS Program Advisory Committee (APAC), the predecessor to the new OAR Advisory Council (OARAC), established an "Evaluation Working Group" to undertake a systematic review of the NIH AIDS research program.

The Working Group is committed to developing recommendations and issuing a report to the OARAC by January 1996. This evaluation then will be forwarded to the OAR Director and the NIH Director in order to provide critical guidance for the preparation of the comprehensive FY 1998 AIDS research plan and related budget proposals.

The Working Group was convened last January 29 to initiate this review. Chaired by Dr. Arnold Levine, the Working Group is utilizing "Area Review Panels" to gather information on and evaluate the overall NIH programs within six scientific "areas of emphasis":

1. Natural History, Epidemiology, and Prevention;
2. Etiology and Pathogenesis;
3. Vaccine Research and Development;
4. Behavioral, Social Science, and Prevention Research;
5. Drug Discovery; and
6. Clinical Trials.

The Area Review Panels will determine how the various programs fit into the comprehensive trans-NIH effort in each of these scientific categories.

The final report to the OARAC is expected in January 1996, and will be available to the public.

Recommendation A.2: Identify ways to increase and encourage industry efforts in drug discovery and development. For example, fund programs similar to the NCDDG to foster collaborative efforts among industry, academia, and government scientists, improve access to and efficiency of government-supported drug screening programs, and foster productive transfer of technology to industry partners. Continue to fund the National Cooperative Drug Discovery Groups-HIV (NCDDG) program.

DHHS Response: The National Institute of Allergy and Infectious Diseases (NIAID) convened an *Ad Hoc* NCDDG Program Review Panel in 1991 to review the NCDDG-HIV and NCDDG-Opportunistic Infections (NCDDG-OI) programs. The panel recommended a reduction in the number of research groups funded under this program. NIAID therefore has reduced the NCDDG-HIV from 23 to 13 groups, and plans to reduce the number further to a level of 8 - 12 groups by 1997. NIAID intends to maintain the NCDDG-HIV at this recommended level, in addition to 8 - 10 NCDDG-Opportunistic Infection (OI) groups, through program announcements. The NCDDG program will be recompeted in FY 1997.

In the spirit of the NIH-wide rededication to investigator-initiated research, NIAID also funds an extensive portfolio of 173 grants totalling approximately \$65 million to support the discovery and development of AIDS drugs and agents. Many of these grants focus on novel therapeutic targets. NIAID soon will release a program announcement to encourage further investigator-initiated research in this important area.

(On June 29 & 30, 1995, the Task Force issued a new set of recommendations concerning proposed new incentives for private investment in AIDS drug development; see page 11).

Recommendation A.3: Establish online databases of research abstracts to promote early communication of results of basic and applied clinical research that may be relevant to HIV/AIDS drug discovery/development efforts.

DHHS Response: Selected meeting and conference abstracts are currently available online. A pilot program was initiated in the Fall of 1995 to develop an online database through the National Library of Medicine of research abstracts from NIH-supported grants and contracts. Based on an evaluation of the pilot program, the database could potentially be expanded to include all NIH-supported research in 1996.

Recommendation A.4: Periodically survey industry, academia, and government to identify research efforts on promising targets. These surveys may take the form of telephone calls, written surveys, and/or workshops or meetings to obtain information about these efforts.

DHHS Response: Approved by OMB in September, the "AIDS Drug Discovery and Development Industry Survey" was recently sent by the Assistant Secretary for Health to over 400 biotechnology and pharmaceutical companies in an effort to identify under-explored molecular targets for drug discovery and other obstacles to progress. Task Force members will receive the final report and analysis of the survey responses, which is scheduled to be published by the end of the year.

(For additional recommendations concerning Drug Discovery, see B.22 - B.26).

Drug Development

To address obstacles facing women in the drug development process, the Task Force recommends that:

Recommendation A.5.a: FDA must amend existing regulations governing the Investigational New Drug (IND) and New Drug Application (NDA) process to require a sponsor to file gender accrual analysis in the annual IND report. In addition, for the NDA and the product licensing application (PLA), the regulations will require sponsors to analyze clinical data by gender and assess potential differences between genders. The regulatory amendment (proposed rule) should be submitted to the Department of Health and Human Services (DHHS) within thirty days of the January 19, 1995 Task Force meeting and subsequently forwarded to OMB within 30 days of that date.

DHHS Response: The FDA published a proposed rule for investigational new drug applications (IND's) and new drug applications (NDA's) in the *Federal Register* on September 8, 1995. The FDA is proposing to amend its regulations pertaining to IND's and NDA's. The proposed rule would clearly define in the NDA format and content requirements the need to present effectiveness and safety data for important demographic subgroups, specifically gender, age, and racial subgroups. The rule would codify expectations that FDA has previously described in guidance. The proposed amendments would also require IND sponsors of drugs, including biological products, to characterize, in their annual reports, the number of subjects in a clinical study according to age group, gender, and race.

Written comments are being accepted on the proposed rule until December 7 to Deborah A. Wolf, FDA Center for Drug Evaluation and Research (HFD-362), 750 Standish Pl, Rockville, MD 20855.

Recommendation A.5.b: The FDA should appoint a working group comprised of representatives of affected communities, academia, industry and government to address gender analysis. The working group will give a formal report on the results of this meeting to the Task Force.

Gender-based drug effects will not be discerned simply from enrolling women in clinical trials. Certain additional analyses must be designed and implemented. The FDA must develop a scientific approach to gender analysis including implementing trial designs that will yield adequate information regarding the detection of possible gender differences, analyzing existing databases and identifying the pharmacological gender analysis required by the FDA during the IND and NDA process. The establishment of this working group will begin this process. The recommendations of the working group will be monitored by the Task Force.

DHHS Response: The FDA has organized a workshop on gender studies in product development: scientific issues and approaches. This workshop was organized by a group comprised of FDA staff and was supplemented with external consultants (including a Task Force member).

The gender analysis workshop, scheduled for November 6-7, 1995 at the Double Tree Hotel, Rockville, Maryland, is expected to include members of industry, government, academia and interested consumer and health professional communities. Agenda topics for this workshop include:

- Pharmacokinetics and pharmacodynamics;
- hormonal influences; and
- study design and analysis.

Promotional brochures for the workshop were widely distributed to potential audience participants; approximately four hundred participants were expected to attend.

***Recommendation A.5.c:* The FDA must amend the regulations defining circumstances under which it is appropriate to issue a clinical hold or terminate an IND to include instances where a trial sponsor imposes restrictions on the inclusion of women of childbearing potential in any phase of any clinical trial for life threatening illnesses where there is no evidence of reproductive toxicities. The regulatory amendment should allow the FDA to employ these sanctions when there is evidence of reproductive toxicity, but a less restrictive alternative than exclusion of women exists. If the FDA requests that women not be excluded and the exclusion continues, the FDA should first issue a clinical hold on the trial, and then, if the sponsor refuses to correct the exclusion of women, the FDA should force the sponsor to terminate the IND. FDA will submit proposed rule to HHS within 120 days and report progress to the Task Force at the February 1995 meeting.**

DHHS Response: The FDA has drafted a proposed rule that is responsive to this recommendation and ensures that women are not inappropriately excluded from clinical trials. FDA anticipates that the proposed rule will be submitted to DHHS for preliminary review by November 1995.

Recommendation A.5.d: The FDA must create a working group to identify potential models (other than the animal reproduction studies articulated in the international harmonization guidelines) to evaluate reproductive effects (including male mediated effects.)

The amendment in this recommendation reflects an acknowledgement that the FDA did identify the international harmonization guidelines as the agency standard for evaluating reproductive effects but notes that there is little required regarding the analysis of male mediated effects and that this battery of tests is costly and time consuming and is not necessarily predictive of human reproductive effects.

DHHS Response: In addition to the reproductive harmonization guidelines referred to in the recommendation, consensus was reached at the March 28 - 30, 1995 meeting of the International Conference on Harmonisation Steering Committee on male-mediated reprotoxicity effects. It is anticipated that draft guidelines will be released later this year for consultation by tripartite-member regulatory bodies and the public. (For more information, see the Step 2 ICH Harmonised Tripartite Guideline and the September 22, 1994 Federal Register notice).

Scientists at the FDA National Center for Toxicological Research are identifying methods to assess late-occurring effects on the developing fetus. This includes reproductive tract changes that are not assessed by the standard assays now in use because of the gestational differences in test species and humans.

Additionally, FDA staff from the Center for Drug Evaluation and Research (CDER) are preparing a publication which is a review of the literature on fetal harm due to paternal drug exposure. This article is expected to be published in 1996 and may provide a framework for helping to formulate the agency's position on this topic.

Research at the FDA National Center for Toxicological Research is ongoing and is expected to continue through 1996.

Recommendation A.5.e: The Public Health Service (PHS) must develop a list of databanks, accessible to trial sponsors and the public, containing information on the known teratogenicity and mutagenicity of various drugs.

DHHS Response: With assistance from the FDA, the NIH National Library of Medicine (NLM) has developed a descriptive listing of NLM and non-NLM databases containing teratogenicity and mutagenicity information on drugs.

The NLM will make the list available to the scientific community through the many mechanisms by which NLM publicizes its current database services. NLM exhibits at scientific and medical conferences each year. These exhibits are staffed by NLM personnel or by representatives from the

National Network of Libraries of Medicine (NN/LM). Included in each exhibit are fact sheets about NLM's products and services as well as demonstrations of online searching using Grateful Med.

NLM and NN/LM provide training courses on online searching of NLM's databases throughout the country. NLM also produces newsletters and other public announcements that are widely distributed electronically and by mail. All of the non-NLM databases listed are available commercially.

Recommendation A.6: The Task Force recommends that a forum, or "think tank," be convened to develop policy recommendations for the Public Health Service (PHS) on enhancing heterogeneity in AIDS clinical trials. The PHS will provide periodic updates to the Task Force on implementation of these recommendations.

DHHS Response: DHHS will form a planning group for a workshop concerning heterogeneity in AIDS-related clinical trials. This workshop will evaluate the current status of enrollment of heterogeneous populations in AIDS clinical trials in the public and private sectors, and may develop specific recommendations for improving enrollment where necessary and appropriate.

Recommendation A.7: The Task Force recommends that the FDA and NIH consolidate the review process of gene therapy protocols to include the following principal elements:

- ▶ All human gene transfer protocols will be submitted simultaneously to the NIH and the FDA in a single submission format.
- ▶ FDA and NIH will simultaneously evaluate the protocol for possible Recombinant DNA Advisory Committee (RAC) review.
- ▶ Semiannual data reporting procedures will remain the responsibility of NIH Office of Recombinant DNA Activities (ORDA). Semiannual data reports will be reviewed by RAC in a public forum.

DHHS Response: On April 17, the NIH Director approved the changes in the *NIH Guidelines for Research Involving Recombinant DNA Molecules* thus addressing the NIH portion of the NIH/FDA consolidated review process. Principal elements of the consolidated process:

- ▶ All human gene transfer protocols will be submitted simultaneously to the NIH and FDA in a single submission format.
- ▶ FDA and NIH will review the submissions to determine the necessity for RAC review.
- ▶ Factors defining the need for RAC review will include:
 - 1) new vectors/new types of gene delivery;
 - 2) targeting of new diseases;
 - 3) unique applications of gene transfer; and
 - 4) ethical issues requiring public review.

- ▶ Semiannual data reporting will remain the responsibility of the NIH Office of Recombinant DNA Activities (ORDA) with semiannual data reports being reviewed by the RAC in a public forum.
- ▶ The RAC and FDA will broaden the scope of their meeting and discussions beyond individual protocol review to include such topics as a gene transfer patient registry and criteria for *in utero* gene therapy.

At a recent meeting of the RAC, principal investigators of 9 protocols were notified of their exemption from RAC review in accordance with *Appendix M-VII, Categories of Human Gene Transfer Experiments That May be Exempt From RAC Review*, of the *NIH Guidelines*. Four protocols were determined by ORDA to require RAC review and were reviewed during the September meeting. (See *NIH Guidelines for Research Involving Recombinant DNA Molecules and RAC Advisory Committee Meeting minutes September 11-12, 1995*; see also *Recommendation B.13*).

Recommendation A.8: The Task Force recommends that further deliberation on surrogate markers occur during the discussion of protease inhibitors at the February 23 - 24, 1995 Task Force meeting.

DHHS Response: The February meeting of the Task Force was almost entirely dedicated to a review of protease inhibitor development. (See *Summary Minutes*). In addition to other issues, the use of various "surrogate markers" to evaluate efficacy in this promising new class of drugs was discussed extensively.

A workshop was subsequently held to examine issues related to trial design, confirmatory trials, and accelerated approval; each of these are directly related to the utility and evaluation of surrogate markers. Dr. David Feigal, Director of the FDA Division of Antiviral Drug Products, coordinated this workshop. The planning group for the workshop included members of the Task Force and representatives of NIH, FDA and others.

Discussion topics at the workshop included:

- ▶ Resistance and viral load, including implications for study design;
- ▶ End-point methodology, including use of surrogate markers as "outcomes" and end point selection and validation; and
- ▶ Clinical trial design, including experiences to date with dynamics of early drug approval and confirmatory trials, and alternative trial designs.

Participants in the workshop also included members from each of the FDA advisory committees responsible for reviewing AIDS or AIDS-related therapies; several members from the National Task Force on AIDS Drug Development; FDA staff responsible for the regulatory review process of each phase of the clinical trial design for AIDS and AIDS-related therapies; and members of government, industry, academia and AIDS-affected communities.

Also discussed at the February Task Force meeting was the great technical difficulty of producing sufficient quantities of protease inhibitors to meet the demand among people with AIDS. In follow-up to this discussion, the Office of HIV/AIDS Policy is working with the Institute of Medicine to plan a workshop to examine appropriate and ethical means of providing access to potentially life-sustaining therapies of limited supply.

Recommendation A.9: The Task Force recommends that a workshop, or series of workshops, be convened to identify and discuss issues related to the development and use of gene therapies and related novel approaches for the treatment of HIV disease.

DHHS Response: A Task Force Drug Development Subcommittee meeting was convened on September 13-14 to focus on gene therapy Investigational New Drug (IND) issues. This meeting was planned as a workshop by the Drug Development Subcommittee Co-chair, Flossie Wong-Staal, Ph.D., in conjunction with the FDA Office of AIDS and Special Health Issues and the FDA Center for Biologics Evaluation and Research (CBER).

Agenda topics for the workshop included an overview of the CBER IND process, somatic cell and gene therapy, clinical trial design/follow up, toxicology issues, ancillary products, good manufacturing processes, and case studies. Additionally, a presentation on the function of the Recombinant DNA Advisory Committee was made. The meeting was designed as an interactive learning session.

Attendees represented a broad cross section of the gene therapy community, including university investigators, representatives from small gene therapy manufacturing facilities, lawyers, consultants, regulatory review personnel, and representatives of affected communities. (*Transcripts and booklets are available from the FDA Office of AIDS and Special Health Issues*).

(*See B.20. and B.21. for additional recommendations concerning drug development*).

Public / Private Issues

Recommendation A.10: The Task Force supports NIH activities related to the review of the "reasonable price clause" in Cooperative Research and Development Agreements (CRADAs) as a barrier to drug development. The Task Force will review NIH's final recommendations to determine if further action is necessary.

DHHS Response: Based on an extensive consultation involving representatives of academic and industry researchers and patient advocacy groups, the NIH Director has removed the "reasonable pricing" clause from the PHS model Cooperative Research and Development Agreement (CRADA) and the PHS model Exclusive License Agreement. The clause was removed effective April 11, 1995.

Recommendation A.11: The Task Force recommends that patent applications for drugs involved in the diagnosis or treatment of serious or life-threatening disease should undergo an expedited review process by the U.S. Patent and Trademark Office (PTO).

DHHS Response: PTO has announced that patent applications related to AIDS and cancer may be reviewed on an expedited review basis at the applicant's option.

Recommendation A.12: The Task Force recommends that:

- A. PTO develop and implement a course in law for patent examiners;
- B. PTO develop compensation incentives to retain well-trained examiners that allow PTO to compete against the private sector;
- C. Patent filing fees collected by PTO should be applied to improve the administrative and management functions of the patent examiners.

DHHS Response:

- A. PTO maintains an extensive continuing education program in patent law for patent examiners, including payment for half of the cost of law school tuition.
- B. PTO agrees that more competitive compensation packages are needed to attract and retain examiners, and is pursuing a number of options in an effort to do so.
- C. The PTO budget is entirely supported by filing fees; no taxpayer dollars are budgeted.

Recommendation A.13: The Task Force recommends that the PTO accept *in vitro* efficacy data or *in vivo* surrogate marker data, as well as evidence of utility, for patent purposes. The evidence for utility should be determined by experts in the field.

DHHS Response: PTO has recently published guidelines announcing that *in vitro* efficacy data or *in vivo* surrogate marker data, as well as evidence of utility, will be accepted for patent purposes.

Recommendation A.14: The Task Force recommends that a focus group be convened to define incentives for pharmaceutical companies to perform early safety and pharmacokinetic studies to develop pediatric drugs and formulations for treating life-threatening disease. Progress from the focus group will be presented to the Task Force.

DHHS Response: A working group was formed, chaired by Task Force member Art Ammann, M.D., which created a list of marketed drugs for which no pediatric formulation exists. The list was prioritized based on the need for pediatric formulations, and submitted to the FDA and NIH. The working group also proposed incentives for private investment in the development of pediatric formulations; this proposal was adopted by the Task Force (see Recommendation B.3).

Recommendation A.15: The Task Force recommends that the role of the AIDS Clinical Trials Group (ACTG), as well as other government-sponsored clinical trials mechanisms, be reviewed after the ACTG recompetition. The ACTG must define its role relative to: a) small companies that may not have the resources to develop their own drug and, b) a drug where the patent exclusivity is unavailable.

Response: The Adult ACTG currently is being recompeted and restructured. Future ACTG studies will focus on the evaluation of innovative therapies and multi-agent regimens. The anticipated award date for the Adult ACTG is January 1, 1996. The Pediatric ACTG will be recompeted in 1997.

As part of the NIH AIDS Research Program Evaluation Working Group review, the ACTG and other NIH-funded AIDS clinical trials programs will be evaluated by the Clinical Trials Area Review Panel. The Panel will assess the effectiveness of the various clinical trials programs from a trans-NIH perspective and develop recommendations prioritizing each clinical trial system and the appropriate funding mechanisms to support such programs as part of the NIH AIDS research program for FY 1998. The final report from the Working Group is expected in January 1996.

Additionally, the NIH AIDS Clinical Drug Development Committee reviews applications from small and large companies and, based on the data submitted, makes recommendations to NIH on whether clinical trials for the companies' products should be prioritized for funding.

The National Task Force on AIDS Drug Development

June 1995 Recommendations and DHHS Responses

Preface

Based on testimony and evidence presented to the National Task Force on AIDS Drug Development, the Task Force has determined that additional incentives for private investment in HIV/AIDS drug development may be required* in order to help ensure the rapid discovery and development of safe and effective treatment for this disease, a continuing public health crisis in the United States and throughout the world.

The Task Force recognizes that there are significant economic factors that may increase or diminish incentives for investment in much broader areas that could have an indirect or "trickle-down" impact on investment in AIDS-related research specifically. Nevertheless, most of the mechanisms selected for consideration at this time were chosen based on their potential for a focused effect on the investment climate for HIV and AIDS-related research, while often potentially benefiting research on other diseases as well.

The Task Force believes that the biotechnology industry can play an important role in creating new therapeutics for HIV and, hence, is extremely concerned about the current state of the health of this industry.

Factors contributing to the Task Force's perception that investment in AIDS-related research and development may be of greater risk to investors, and of diminished potential for financial return compared to many other areas of investment, include the following:

- ▶ **the relatively small market potential (particularly within the developed world);**
- ▶ **the need for a more complete scientific knowledge base associated with this complex disease, first identified 14 years ago;**
- ▶ **accumulating evidence that, following several key disappointments in product development, investors and drug developers are moving away from investment in new and innovative classes of drugs targeting HIV; and**
- ▶ **the uncertain future of policies for reimbursement for HIV/AIDS drugs for both public and private payors.**

Particularly given the uncertain outlook for increased Federal investment in biomedical research, the Task Force believes that there are special public health considerations of the HIV/AIDS epidemic justifying targeted incentives for private sector investment. Among these are the following:

- ▶ the disease is debilitating, costly and fatal;
- ▶ the disease destroys the human immune system, leaving populations vulnerable to other infections;
- ▶ the disease is infectious, and is often outwardly undetectable for many years, contributing to difficulties in controlling the spread of the virus through sexual contact, contaminated syringes, and perinatal transmission; and
- ▶ the disease disproportionately affects young people, leading to loss of productivity and premature death.

All of these and other factors contribute to the need for special targeted incentives to maintain and increase private investment in HIV/AIDS research.

The Task Force also believes that the investment climate for treatment research for other public health emergencies, such as multi-drug resistant tuberculosis and substance abuse addiction, may justify qualification for similar incentives for private investment.

** Please note that the Assistant Secretary for Health, the NIH Director and the FDA Commissioner abstained from voting on several recommendations concerning new incentives for private investment.*

Patent & Market Exclusivity Incentives

Recommendation B.1: The Administration should evaluate the potential impact of proposed amendments to the Hatch-Waxman Patent Term Restoration Act designed to ensure that biotechnology and pharmaceutical products do not lose patent term due to delays in the drug approval process.

DHHS Response: The Department of Health and Human Services is evaluating these proposed amendments to the Hatch-Waxman Patent Term Restoration Act in consultation with the Commissioner of Patents and Trademarks, and will continue to consult with other appropriate officials in order to develop an Administration position on these proposals.

Recommendation B.2: The Administration should propose legislation providing a fixed period of extended market exclusivity for all treatments for HIV and AIDS.

DHHS Response: The Department of Health and Human Services is deeply concerned by the perception that there may be inadequate market incentives for private investment in HIV/AIDS-related research, and that this situation could be slowing the development of new classes of HIV therapies. Thorough research needs to be conducted into the current economic outlook for HIV/AIDS drug discovery and development in the private sector, including an examination whether there are inadequate incentives for investment, and whether research could be accelerated through the initiation of new incentives.

The Department is preparing to sponsor a more detailed study of this issue in an effort to explore the extent of this problem with respect to AIDS and, if there is a need, to develop a set of targeted policy initiatives that could most effectively correct the problem. The potential impact of the Task Force's various proposed incentives on AIDS-related and other areas of biomedical research, on access to health care, and on the economy as a whole will be considered. The Department will ask for participation in this research project by other Federal agencies, as well as non-governmental experts.

Additionally, as part of this analysis, consideration will be given to other proposals, including the creation of a mechanism that would provide for the introduction of targeted biomedical research investment incentives in the event of certain "public health emergencies". Such emergencies might be defined according to a set of quantifiable epidemiological and economic criteria, such as rate of increase of premature deaths, or projected annual cost to the nation of treatment. Under this proposal, when clear evidence of market failure is identified and existing incentives are determined to be inadequate to meet this urgent public health need, targeted market exclusivity, tax and/or other incentives could be proposed. These measures would be designed to stimulate greater competition within the private sector, and to enhance the investment of public funds to more promptly respond to the public health crisis; the incentives would "sunset" when the crisis was resolved. Enhanced incentives targeted to pediatric and other special subpopulations (B.3) will also be considered.

The Department agrees that, in addition to HIV/AIDS, there may be other current, emerging and future life-threatening and costly epidemics, such as substance abuse and multi-drug resistant tuberculosis, that could benefit from a more prompt and vigorous biomedical research response in the private as well as the public sectors. It is critical that we learn from our experiences with AIDS, and improve on existing mechanisms to ensure an adequate and timely response to epidemics that threaten the lives of hundreds of thousands of Americans, and many millions around the globe.

Recommendation B.3: The Administration should propose market exclusivity incentives for manufacturers to successfully complete infant formulation, safety, pharmacokinetic and, as appropriate, efficacy studies of HIV and AIDS drugs. These studies should include adequate numbers of infants and children. These incentives should apply to new drugs as well as to drugs currently approved for adults.

DHHS Response: (see Response to B.2 above).

Tax Credit Incentives

Recommendation B.4: The Administration should propose legislation making the Orphan Drug Tax Credit permanent, restructured so that it can be carried forward by companies with no tax liability.

DHHS Response: In testimony before the Subcommittee on Oversight of the House Committee on Ways and Means, the Administration reiterated its support for making the orphan drug credit permanent and announces its willingness to consider allowing excess orphan drug credits to be carried forward or backward under the generally applicable rules for business credits. As Deputy Assistant Secretary of Treasury Cynthia Beerbower indicated in her May 9 testimony, the Administration's support for a permanent credit and for a carryover provision is subject to identifying acceptable revenue offsets for any package that extends, and otherwise modifies, expired and expiring provisions.

Recommendation B.5: The Administration should propose legislation making the Research and Experimentation (R&E) tax credit permanent.

DHHS Response: The Administration proposed making the R&E credit permanent in its 1993 tax proposals, but in the Omnibus Reconciliation Act of 1993 Congress extended the credit only through June 30, 1995. The Administration's FY 1996 budget endorsed the revenue neutral extension of the R&E credit. Deputy Assistant Secretary of the Treasury Cynthia Beerbower reiterated that support in her May 9 Congressional testimony, pointing out that the cost of any temporary extension or of making the credit permanent must be fully offset.

Recommendation B.6: The Administration should propose legislation providing for a 50% tax credit for all HIV/AIDS-related clinical research expenditures incurred prior to marketing approval. The credit should be made permanent, and could be carried forward.

DHHS Response: The expenditures referenced in this and the following recommendation would likely qualify for the R&E credit (B.5) if that more generalized incentive for research and experimentation is extended by the Congress. Moreover, drugs related to some specific HIV/AIDS-related conditions would still be eligible for the orphan drug credit (B.4), if the credit is extended beyond its December 31, 1994 expiration date, because those conditions affect less than 200,000 residents.

As part of the study referenced under B.2, it will be important that any new tax credit proposals considered concisely define the scope of the expenditures eligible for a credit. New tax provisions must avoid disputes between taxpayers and the Internal Revenue Service regarding the eligibility of particular expenditures.

Under the Omnibus Reconciliation Act of 1993, new tax credits are considered additive to the projected deficit, and must be offset with tax increases or spending reductions in the same way that budget increases for Federal agency programs are considered expenditures and must be offset. Therefore, keeping the goal of stimulating drug development in mind, balanced consideration must be given to the strategy of increasing the Federal investment in biomedical research. Investment in NIH research produces the scientific findings which create opportunities for drug development, stimulating greater investment and competition in the private sector.

Recommendation B.7: The Administration should propose legislation providing for a 50% tax credit for all HIV/AIDS-related clinical research expenditures incurred following accelerated approval as required by the FDA and/or which examine new indications or formulations post-approval. This credit should be made permanent, and could be carried forward.

DHHS Response: (see B.2 and B.6 above).

Regulatory Incentives

Recommendation B.8: The Food and Drug Administration (FDA) should continue to achieve its excellent record of rapid review and initial approval of antiretroviral drugs, and ensure that it meets the same high performance standards for anti-infective drugs and biological products for treatment of HIV/AIDS and related conditions. These performance standards should be consistent with the Prescription Drug and User Fee Act targets.

DHHS Response: Since the implementation of the Prescription Drug User Fee Act (PDUFA) of 1992, the Food and Drug Administration (FDA) has committed to shortening the review time of sponsor's applications significantly by 1997. The agency is committed to a six month review period for new drug applications considered a "priority". Priority applications represent drugs offering a significant advance over existing treatments. Additionally, for life-threatening therapies, the agency's policy is to work closely with sponsors during the design phase of pivotal clinical trials to ensure the quickest application review for approval.

Recommendation B.9: The FDA should evaluate more flexible criteria for approval of additional claims. A working group should be established to develop more specific recommendations.

DHHS Response: A working group is being established to develop more specific recommendations pertaining to criteria for approval of AIDS drugs. Dr. Stephen Carter of Boehringer-Ingelheim (formerly of Bristol-Myers Squibb), will work with the FDA Office of AIDS and Special Health Issues to coordinate this working group's efforts.

Recommendation B.10: The FDA should collaborate with industry and patient groups to conduct a review of experiences to date with early access initiatives and determine whether to modify or expand these programs. As part of this review, proposals should be developed to enhance the quality of data generated by early access protocols.

DHHS Response: FDA has taken significant steps toward making experimental drugs for HIV/AIDS more widely available and has initiated expedited procedures to speed the review and approval of promising therapies for HIV/AIDS.

A recent article (*Scientific American* March, 1995 Vol. 272 No.3 entitled, "Faster Evaluation of Vital Drugs," by David A. Kessler and Karyn L. Feiden) reviews the experience of early access initiatives such as treatment investigational new drug (IND) regulation and accelerated approval. This article describes efforts by the FDA to encourage efficient drug development strategies by increasing the range of trial designs that may be acceptable.

Also, in collaboration with the FDA, the Task Force sponsored a workshop on September 6-8 which examined current issues in the design and analysis of AIDS clinical trials. The workshop, which included representatives of industry, academia, government and the patient community, provided a forum for a review of AIDS clinical trials experiences to date. FDA will review and evaluate the major discussion points from the workshop (held in response to January 1995 recommendation A.8).

In addition, the Task Force has received copies of a pre-published article related to this issue by Sheila R. Shulman and Jeffrey S. Brown of the Tufts Center for the Study of Drug Development entitled, "The Food and Drug Administration's Early Access and Fast Track Approval Initiatives: How Have They Worked?"

Recommendation B.11: The FDA should provide a single written statement concerning the conditions under which one pivotal trial can be considered as the basis of approval for breakthrough drugs or biologics for serious and life-threatening diseases.

DHHS Response: FDA works closely with sponsors throughout the drug development process, so that necessary data are developed expeditiously and efficiently. For approval purposes, it is important that the results of a clinical study can be independently corroborated. Oftentimes, two studies are required for corroboration.

Under certain circumstances, however, the FDA may base approval of a drug on results from a single study rather than two independent trials. The following statement is included as part of a much larger review in "Reinventing Drug and Medical Device Regulations", published by President Clinton and Vice President Gore's National Performance Review in April 1995:

"FDA believes that a showing of effectiveness must be replicated to constitute adequate demonstration of effectiveness for a new product. While a second study may well be needed to replicate results demonstrated in a first study, in some instances it is possible to replicate results within one large, well-designed multi-center study. It should be emphasized that this approach can be successful only when results are strong. A statistically marginal result, even in a very large study, cannot provide convincing evidence of replication.

"The biotechnology drug Pulmozyme was recently approved to treat cystic fibrosis on the basis of one multi-center study with features that provided elements of replication. Similarly, the drug timolol was approved to treat people after a heart attack following a demonstration of improved survival in a single study. In that study, the favorable effect was seen in patients at several levels of severity at three different hospitals. A simple multi-center double-blind placebo-controlled trial led to prompt approval of zidovudine for AIDS in 1987 when it was found that 16 deaths had occurred in the placebo group, as opposed to one death in the group receiving the drug. FDA has also approved vaccines, including a vaccine for hepatitis A, that have been studied for effectiveness in a single multi-center study."

Recommendation B.12: The HIV/AIDS community urgently needs an approved viral load diagnostic kit. The FDA should articulate clear policies and a single mechanism for approval of HIV-related diagnostic test kits. Companies should be encouraged to submit data to the agency in response to this need.

DHHS Response: FDA's general mechanisms regarding the review classes of test kits are summarized below. This information has been described to the Task Force.

Retroviral; Blood Bank Use	Product License Application (PLA) Reviewed at the Center for Biologics Evaluation and Research (CBER)
Retroviral; Non-Blood Bank (diagnostic use only)	Pre-Marketing Application (PMA) Reviewed at CBER
Non-Retroviral; Blood Bank	PLA Reviewed at CBER
Non-Retroviral; Non-Blood Bank (diagnostic use only)	PMA or 510(k) Reviewed at the FDA Center for Diagnostics and Radiologic Health (CDRH)

At a September 6-8, 1995 workshop sponsored by the Task Force, members from the Center for Biologics Evaluation and Research, Division of Blood Products, reviewed the agency's policy relating to diagnostic test kits. Representatives of the diagnostic-test kit industry were present and participated in the interactive forum.

FDA is aware of the very promising data on the significance of HIV viral load as a research tool in the antiviral drug trials, as well as a clinical marker for prognosis, and potentially also as a

monitor of therapy. FDA is hopeful that these same data soon will be made available to the agency in the context of product applications where they can be used to support specific medical claims.

FDA is working closely with sponsors, places a high priority on these submissions, and is hopeful that this will result in acceleration of the product development process.

Recommendation B.13: The Public Health Service should develop an integrated policy for the rapid review, as well as the reporting requirements, for gene therapy research. The policy should clearly define the roles of FDA and the National Institutes of Health (NIH), and minimize duplication of effort.

DHHS Response: The Department strongly supports this recommendation, and is in the process of developing an integrated policy for the rapid review and reporting requirements for gene therapy research. The NIH Director has appointed a review panel that is currently examining ways to expedite the NIH portion of the NIH/FDA consolidated review process of gene therapy. The panel's report is due shortly.

NIH will continue to work with FDA in further developing an effective and efficient review process of gene therapy protocols that ensures continued protection of the public health.

Reimbursement Incentives

Recommendation B.14: The Administration should propose legislation requiring that full coverage of prescription medications used in the treatment of HIV/AIDS and other life-threatening diseases is provided in state Medicaid plans. This coverage should include off-label uses of medications.

DHHS Response: Drug coverage is an optional service under the State Medicaid plan. All States currently cover prescription drugs under Medicaid or under their section 1115 demonstration waivers. Under section 1902(a)(54) of the Social Security Act, States must cover all covered outpatient drugs of manufacturers participating in the drug rebate program. The statute allows states to exclude or restrict certain outpatient drugs, such as fertility drugs or smoking cessation drugs. States can also subject any drug to prior authorization and place limits on the number of refills per month, number of pills per prescription, and the number of prescriptions per month.

These limits are allowed by statute to promote efficiency and economy within the State plan and to deter prescription fraud and abuse. If a beneficiary needs additional prescriptions which exceed the monthly limit, States generally have a process in place which allows a physician to certify to the State agency when additional prescriptions are medically necessary. This allows medically necessary drugs in excess of the monthly limits to be accessible to beneficiaries.

Medicaid covers FDA-approved label indications and off-label uses of drugs only if those off-label uses are published in one of three major compendia: American Hospital Formulary Service Drug Information, American Medical Association Drug Evaluations, and United States Pharmacopeia Drug Information.

Except for certain statutory restrictions, the Medicaid program provides coverage of prescription drugs regardless of disease or illness. Many States also have pharmaceutical assistance programs available for people who do not yet qualify for Medicaid but who need assistance with drug coverage, such as:

- ▶ AIDS Drug Assistance Programs (ADAP);
- ▶ ADAP Plus (for primary care); and
- ▶ AIDS Drug Reimbursement Programs (ADRP).

Legislation which would prohibit States from imposing any restrictions currently allowed by statute could have adverse effects on their Medicaid programs, since States would lose the limited flexibility necessary to achieve efficiency and economy within the State plan. These restrictions are an aid to States in controlling prescription fraud and abuse among providers, pharmacies and beneficiaries.

Legislation is not necessary to achieve this objective. As described above, the Medicaid drug rebate program allows access to all medically necessary prescription drugs for HIV/AIDS and other life-threatening diseases.

While it is important to be sensitive to the needs of these populations, we do not believe that the Medicaid program should provide varying levels of drug coverage restrictions, or lack of restrictions, based solely on the disease or illness involved. Providing the same level of coverage to enhance the quality of life for our beneficiaries with other debilitating diseases, such as multiple sclerosis, is equally as important. Thus, the Department will not begin to establish different formulary rules based on disease or illness.

Recommendation B.15: The Department of Health and Human Services (DHHS) should establish a policy requiring full coverage of all medically necessary prescription medications used in the treatment of HIV/AIDS and other life-threatening diseases, including FDA-approved treatment IND medications, in State Medicaid waiver applications. This coverage must include off-label uses of these medications, and such policies should ensure that managed care systems do not constrain such coverage.

DHHS Response: Individuals who meet current Medicaid eligibility criteria retain access to traditional Medicaid benefits, including prescription medications, under State section 1115 health care reform demonstration projects. The Health Care Financing Administration (HCFA) encourages States to include the broadest possible range of covered services and drugs for those individuals who would not otherwise be eligible for Medicaid in the absence of a waiver.

States have the flexibility to waive the provisions of the drug rebate program for either their entire section 1115 waiver program or for specific populations only. In the majority of cases, populations such as persons with HIV/AIDS remain under the fee-for-service system. As a result, these drugs are covered under the drug rebate program, as described in proposal number 14 above. Because the drugs used to treat these special populations are very expensive, States generally collect significant rebates for these drugs under the drug rebate program. Therefore, depending on the size of the State and its ability to negotiate large rebates outside of the national program, States may find it more advantageous to remain under the rebate program for the guaranteed best price under Medicaid.

Some States have made proposals to phase these special populations into managed care over an extended period of time. An HCFA review of these waivers has indicated that drug coverage under the health maintenance organizations (HMOs) may be more liberal, in some respects, because the HMO may not require a physician override when the person exceeds the number of prescriptions allowed per month.

More significantly, HCFA has not approved a waiver which did not provide the same level of drug coverage available to beneficiaries before the waiver. This includes the requirement that States cover off label uses normally covered under the traditional Medicaid program.

States should not be mandated to cover all treatment investigational new drugs (INDs). States currently have the option to cover experimental and investigational drugs during any phase of the investigational process. If a State chooses to cover these drugs, Federal matching funds are available. However, since these drugs have not been determined to be safe and effective, we believe that States should be able to evaluate these INDs individually to determine which treatment INDs they will cover. Also, drugs which have received "accelerated approval" status by the FDA are considered an FDA-approved drug for marketing purposes and, therefore, must be covered under Medicaid if the manufacturer participates in the rebate program.

Legislation which would require States to cover treatment INDs, regardless of whether States believe an IND is medically necessary, could have a significant impact on their budgets. Manufacturer rebates or discounts are not available for these drugs. While a manufacturer of a treatment IND may only charge a payer an amount which is generally sufficient to recover its costs, these drugs are generally very expensive. Thus, both States and the Federal government would be mandated to assume a large financial liability for drugs which States may not believe are in the best interest of the beneficiaries. Therefore, the Department supports the position that States should maintain the flexibility to determine which treatment INDs they will cover.

Recommendation B.16: The Administration should insist that full coverage of medically necessary prescription medications used in the treatment of HIV/AIDS and other life-threatening diseases be included in any Medicaid block grant proposals. This coverage must include off-label uses of these medications.

DHHS Response: The Department believes that States should continue to provide adequate access to medically necessary drugs for all diseases and illnesses under any possible Medicaid block grant proposal. However, since the future of block grant proposals are undecided, and it is unclear whether drugs would be part of block grants proposals, it is premature to make further policy recommendations at this time.

The Department is very concerned about the choices States would make regarding drug coverage under a block grant scenario, and will focus on assuring adequate access to all medically necessary drugs for the entire population which a State serves.

Recommendation B.17: The Administration should propose legislation providing coverage for treatment IND medications for HIV/AIDS under Medicare similar to coverage provided for group "C" cancer drugs.

DHHS Response: Once approved for marketing by the Food and Drug Administration (FDA), drugs and biologicals are considered safe and effective (and, as the law requires for Medicare coverage purposes, reasonable and necessary) when used for indications specified in the labeling. If the drug or biological is prescribed for an indication other than those specified in the labeling, coverage is determined by the local Medicare contractor. In doing so, the contractor takes into consideration the advice of its own medical consultants and the generally accepted medical practice in the community.

Treatment INDs are considered experimental and investigational and, therefore, are not covered by Medicare. Arguments have been made in the past that treatment INDs are analogous to Group C cancer drugs and, therefore, HCFA should cover treatment INDs in the same manner that it covers Group C drugs. It is important to understand that at the time HCFA agreed to cover Group C cancer drugs, a major factor behind the decisions was an assurance that these drugs had either completed or virtually completed all of the FDA safety and efficacy clinical testing requirements.

Also, the Group C classification differs from the Treatment IND because Group C cancer drugs are provided free, while manufacturers of treatment INDs charge on a cost basis under FDA guidelines. While it is true that HCFA provides full reimbursement for care associated with Group C therapy, the Group C cancer drugs are always provided free of charge. Therefore, Group C drugs and treatment INDs are not equivalent.

For the reasons described above, the Department will not propose legislation requiring that Medicare cover treatment INDs in the same manner that Medicare covers Group C cancer drugs.

Recommendation B.18: The Administration should ensure that all costs of medically necessary care for the treatment of HIV/AIDS and other life-threatening illnesses provided during the course of participation in clinical trials should be eligible for reimbursement under private insurers.

DHHS Response: The Department maintains the position that private insurers should be allowed the flexibility to determine which investigational or experimental drugs and associated care they will cover. The private insurance industry should analyze the costs and benefits associated with clinical trials for the populations it serves. Private insurers should comment on this proposal.

Recommendation B.19: The Administration should ensure that all costs of medically necessary care associated with the use of an investigational agent for the treatment of HIV/AIDS and other life-threatening illnesses should be eligible for reimbursement under Medicare and private insurance.

DHHS Response: For the reasons cited in response to recommendations B.17 and B.18, the Department does not recommend any policy which would mandate the coverage of all costs of medically necessary care associated with the use of experimental or investigational new drugs. Before any policy as broad as this should be considered, a thorough analysis must be conducted to determine the financial impact on the Medicare program and private insurance plans.

Drug Development

Recommendation B.20: The FDA should include as part of its routine audits of Institutional Review Boards (IRBs) an evaluation of whether there are unnecessary exclusions of women from clinical trials that alter the exclusions specified in the protocol. In addition, the FDA should be responsive to complaints of possible exclusions by examining procedures of specific IRBs.

DHHS Response: FDA's efforts in this area are ongoing. FDA staff have met internally several times to develop proposals to supplement the current compliance programs related to IRBs. Various proposals that would be responsive to this recommendation are currently under evaluation.

Recommendation B.21: DHHS must amend its "Regulations Governing Human Subject Research" which limits research on fetuses and pregnant women. In particular, DHHS must eliminate the requirement that the father of the fetus must consent before a woman may participate in a clinical trial.

DHHS Response: The Office of Protection from Research Risks (OPRR) of the Department of Health and Human Services has completed a review of this issue. OPRR has recently forwarded a rule consistent with this Task Force recommendation to the Assistant Secretary for Health. Following additional Departmental review, it is anticipated that the proposed rule will be published for comment very soon in the *Federal Register*.

Drug Discovery

Recommendation B.22: The Task Force recommends that NIH continue to vigorously support meritorious research on HIV-encoded proteins, regulatory elements of HIV, cellular factors and other targets involved in HIV replication to determine which of these would be promising targets for drug development. As such targets are identified and sufficient scientific information is obtained, screening assays should be developed to identify potential agents that inhibit or block key steps in the viral life cycle thus halting viral replication and/or the production of infectious diseases.

DHHS Response: The NIH continues to vigorously support investigator-initiated research, especially in the area of basic research, which provides the crucial scientific research needed to discover and develop new therapeutic agents and regimens against HIV infection and its associated opportunistic infections and malignancies. The NIH, through its Institutes, Centers and Divisions, continues to vigorously support research that identifies new targets for drug development as well as screening assays to identify such compounds.

Recommendation B.23: The Task Force should encourage increased communication between the NIH and industry and among industrial organizations in the area of AIDS drug discovery and development. It should be noted that the NIH director has requested and has been recently invited to participate in an upcoming Intercompany Collaboration (ICC) meeting to facilitate future communication.

DHHS Response: The NIH agrees with the need for ongoing communication between NIH and industry, as well as between industrial organizations, in the area of AIDS drug discovery and development. The Director met with the ICC on August 15 and discussed possible mechanisms to ensure maximum information exchange between the NIH and the pharmaceutical industry. It also was proposed that Dr. William Paul, Director of the NIH Office of AIDS Research, would meet with the ICC in the near future.

The Department encourages industry representatives on the Task Force to facilitate continued cooperation among their industry colleagues in exchanging information related to HIV/AIDS drug development.

Recommendation B.24: The Task Force encourages industry, perhaps through the ICC, to formulate a consensus materials transfer agreement (MTA) to facilitate the rapid exchange of reagents and reference standards for assays as well as candidate anti-HIV agents.

DHHS Response: The NIH Office of Technology Transfer (OTT) is available to discuss with industry the development of an agreement for material transfers between nonprofit and for-profit entities.

Recommendation B.25: The Task Force encourages increased sharing of reagents, cell lines, coordinates of cell structures, screening assays, and protocols among industry, academia, and the Federal government to permit identification and progress developing potentially new compounds with anti-HIV activity.

Similarly, the Task Force encourages industry and academic researchers to deposit reagents, assays, cell lines, molecular clones, reference standards for proteins, and panels of drug-resistant viruses in the National Institute of Allergy and Infectious Diseases (NIAID) AIDS Research and Reference Reagent Program for sharing with industry and academic researchers. Alternatively, the ICC or other organizations should be asked to develop mechanisms to facilitate the transfer of such material.

DHHS Response: The NIAID Research and Reference Reagent Program was established during the early stages of the pandemic to encourage sharing between researchers of reagents, technical information, and assays. This sharing of reagents is crucial in developing future compounds against HIV and its sequelae. The NIAID Reagent Program continues to encourage researchers in industry and academia to provide materials to this program for sharing with other investigators involved in AIDS-related research.

Recommendation B.26: The Task Force should proceed with the distribution of a questionnaire to determine industry's efforts in AIDS drug discovery and development. The questionnaire should be submitted to the Office of Management and Budget (OMB) for clearance prior to distribution to pharmaceutical and biotechnology companies to identify the targets and level of effort currently supported by industry in this area.

DHHS Response: Approved by OMB in September, the "AIDS Drug Discovery and Development Industry Survey" was recently sent by the Assistant Secretary for Health to over 400 biotechnology and pharmaceutical companies in an effort to identify under-explored molecular targets for drug discovery and other obstacles to progress.

Task Force members will receive the final report and analysis of the survey responses, which is scheduled to be published by the end of the year.

Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised controlled trial

Heiner Grosskurth, Frank Mosha, James Todd, Ezra Mwijarubi, Arnoud Klokke, Kesheni Senkoro, Philippe Mayaud, John Changalucha, Angus Nicoll, Gina ka-Gina, James Newell, Kokugonza Mugeye, David Mabey, Richard Hayes

Summary

A randomised trial was done to evaluate the impact of improved sexually transmitted disease (STD) case management at primary health care level on the incidence of HIV infection in the rural Mwanza region of Tanzania. HIV incidence was compared in six intervention communities and six pair-matched comparison communities. A random cohort of about 1000 adults aged 15–54 years from each community was surveyed at baseline and at follow-up 2 years later. Intervention consisted of establishment of an STD reference clinic, staff training, regular supply of drugs, regular supervisory visits to health facilities, and health education about STDs.

12 537 individuals were recruited. Baseline HIV prevalences were 3.8% and 4.4% in the intervention and comparison communities, respectively. At follow-up, 8845 (71%) of the cohort were seen. Of those initially seronegative, the proportions seroconverting over 2 years were 48 of 4149 (1.2%) in the intervention communities and 82 of 4400 (1.9%) in the comparison communities. HIV incidence was consistently lower in the intervention communities in all six matched pairs. Allowing for the community-randomised design and the effects of confounding factors, the estimated risk ratio was 0.58 (95% CI 0.42–0.79, $p=0.007$). No change in reported sexual behaviour was observed in either group.

• We conclude that improved STD treatment reduced HIV incidence by about 40% in this rural population. This is the first randomised trial to demonstrate an impact of a preventive intervention on HIV incidence in a general population.

Lancet 1995; 346: 530–36

Introduction

The cumulative total of adult HIV infections rose to an estimated 18 million by late 1994, and is projected to reach 30 to 40 million by the year 2000.^{1,2} Most new infections are acquired in the developing world and are heterosexually transmitted. Large numbers of infections continue to occur in sub-Saharan Africa, the region most severely affected during the first decade of the epidemic. Recently, the epidemic has begun to spread rapidly in some parts of southern Asia, and the number of new infections there may exceed that in Africa within the next 10 years.²

In the face of this severe and worsening epidemic, AIDS prevention programmes of varying intensity and efficiency have been set up in most affected countries. However, the impact of these programmes is unclear, due largely to lack of well-designed evaluation studies.³

In the absence of an effective cure or vaccine, the main preventive strategy has been health education aimed at achieving a reduction in risky sexual behaviour and, in some countries, the promotion of condom use. Other sexually transmitted diseases (STDs) are highly prevalent in many of the worst affected populations,⁴ and observational studies suggest that the sexual transmission of HIV may be enhanced in the presence of such STDs.^{5–8} For this reason, the WHO has recommended programmes to improve the management of STDs as an additional HIV control tool, and it has been suggested that the treatment of bacterial STDs may be one of the most cost-effective health interventions available in some developing countries.^{9,10} However, no empirical data have been available on the impact of such measures on the incidence of HIV infection, or on their cost-effectiveness as a public-health strategy.

It was against this background that we undertook a community-based randomised intervention trial in a rural area of north-western Tanzania. The objectives of the trial were to establish a programme for the improved diagnosis and treatment of STDs in the general population, and to measure the impact of this intervention on the incidence of HIV infection and on the prevalence and incidence of STDs. The improved STD services were designed to be feasible rather than optimal, were integrated with the Tanzanian primary-health-care system, and were based on syndromic treatment algorithms as recommended by WHO.¹¹ We report the impact of the programme on HIV incidence.

Methods

The trial was conducted between November, 1991, and December, 1994, in the Mwanza region of Tanzania, which is situated on the southern shores of Lake Victoria. The study population, and the rationale and design of the trial and of the intervention programme, have been described,¹² but the most important aspects are summarised below.

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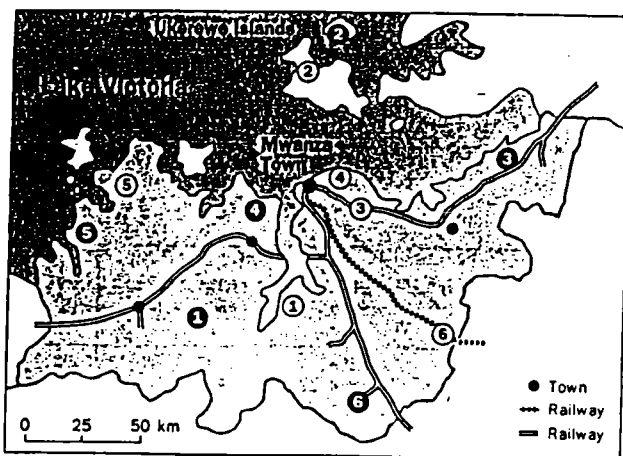


Figure 1: Map of Mwanza region

Numbered circles indicate location of six pairs of study communities; intervention communities are shown in black circles.

STD intervention programme

The programme had five components. First, establishment of an STD reference clinic and laboratory in Mwanza town to monitor the aetiology of STDs and the effectiveness of the treatment algorithms. Second, training of existing staff from health centres and dispensaries in the intervention areas in the diagnosis and treatment of STDs with syndromic treatment algorithms. The training comprised 1 week of classroom teaching followed by 2 weeks of practical training at the STD reference clinic in Mwanza town. The staff were also trained to provide patients with STDs with health education and to offer free condoms for use during the current STD episode. Third, regular supply of the drugs needed to treat STDs effectively. To ensure continuous availability of drugs, a special delivery system was set up to supplement the supplies provided through the national essential drugs programme. Fourth, regular supervisory visits by a programme officer to each health facility to provide in-service training, and to check drug supplies and patient records. Finally, periodic visits by a team of health educators to the villages served by each health facility to provide information on STDs, focusing on the availability of effective treatment and encouraging prompt attendance for treatment of symptomatic STDs.

Impact evaluation

12 large communities, each consisting of the catchment population of a health centre and its satellite dispensaries, were selected as the elements for randomisation. A previous survey in the region had demonstrated substantial geographical variations in HIV prevalence, with a higher prevalence in roadside settlements than in rural villages,¹¹ and a raised prevalence was also observed in villages close to the lake shore. To help ensure comparability of the intervention and comparison communities with respect to baseline HIV and STD prevalences and risk factors for infection, the communities were matched into six pairs according to the following criteria: roadside, lakeshore, island, or rural location; geographical area (paired communities were generally in the same district and less than 50 km apart); and prior STD attendance rates at the health centre, mainly to eliminate those health centres that were barely functioning.

In each matched pair, one community was randomly chosen to receive the STD intervention immediately following the baseline survey, whereas the comparison community received the intervention after the follow-up survey 2 years later. Locations of the study communities are shown in figure 1.

The impact of intervention on the incidence of HIV infection and on the prevalence and incidence of STDs was measured in a random cohort consisting of 1000 adults from each community. Clusters of households were sampled randomly from the population residing within 90 min walking distance of the health centre, by a sampling scheme described previously.¹⁴ All adults

aged 15–54 years in the selected households were eligible for inclusion.

Surveys of the study cohort were conducted at baseline and at follow-up 2 years later. Informed oral consent was obtained from each adult at enrolment, and personal characteristics, circumcision status, and history of STDs were recorded through a confidential interview. A sample of venous blood was taken from all consenting subjects. Men were asked to provide a first-void urine sample, which was tested on the spot with a leucocyte esterase dipstick (LED, Nephur-Test+Leuco, Boehringer-Mannheim). Men with a positive LED test, and those reporting or found on examination to have urethral discharge, were asked to provide a urethral swab. All participants were seen by a clinician, who provided treatment for symptomatic STDs and other illnesses.

Laboratory methods

Serum was separated and tested for HIV antibodies by ELISA assay (Vironostika HIV MIXT Microelisa, Organon, Teknika, Baxel, Netherlands). All positive samples underwent confirmatory testing with a methodologically independent ELISA (Wellcozyme HIV 1+2 GACELISA, Murex Diagnostics, Dartford, UK) and, in case of discrepant or indeterminate ELISA results, a western blot test (HIV-1 Westernblot, Epitope, Beaverton, Oregon, USA). Western blot results were considered positive if WHO criteria were fulfilled.¹⁵ Indeterminate western blot results were considered negative in the analysis. HIV-2 has yet to be observed in this area, and data on HIV prevalence and incidence can be taken to refer to HIV-1 infection.

Serological tests for syphilis were carried out by the rapid plasma reagin (RPR) test (with VD 25 VDRL Carbon Antigen, Murex, Dartford, UK) and the *Treponema pallidum* haemagglutination test (TPHA, Fujirebio, Tokyo, Japan). TPHA seropositivity was considered to indicate past or current syphilis infection, while positivity on both TPHA and RPR tests was considered indicative of active syphilis. An initial RPR test was done in the field, and subjects with a positive RPR test were treated on the spot for syphilis.

Urethral swabs were tested for *Neisseria gonorrhoea* by gram stain, and for *Chlamydia trachomatis* by an antigen capture enzyme immunoassay (IDEIA Chlamydia, Novo Nordisk Diagnostika, Cambridge, UK). Gonorrhoea was diagnosed when intracellular gram negative diplococci were seen in urethral smears. For logistical reasons, it was not possible to attempt isolation of *N. gonorrhoea* in this rural population-based study. Chlamydia infection was diagnosed after a confirmatory blocking assay on all positive samples. Urethritis was defined as *N. gonorrhoea*/C *trachomatis* infection and/or the presence of five or more polymorphs per high power field in urethral smears.

Sexual behaviour survey

To determine whether any differences in HIV incidence between intervention and comparison groups may have resulted from differences in sexual behaviour, separate random sampling of one in eight cohort members was done after the baseline and follow-up surveys. The selected individuals were revisited and interviewed concerning sexual attitudes and practices with a detailed questionnaire.

Statistical methods

Since randomisation was applied at the community level, statistical inference needed to take account of between-community variations in HIV incidence. Within each matched pair, the risk ratio (RR) of HIV incidence in the intervention community relative to the comparison community was computed. A point estimate of the overall RR was calculated as the geometric mean of the pair-specific RRs. Statistical significance was assessed with the paired *t* test on the logarithms of the RRs, and corresponding 95% CIs for the RR were obtained. Significance was further evaluated with the non-parametric sign test.

	Men		Women	
	Intervention (n=2881)	Comparison (n=2998)	Intervention (n=3261)	Comparison (n=3397)
HIV positive	3.4	4.1	4.1	4.7
Syphilis (TPHA+)	15	14	17	16
Active syphilis (TPHA+/RPR+)	7.9	7.8	9.5	8.8
NG/CT	2.4	3.2	..	..
Symptomatic NG/CT	0.3	0.5	..	..
Urethritis	10	11	..	..
Symptomatic urethritis	1.0	1.3	..	..
Reported GUS ever	14	16	5.1	6.1
Reported GDS ever	24	31	7.7	8.7

NG/CT=*N gonorrhoea*/C *trachomatis*, GUS=genital ulcer syndrome, GDS=genital discharge syndrome.

Table 1: Baseline prevalence (%) of HIV infection and other STDs by sex, in intervention and comparison communities

To adjust for differences between the intervention and comparison communities that might bias the estimate of impact, a logistic regression model was fitted using data on individuals and including terms for the matched pair, age-group (15-19, 20-24, 25-29, 30-34, 35-44, 45-54 years), sex, travel out of the village during the follow-up period, reported history of STD (ever) at the baseline survey, and male circumcision status. By computing observed and expected numbers of HIV seroconversions in the intervention (O_i , E_i) and comparison (O_o , E_o) communities, an adjusted RR was obtained for each pair as $(O_i/E_i)/(O_o/E_o)$. Adjusted significance tests and confidence intervals were calculated as before.

Evaluation of the impact of the intervention on the prevalence of STDs at follow-up was based on the seroprevalence of active syphilis, and on the prevalence of confirmed urethritis and *N gonorrhoea*/C *trachomatis* infection in men. Since many urethral infections were symptomless,¹⁴ additional analyses were done of the prevalence of symptomatic urethritis and *N gonorrhoea*/C *trachomatis* infections in men. Statistical methods were as for HIV incidence.

The number of communities and the size of the cohort were chosen to provide 80% power of detecting a 50% reduction in annual HIV incidence from 1% to 0.5%, taking account of the expected level of between-community variation in incidence rates.¹²

Results

Cohort enrolment and baseline comparability

12 537 adults were enrolled at the baseline survey, representing 85% of eligible individuals from the sampled households. Detailed results of the baseline survey have been presented previously.¹⁴ The randomisation and matching procedures were shown to have provided intervention and comparison groups that were generally similar at baseline with respect to HIV prevalence, history and prevalence of STDs, and measured risk factors for HIV infection. However, there was some imbalance in reported history of STDs (ever), travel away from the village, and male circumcision, and so these variables were adjusted for in the impact analysis.

	Intervention	Comparison	Total
Men			
Recruited	2881	2998	5879
Seen at follow-up	2052	2187	4239
Coverage (%)	71	73	72
Women			
Recruited	3261	3397	6658
Seen at follow-up	2234	2372	4606
Coverage (%)	69	70	69
Total			
Recruited	6142	6395	12 537
Seen at follow-up	4286	4559	8845
Coverage (%)	70	71	71
Losses to follow-up	1856	1836	3692
Moved	814 (13%)	924 (14%)	1738 (14%)
Temporary absence	291 (5%)	459 (7%)	750 (6%)
Died	87 (1%)	109 (2%)	196 (2%)
Other	664 (11%)	344 (5%)	1008 (8%)

Table 2: Numbers recruited to cohort, coverage at follow-up survey, and reasons for loss to follow-up in intervention and comparison communities

Baseline prevalences of HIV and STDs are summarised in table 1. Overall HIV prevalences at baseline were 3.8% and 4.4% in the intervention and comparison groups, respectively, while prevalences of active syphilis were 8.7% and 8.3%, respectively. HIV prevalence was higher in the intervention community in three matched pairs, and in the comparison community in the other three pairs.

Implementation of intervention

The intervention programme was successfully established in all six intervention communities. Clinic records showed that 11 632 cases of STDs were treated in the intervention health units during the 2 years of follow-up. Previous data¹⁷ (unpublished observations) have shown that the treatment regimens would be expected to achieve cure in over 90% of cases.

Coverage at follow-up survey

8845 (71%) cohort members were seen again at the follow-up survey 2 years later. 1738 (14%) had moved permanently away, 750 (6%) were temporarily away, 196 (2%) had died, and 1008 (8%) did not participate for other reasons (refusals, inaccessibility due to heavy rains, or reason not recorded). Coverage rates were very similar in the intervention (70%) and comparison (71%) groups (table 2). Reasons for non-participation were broadly similar in the two groups, although losses due to "other" reasons occurred somewhat more frequently in the intervention group.

Impact on HIV incidence

HIV prevalence at baseline, and HIV seroconversions over the 2 years of follow-up, are shown for each community in

	HIV baseline prevalence (%)		HIV seroconversions		Crude RR (95% CI)	Adjusted RR* (95% CI)
	Intervention	Comparison	Intervention	Comparison		
Matched pair/stratum						
1 Rural	3.9	3.0	5/568 (0.9%)	10/702 (1.4%)	0.62	0.59
2 Islands	2.0	1.6	4/766 (0.5%)	7/833 (0.8%)	0.62	0.65
3 Roadside	6.8	8.6	17/650 (2.6%)	20/630 (3.2%)	0.82	0.88
4 Lakeshore	5.4	4.3	13/734 (1.8%)	23/760 (3.0%)	0.59	0.62
5 Lakeshore	2.8	4.7	4/732 (0.5%)	12/782 (1.5%)	0.36	0.35
6 Rural	1.8	4.5	5/699 (0.7%)	10/693 (1.4%)	0.50	0.50
Overall	3.8	4.4	48/4149 (1.2%)	82/4400 (1.9%)	0.57† (0.42-0.76)	0.58† (0.42-0.79)

*Adjusted for age, sex, travel during follow-up period, history of STD (ever) at baseline, and male circumcision. †Geometric mean.

Table 3: HIV incidence over 2 years in intervention and comparison communities, and crude and adjusted risk ratios

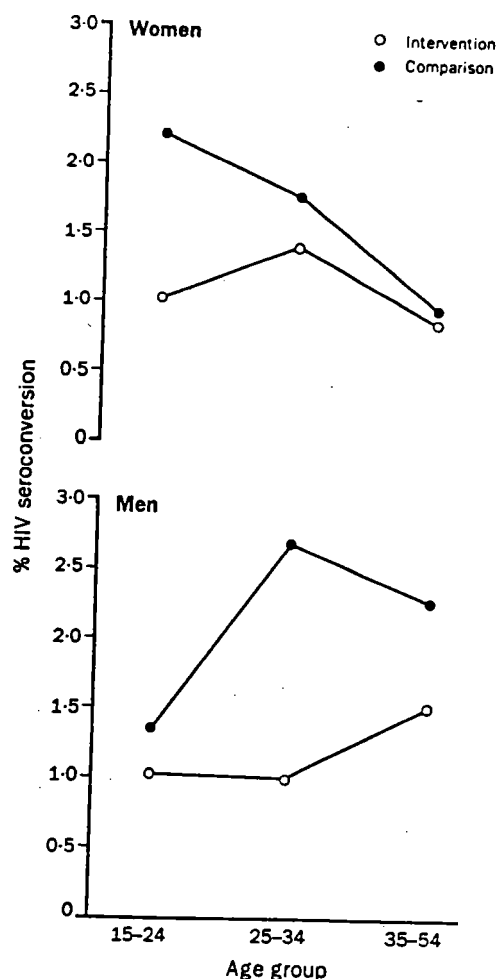


Figure 2: Incidence of HIV infection over 2 years by age and sex in intervention and comparison communities

table 3. HIV results were available at both baseline and follow-up for 8825 (99.8%) of those seen at follow-up. Of these, 276 (3.1%) were HIV positive at baseline, so that HIV incidence calculations were based on 8549 initially seronegative individuals—4149 in the intervention group and 4400 in the comparison group.

Over the 2 years of follow-up there were 48 seroconversions (1.2%) in the intervention group and 82 (1.9%) in the comparison group. HIV incidence varied substantially between matched pairs, but was consistently lower in the intervention community than the comparison community in all six matched pairs (table 3). When the data were analysed to take account of between-community variation, the RR for seroconversion in intervention compared with comparison communities was 0.57 (95% CI 0.42–0.76, $p=0.004$). When the analysis was adjusted for variables showing an imbalance between the two treatment groups at baseline, the RR was virtually unchanged (0.58, 0.42–0.79, $p=0.007$). A non-parametric test gave similar results (two-sided $p=0.03$ for both unadjusted and adjusted analyses).

Seroconversion rates are shown by age and sex in figure 2. HIV incidence in the comparison group was highest in women aged 15–24 years and men aged 25–34 years. In the intervention group, the greatest proportionate reductions in incidence occurred in the same two age/sex groups. However, numbers of seroconversions at each age were small, and the differences in effect between age/sex groups were not statistically significant (test for

Marker	Prevalence		Crude RR* (95% CI)	Adjusted RR*† (95% CI)
	Intervention	Comparison		
Active syphilis	445/4260 (10.4%)	516/4539 (11.4%)	0.90 (0.76–1.06)	0.92 (0.78–1.07)
NG/CT‡	52/2052 (2.5%)	66/2187 (3.0%)	0.68 (0.27–1.68)	0.65 (0.26–1.62)
Symptomatic NG/CT‡	19/2052 (0.9%)	26/2187 (1.2%)	0.58 (0.14–2.51)	0.72 (0.25–2.07)
Urethritis‡	119/2052 (5.8%)	152/2187 (7.0%)	0.84 (0.31–2.26)	0.84 (0.32–2.20)
Symptomatic urethritis‡	32/2052 (1.6%)	54/2187 (2.5%)	0.48 (0.09–2.70)	0.49 (0.09–2.55)

NG/CT=*N gonorrhoea*/*C trachomatis*.

*Geometric mean of pair-specific risk ratios. †Adjusted for age, sex, travel during follow-up period, history of STD (ever) at baseline, and male circumcision.

‡Men only.

Table 4: Markers of STD prevalence at follow-up in intervention and comparison communities, and crude and adjusted risk ratios

interaction obtained by logistic regression, ignoring between-community variation, gives $\chi^2=2.69$, 5 df, $p=0.75$).

Impact on STD prevalence

Markers of STD prevalence at follow-up in the intervention and comparison communities are shown in table 4. Prevalence was consistently lower in the intervention group for all markers. However there was substantial between-community variation, and none of the differences were statistically significant when this variability was taken into account. The greatest effect observed was on symptomatic urethritis in men, with prevalences at follow-up of 1.6% in that intervention group and 2.5% in the comparison group, giving an adjusted RR of 0.49 (CI 0.09–2.55, $p=0.32$).

Sexual behaviour

Results from the sexual behaviour surveys at baseline and follow-up are summarised in table 5. At baseline,

	Men		Women	
	Intervention	Comparison	Intervention	Comparison
Baseline				
n	237	281	298	301
Lifetime partners (%)				
0	1	3	3	4
1	7	5	28	26
2–4	18	22	47	53
5–19	44	44	19	16
20+	31	26	3	1
Partners past year (%)				
0	7	10	9	10
1	44	36	78	83
2	22	25	9	6
3–4	18	22	3	1
5+	10	8	1	0
Follow-up				
n	216	268	248	255
Partners past year				
0	5	4	10	10
1	42	46	81	75
2	27	26	7	12
3–4	18	19	2	2
5+	8	6	0	0
Casual partners past 2 years				
0	62	55	89	87
1	14	17	6	7
2	10	11	3	3
3+	14	17	2	3

Table 5: Numbers of sexual partners reported in intervention and comparison communities at baseline and follow-up

reported numbers of lifetime sex partners and of sex partners during the past year were similar in the intervention and comparison groups in both sexes. At follow-up, reported partners during the past year showed no change from baseline, and there was still no material difference between the intervention and comparison groups. Data were also collected at follow-up on reported "casual" partners during the past 2 years, defined as all sex partners other than those described as "regular" or living with the respondent. Similar results were again obtained in the intervention and comparison groups.

At baseline only 2% of men reported sexual contact with bar girls or prostitutes during the past year, and this question was not repeated at follow-up. Information was collected at follow-up on condom use during the follow-up period. Condom use with sex partners other than their spouse was reported by only 2.4% of men (intervention 1.6%, comparison 3.0%) and 2.3% of women (intervention 2.7%, comparison 1.8%). Only three individuals reported regular use of condoms.

Discussion

Rational health policy decisions depend on reliable data on the cost-effectiveness of different health interventions. Because of the urgency of the AIDS epidemic, interventions have had to be made without the benefit of such data. Although a few evaluation studies have been published,¹⁸⁻²⁰ these have been observational in design, and this is the first report of a randomised controlled trial of a preventive intervention against HIV in the general population anywhere in the world.

Although WHO has advocated improved STD treatment as an additional HIV control strategy for some years, the empirical basis for this policy has been slender. While evidence from observational studies is consistent with the hypothesis that STDs act as a biological cofactor for HIV transmission,¹ there are substantial difficulties in interpreting such data, and the magnitude of any such effect is unknown.²¹⁻²³ The impact of improved STD treatment depends on the proportion of HIV infections in the general population that are attributable to the cofactor effect of STDs, and on the reduction in STD prevalence that might be achieved by an intervention programme, and neither is easy to predict. By incorporating randomisation within the phased introduction of an STD intervention programme in the Mwanza region of Tanzania, we have been able to obtain reliable data on the impact of this programme on HIV incidence.

We have demonstrated an overall reduction in HIV incidence of about 42% over 2 years of follow-up. The reduction occurred in both sexes, and was observed consistently in all matched pairs of study communities. The observed annual incidence of 0.9% in the comparison group was close to the 1% assumed in the study design, and similar to the incidence observed in the rural population of neighbouring Kagera region.²⁴ Since the intervention was randomised at the community level, it was essential to use statistical methods that took account of between-community variation in incidence. Such analysis demonstrated a highly significant impact, and it is therefore very unlikely that chance accounted for the observed differences. Are there any sources of bias which might account for the findings?

These results might be explained by a lack of comparability between the treatment and comparison communities, such that HIV incidence would have

differed in the absence of intervention. Although matching and randomisation should have minimised this problem, with 12 study communities some differences cannot be ruled out. However, data collected at baseline support the comparability of the two groups and, in particular, baseline prevalences of HIV and syphilis were similar.¹⁴ Where imbalances in risk factors were identified, these were adjusted for in the analysis, with little effect on the impact estimates.

Losses to follow-up are an important source of bias in prospective studies, since those lost may differ in risk from those continuing under follow-up. Of our cohort, 71% were seen at follow-up, or 83% after excluding those who had died or moved away permanently. These coverage rates are within the range generally considered acceptable in population-based studies. Coverage rates were almost identical in the intervention and comparison groups, and reasons for loss to follow-up were broadly similar, although losses due to "other reasons" were somewhat higher in the intervention group. This discrepancy was due mostly to a low coverage rate in one intervention community, which became inaccessible due to onset of the rains, and to field worker error in another intervention community resulting in failure to record reasons for some losses. It seems unlikely that the comparison of the two groups has been influenced substantially by losses to follow-up.

The HIV testing algorithms employed were highly sensitive and specific, but a small number of false positives or negatives cannot be ruled out. Since the HIV testing laboratory was kept blind to the origin of the serum specimens, any such misclassification should not be different between the two study groups, and the effect of misclassification would be modest dilution of the intervention effect.

Further bias may have resulted from "contamination" effects—for example, if individuals from comparison communities travelled to intervention villages to take advantage of the improved services. In our trial, the study communities were carefully chosen with respect to the geography of the region, so that distances between communities were large, and travel between them difficult and time-consuming. To check for this possibility, however, data were collected at the intervention health units on the place of residence of patients treated for STDs. During the 2 years of follow-up, only 59 patients from the comparison communities were recorded at these units, representing only 0.5% of those treated for STDs. The effect of any contamination bias would again be to dilute the effect of the intervention. The estimate of impact may therefore be an underestimate.

We conclude that there is strong evidence that our STD intervention programme has a substantial effect on HIV incidence in this rural population. Might this be explained by changes in risk behaviour in the intervention communities? The main focus of the intervention was on the provision of improved STD treatment services. Periodic visits were made by the project team to the intervention villages to inform the population about STDs, the main emphasis being on the importance of seeking treatment promptly and on publicising the improved treatment services available. These visits were not expected to have a substantial impact on patterns of sexual behaviour. Health education activities of the National AIDS Control Programme continued equally in the intervention and comparison communities during the

follow-up period. Although health workers in intervention units were trained to offer condoms to patients attending with STDs, patient registers indicate that only 0.9% of patients took condoms. To provide empirical data on behavioural change, special surveys of sexual behaviour were conducted at both baseline and follow-up in random samples selected from the study cohort. These data indicated no change in sexual behaviour over the 2-year follow-up period, and no material difference between the intervention and comparison communities. Furthermore, condom use remained at a very low level in both groups. Whereas condoms now seem to be relatively well-accepted in Mwanza town, due partly to the intensive condom promotion activities there, acceptability and use of condoms remain low in rural areas and more intensive interventions will be needed to change this pattern.

In the absence of sexual behaviour change, the most plausible explanation for our results is that the STD treatment programme reduced HIV incidence by shortening the average duration of STDs, thus effectively reducing the probability of HIV transmission. The data on STD prevalences were consistent with this hypothesis, all measured indicators showing a lower prevalence in the intervention group than in the comparison group at follow-up, but none of these effects was statistically significant. Moreover, some indicators showed some imbalance at baseline.

An intervention based on syndromic treatment of self-reporting cases would not be expected to have a substantial effect on the prevalence of symptomless infections. The high frequency of symptomless infections in men in this population was not recognised when the trial was designed,¹⁰ and the sample size was too small to detect a significant effect on symptomatic infections. The most reliable measure of symptomatic infections in our study cohort was the prevalence of confirmed urethritis in men reporting symptoms at the time of our survey, and it is of interest that this indicator showed the greatest reduction in the intervention group compared with the comparison group.

Our data on STDs were limited by logistical constraints on the diagnostic methods that could be employed in a rural field survey, and by the subjective nature of responses on symptomatic infections. Future trials will need to pay careful attention to these difficulties.

The magnitude of the effect on HIV incidence is the clearest evidence to date that a large proportion of HIV infections in this population are attributable to the cofactor effect of STDs, and this may help to explain the rapid heterosexual spread of HIV in many parts of sub-Saharan Africa. The largest impact of intervention was seen in women aged 15–24 and men aged 25–34; these are the age/sex groups in which the highest incidences of HIV were observed in the comparison communities, and STDs might play a particularly important part in facilitating HIV transmission in these groups. If an STD intervention strategy that relied on effective treatment of self-presenting symptomatic cases is able to reduce HIV incidence by almost half, more intensive STD control measures might have a greater effect.

How generalisable are our results to other rural populations in Africa? With an adult HIV prevalence of around 4% and an annual incidence of around 1%, the rural population of Mwanza region is fairly typical of many other parts of eastern and southern Africa.

Although information on the prevalence of STDs in African population is sparse, our data are similar to other published results.^{4,21} Furthermore, the intervention strategy we adopted was chosen for its potential replicability in low-income countries, and was designed to be implemented through routine primary-health-care services. However, ease of implementation will clearly vary according to the structure and functioning of the health services. To ensure a constant supply of the drugs needed for STD treatment, the intervention in Mwanza region incorporated a special delivery system to supplement the supplies provided through the national essential drugs programme. The cost analysis will need to examine likely variations in cost and effectiveness if a less intensive intervention were established—for example, if the programme were to rely on the routine drug supply system, or if supervisions were carried out less frequently.

Many other parts of the developing world, including southern Asia where the HIV epidemic is now spreading rapidly, have high rates of STDs and poor STD treatment services, so our intervention strategy is potentially of much wider applicability. Educational interventions, aimed at modifying risk behaviour, were not evaluated in this trial, but should in our view remain an important priority for national AIDS control programmes. However, our results suggest the importance of complementing these activities with improvements to STD treatment services wherever STDs are highly prevalent. Commentators have emphasised the inadequacy of the resources being directed globally to HIV prevention, in particular in the developing countries most affected by the epidemic. This failure may partly reflect “donor fatigue” and doubts about the impact of control activities. The demonstration that HIV incidence can be almost halved by a modest intervention in one of the world's most disadvantaged countries should provide a message of hope, and help stimulate renewed efforts to control this epidemic throughout the developing world.

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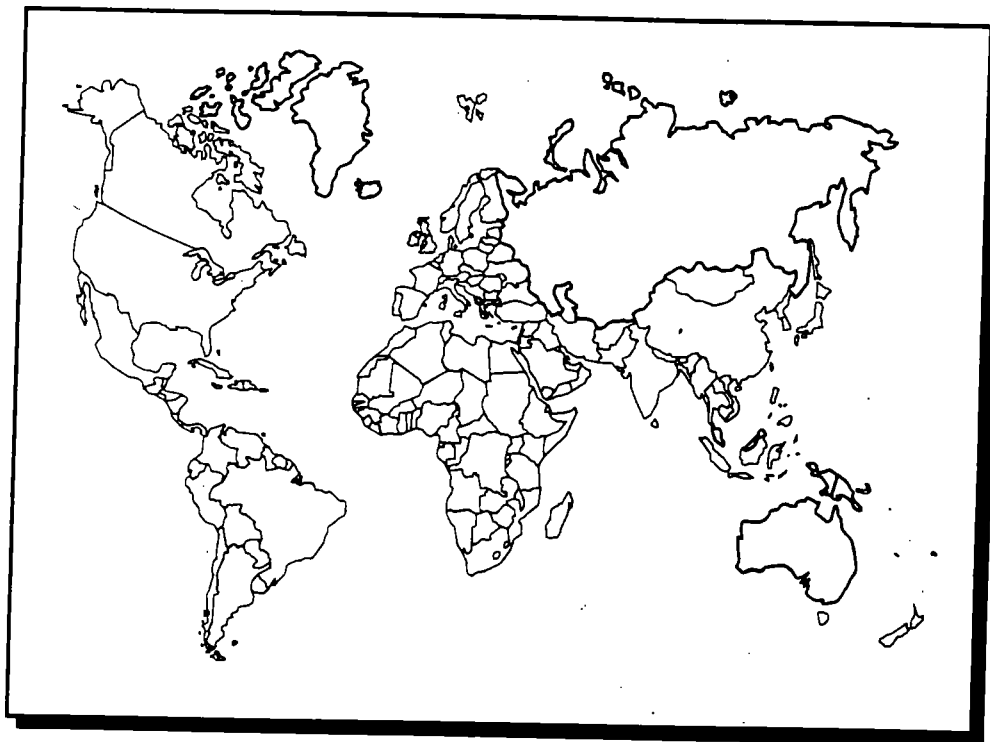
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HIV/AIDS POLICY GUIDANCE

USAID



SEPTEMBER 1995

Youth represent a unique set of challenges, as the combination of their biological, emotional, economic and legal situations make them particularly vulnerable to HIV transmission. WHO estimates that half the people infected with HIV acquired it between the ages of 15 and 24. To prevent infection in this population USAID supports efforts using messages, channels and methods specific to youth. The intervention opportunities for young adults range from peer counseling, and education and vocational skills building, to legislative efforts related to youth. Prevention strategies, especially for youth, should include opportunities to build so-called "life skills" in communication, decision making, negotiation, and abstinence.

Urbanization and Migration draw persons and populations from their rural communities and place them at increased risk of HIV infection. Individuals separated from family and traditional values can be affected by drastic changes in socio-economic and cultural influences. The epicenters of the HIV epidemic have been found to follow migrant labor flows, suggesting that high risk behavior may be associated with displaced communities. Additionally, involuntary migration in response to civil war or disasters increases the vulnerability of communities to HIV infection. There are, however, potential dangers in focusing on the movements of persons and populations as part of HIV prevention efforts. It could lead to discrimination against certain groups and the creation of inappropriate and counterproductive immigration screening regulations. Therefore, more enlightened methods need to be developed to intervene with "travellers" that do not lead to stigmatization but that arm them with the knowledge and tools to protect themselves and their partners.

Sexually Transmitted Infections significantly increase the efficiency of HIV transmission. Therefore, improving STI services and providing education for people with sexually transmitted infections are the logical focus of prevention efforts. The presence of an STI, particularly one that causes genital ulcers (syphilis, chancroid), increases the likelihood of sexual transmission of HIV by 5 to 20 times. In addition, persons with recurrent STIs are effective targets for communication campaigns to induce behavior change because they are more likely to be engaging in frequent casual high risk sexual encounters. Educational campaigns that focus on STI patients have been shown to have up to eight times as large a preventive impact as those aimed at the general adult population. Recent data from Tanzania demonstrated a 40% reduction in incidence of new HIV infections among communities in which an effective STI intervention program was being conducted.

USAID recognizes that individuals who are marginalized by society (including

Global Update

continued

one in three pregnant women has HIV. These women are overwhelmingly monogamous and have contracted the disease from their husbands who, following African tradition, are not so faithful. "Women have to be able to protect themselves, to have enough power to say no or to insist on using a condom," observes Judith Senderowitz, a reproductive-health consultant to the United Nations. The push for independence and "sexual freedom" has resulted in the increased momentum of local feminist movements, the opposition by many of female mutilation and other violence against women, and in some nations, the acquisition of high-profile jobs by women in government or powerful nongovernmental organizations. (*Newsweek*, 9/25.95, Vol. 126, No.13)

South Africa

Researchers from the University of Natal said in a study that nearly 1 million people in KwaZulu-Natal, the most populous province of South Africa, may be infected with HIV by 1996. "The HIV/AIDS epidemic is at a more advanced stage in KwaZulu-Natal than in the rest of South Africa," the survey said. The study was conducted to determine the impact of AIDS on the 8.7-million person province. Project leader Alan Whiteside said that based on the group's projections, 920,000 residents will have HIV by next year. In addition, the researchers predicted a surge in deaths in the under five-year age group and in the 25- to 40-year age group, and that the majority of the infections would be in poorer socio-economic groups, particularly blacks in townships or impoverished rural villages. (*Reuters*, 10/26/95)

Uganda

Last November, in the Rakai district of Uganda, teams of African and American researchers began recruiting 11,000 people for a five-year study of whether the spread of HIV can be controlled by treating large groups of people for other sexually transmitted diseases (STDs). Maria Wawer of Columbia University and Nelson Sewankambo of the University of Makerere in Kampala have developed a trial in which everyone between the ages of 15 and 38 from nearly 30 area villages is treated with a combination of oral antibiotics for such STDs as gonorrhea, chlamydia, trichomoniasis, and syphilis, regardless of whether or not the subjects show symptoms of the diseases. But the trial—which is funded, in part, by the U.S. National Institutes of Health (NIH), the World Bank, and the Rockefeller Foundation—has sparked controversy because two of the drugs used are too expensive for most Ugandans. This practice is contrary to internationally accepted standards which state that "as a general rule," there should be some guarantee that if the treatment does prove effective, "it will be made reason-

ably available to the inhabitants of the host community or country." The trial, however, has been approved by scientific and ethical review panels at the AIDS Research Subcommittee of the Medical Research Council of Uganda, Columbia University, NIH, and Johns Hopkins University. The study was approved, said Wawer, because it will help identify which STDs are associated with the highest risk of HIV infection. (*Science*, 9/08/95, Vol. 269, No. 5229)

Zimbabwe

According to a statement made to the independent Sunday Gazette newspaper by Zimbabwe Health Minister Timothy Stamps, at least 100,000 Zimbabweans will die of AIDS-related diseases over the next 18 months. "I am not trying to be alarmist," he said, "but this is the reality we are facing." Stamps added, "At present ... 25 to 30 bodies of victims of AIDS are put [daily] into mortuaries of Harare and Mpilo hospitals where authorities are now failing to cope with the congestion." (*Reuters*, 10/22/95)



Timothy Stamps, Zimbabwe's Minister of Health and Child Welfare, will auction his hair next weekend to raise funds for a campaign against AIDS. According to the state news agency ZIANA, Stamps shaved his head in memory of people who have died from AIDS. Under African custom, people demonstrate their grief over the death of a relative by cutting off their hair. Ministry of Health statistics show that more than 100,000 in Zimbabwe have died from AIDS-related causes in the past decade. Stamps predicted that another 100,000 Zimbabweans, or 1 percent of the country's population, would die from AIDS in the next year and a half. (*Reuters*, 11/13/95)

Europe

Italy

The Constitutional Court in Rome has overturned legislation that permitted criminals with AIDS to be freed from jail. The ruling follows a slew of robberies by so-called AIDS gangs this summer in northeastern Italy. The court said that the law "granted a sort of impunity to the ill [inmates] that did not respect the defense of the health of the entire community." Whether or not prisoners infected with HIV or AIDS should be freed will now be decided on a case-by-case basis. Judges will also now be required to determine whether prisoners with the disease are adequately cared for and whether the risk of contagion is controlled. In addition, Thursday's ruling overturns laws that exempted people with AIDS from detention without trial. Now, they are subject to preventive detention if they are suspected of serious offenses. (*Washington Post*, 10/19/95)

THE LANCET

COMMENTARY

STD control for HIV prevention—it works!

See page 530

Prevention and management of sexually transmitted diseases (STDs) have seldom ranked high on national healthcare priority lists, despite their serious threat to health, especially of women and newborn babies.¹ With the emergence of a new lethal STD, HIV, and the increasing evidence that sexually acquired lesions and inflammation could facilitate HIV transmission, the picture has changed.² STD case-management has increasingly been included in HIV-prevention strategies but its potential impact on the spread of HIV remained controversial. Furthermore, STD control is often thought to be a complex and expensive strategy that drains resources from promotion of condoms and other safer sex behaviours.

In this issue, Grosskurth and colleagues report the results of a well-designed community randomised trial which show a 42% reduction of HIV incidence as a result of improved STD case-management in a rural area of Tanzania. As the researchers note, the magnitude of the effect on HIV incidence observed in this trial is the clearest evidence so far that a large proportion of HIV infections in this population are attributable to the enhancing effect of STDs. Even more important, this study shows that simple replicable STD care activities integrated into primary healthcare services can lead to a considerable reduction of HIV. Although there were earlier reports of a significant decline of HIV incidence as a result of STD case-finding in high-risk women, the Mwanza trial shows convincingly for the first time that the concept of STD control for HIV prevention works in the general population. If shortening the duration of self-reported STDs, mainly in males, results in a 42% reduction of HIV incidence, what would have happened if more aggressive strategies had been implemented—eg, addressing symptomless STDs via case-finding among vulnerable groups? One could reasonably expect an even greater effect.

What lessons can we learn from this study? With an apparently low key intervention (including training of healthcare workers in STD syndrome management, making available effective antibiotics for STDs, and promoting healthcare-seeking behaviour) a large effect can be obtained in terms of the proportion of STDs cured by the health services, especially when baseline quality of STD care is poor.³ However, the replicability and sustainability of this minimal package should be seen in the context of declining quality of health systems in many developing countries. For example, access to STD drugs is primarily a function of general access to drugs, except if separate distribution systems are established, which was the case in the Mwanza trial.

In the Tanzanian study there was no difference in sexual behaviour and condom use in the intervention and control communities. From a methodological point of view, this observation makes a more convincing case for the role of STDs as cofactors in HIV incidence, but in public health terms this finding is worrisome. Healthcare workers confronted with STD patients should not miss the opportunity to talk about safe sex and promote condoms.⁴ The disappointingly low condom uptake among the trial participants in Mwanza contrasts with

experience in other HIV/STD prevention projects.^{5,6} Promotion of behaviour change during clinic visits, although limited by time constraints, remains one of the most neglected components of STD/HIV prevention activities in developing countries.

One of the most striking findings of this intervention trial was that the largest impact on HIV incidence occurred among the very young women (15–24 years). The potential for STD/HIV reduction is the largest among young women, who are at increased risk for STD and HIV acquisition because of both behavioural and biological mechanisms (immature cervix with large area of ectopy).⁷ Special attention should be given to this highly neglected group of patients, many of whom are adolescents, in terms of comprehensive reproductive health education and delivery of services. Recent interest in integrating STD services in family planning and maternal and child health may work well for older women, but unmarried adolescents are often not welcome or make little use of such facilities.

We still do not know how best to provide accessible and effective STD care for groups such as adolescents or sex workers. The lack of simple technical tools to detect gonococcal and chlamydial infections in women is a first obstacle, and the syndromic approach to case-management works poorly in symptom-free women. With respect to service delivery, waiting for clients to come to the clinic is not enough. Outreach activities, community involvement, and low-threshold services are important components if we want to influence these hard-to-reach populations.

HIV is still spreading fast; the problem is urgent. We have learnt that no single approach will contain the epidemic, and we need all the means that are available, how imperfect they may be. The Mwanza study confirms that improving STD care-management is an important additional HIV prevention strategy. Its potential benefit will clearly depend on the prevalence of STD in the population, and the effectiveness of the STD programme. Rather than focusing our efforts on further quantifying the attributable risk of STD control, we should now put all our energies into determining how best to deliver STD care, especially to highly vulnerable populations.

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④ Census Bureau --

- What percentage of the general population is African American?
- What percentage of the general population is Hispanic?

~~301-457-1403~~
301-457-2403

~~Denise Sam~~

1990 Census

Black 12.1%

Hispanic 9%

Afro-Amer

23 mil

777,098

23,777,098

Entire pop

248 709 873

A Randomized Controlled Trial of an HIV Sexual Risk-Reduction Intervention for Young African-American Women

Ralph J. DiClemente, PhD, Gina M. Wingood, ScD, MPH

Objective.—To evaluate the efficacy of a community-based social skills human immunodeficiency virus (HIV) prevention intervention to enhance consistent condom use.

Design.—A randomized, single-blind controlled trial.

Setting.—Bayview-Hunter's Point neighborhood of San Francisco, Calif, a predominantly African-American community that is economically disadvantaged.

Participants.—A sample of 128 sexually active, heterosexual, African-American women 18 through 29 years of age was recruited using street outreach techniques. Participants completed a structured baseline interview; 100 women (78.1%) completed 3-month follow-up interviews.

Intervention.—Women randomized to the social skills intervention completed five sessions that emphasized ethnic and gender pride, HIV risk-reduction information, sexual self-control, sexual assertiveness and communication skills, proper condom use skills, and developing partner norms supportive of consistent condom use. Women randomized to the HIV education condition participated in a single session that provided HIV risk-reduction information. Women randomized to the delayed HIV education control condition received no HIV risk-reduction information until all follow-up interviews were completed.

Main Outcome Measures.—Consistent condom use, HIV risk-reduction knowledge, sexual self-control, sexual assertiveness, sexual communication, and partner norms supportive of consistent condom use.

Results.—Compared with the delayed HIV education control condition, women in the social skills intervention demonstrated increased consistent condom use (adjusted odds ratio [OR], 2.1; 95% confidence interval [CI], 1.03 to 4.15; $P=.04$), greater sexual self-control (adjusted OR, 1.9; 95% CI, 1.00 to 3.60; $P=.05$), greater sexual communication (adjusted OR, 4.1; 95% CI, 1.67 to 10.01; $P=.002$), greater sexual assertiveness (adjusted OR, 1.8; 95% CI, 1.01 to 3.27; $P=.05$), and increased partners' adoption of norms supporting consistent condom use (adjusted OR, 2.1; 95% CI, 1.08 to 3.87; $P=.03$). No statistically significant differences in outcome variables were observed between the HIV education condition relative to the delayed HIV education control condition.

Conclusion.—Community-based HIV risk-reduction programs that are gender relevant and culturally sensitive and provide social skills training can effectively enhance consistent condom use.

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AFRICAN-AMERICAN women are disproportionately affected by the acquired immunodeficiency syndrome (AIDS) epidemic.¹ Surveillance data for 1994 indicate that African-American women were approximately 16 times more likely to be diagnosed with AIDS than white women (63 per 100 000 vs four per 100 000). More-

over, seroepidemiological surveys from various populations indicate that, relative to other ethnic groups, African-American women have markedly higher human immunodeficiency virus (HIV) prevalence rates. In a study of childbearing women, seroprevalence rates for African-American women were six to 15 times higher than for white women.² Similarly, HIV prevalence rates among African-American women applicants to the Job Corps training program more than doubled between 1988 and 1992, not only exceeding rates for white and Hispanic women, but also exceeding rates for African-American men.³

Reducing the risk for HIV among sexually active African-American women requires the use of prevention strategies that effectively inhibit viral transmission.^{4,5} A primary HIV prevention strategy is to use a condom during each episode of sexual intercourse.⁶ When used correctly and consistently, condoms effectively prohibit the transmission of viral pathogens, including HIV.⁷⁻¹⁰ For economically disadvantaged African-American women, numerous behavioral, sociocultural, and gender-related factors may reduce their compliance with consistent condom use and increase their risk for HIV infection. These factors include competing socioeconomic stressors and power imbalances experienced by many African-American women in heterosexual relationships.¹¹⁻¹⁴ Unfortunately, the development and implementation of culturally sensitive, gender-relevant HIV prevention programs designed to promote the adoption and maintenance of consistent condom use among African-American women lags behind prevention efforts for other risk populations.^{15,16}

The present study used a randomized, single-blind controlled design to evaluate the efficacy of a community-based HIV sexual risk-reduction intervention to enhance the adoption and maintenance of consistent condom use

among economically disadvantaged young adult African-American women.

METHODS

Participants

A total of 128 women were recruited from the Bayview-Hunter's Point community of San Francisco, Calif. The Bayview-Hunter's Point neighborhood is 84% African American. Twenty-four percent of the total households are below the poverty line, and the median family income is 34% lower than the median family income for the rest of San Francisco.¹⁷

Women were recruited over an 11-month period from February 1993 through December 1993, using street outreach and media advertisements placed throughout the community. Indigenous African-American women field recruiters, familiar with the Bayview-Hunter's Point neighborhood, approached and screened women for eligibility at the local unemployment office, the Social Security office, public laundry facilities, beauty salons, grocery stores, health clinics, and the local Aid to Families With Dependent Children (AFDC) office. Inclusion criteria consisted of being a sexually active, heterosexual African-American woman 18 through 29 years of age residing in the Bayview-Hunter's Point neighborhood. Exclusion criteria included use of crack cocaine in the previous 3 months or a history of injection drug use. After assessing a woman's willingness and eligibility for study participation, field recruiters recorded the woman's name and telephone number on a recruitment list.

Study Procedures

Recruitment lists were given to the project director, and the project director contacted each potential participant, reconfirmed her eligibility and willingness to participate in the study, and scheduled a baseline interview for the following week. Interviews were conducted at the Bayview-Hunter's Point Foundation, an African-American, community-based organization with a long history of providing social and medical services in this community. Prior to the interview, each participant completed a tracking form that included her name, address, and telephone number as well as the address and phone number of a close confidant. After being informed of the purpose of the investigation and procedures to protect confidentiality and after providing written informed consent, a trained African-American woman interviewer administered a face-to-face, 45-minute private interview. After completing the baseline interview, women were compensated \$10 for their time.

Following the baseline interview, the

project director entered each participant's name, address, telephone number, and assigned case number into a log book. The project director, using a random numbers table, generated a listing that identified the treatment assignment for each participant and entered the treatment allocation into the log book. One week prior to implementation of the treatment conditions, the project director telephoned all participants to inform them of the start date for their treatment condition. To encourage compliance, the project director also telephoned participants the day prior to implementation of their treatment condition.

Three months after the intervention, the project director contacted and scheduled all participants to return for follow-up interviews, using a modified version of the baseline interview to assess changes in consistent condom use and theoretically important constructs thought to mediate condom use. Each participant completed a follow-up interview administered by an interviewer who was blinded to the participant's treatment assignment. A reimbursement of \$20 was provided to all participants after completion of the 3-month follow-up interview. The study was approved by the Committee on Human Subjects at the Bayview-Hunter's Point Foundation and the University of California San Francisco Committee on Human Research.

Study Design

The study was a randomized, single-blind controlled trial. After completing baseline interviews, women were randomly assigned to one of three study conditions: a five-session social skills intervention condition ($n=53$), a single-session HIV education condition ($n=35$), or a delayed HIV education control condition ($n=40$).

Intervention Methods

The social skills intervention was developed by the research team in collaboration with several young adult African-American women from the Bayview-Hunter's Point community. Intervention content was both theoretically and empirically based. Social cognitive theory (SCT) and the theory of gender and power were used as theoretical models to guide the development of the social skills intervention. According to SCT, participants need the appropriate information, social skills, and norms to avoid high-risk sexual behaviors.¹⁸

While current models of behavior change have provided useful guidance for understanding HIV risk-reduction practices, these models have failed to consider a host of contextual social factors that

shape the reality of risk and potential for risk-reduction among women.^{19,20} Therefore, we also used the theory of gender and power,²⁰ a social structural theory that examines the sexual division of labor, the sexual distribution of power and authority, affective influences, and gender-specified norms about what constitutes appropriate sexual conduct within heterosexual relationships, to guide intervention development. Applying this gender-specific theory to HIV prevention takes into account how a woman's lack of power, commitment to a relationship, and role in heterosexual relationships can affect her willingness to use sexual risk-reduction strategies. Additionally, the social skills intervention was based on the results of focus groups that explored the psychosocial and cultural influences on sexual decision making among young adult African-American women.²¹

Women in the social skills intervention received five 2-hour weekly group sessions implemented by two African-American women peer health educators.

The first session emphasized gender and ethnic pride. This was accomplished by discussing the positive attributes of being an African-American woman, identifying personal African-American women role models, and engaging in values clarification exercises.

The second session emphasized HIV risk-reduction information by increasing participants' knowledge about HIV-associated risk behaviors and preventive strategies. Participants viewed and discussed an HIV educational video that encouraged women to take responsibility for sexual decision making.

The third session emphasized sexual assertiveness and communication training. Participants were first taught how to differentiate assertive, passive, and aggressive communication styles. Participants were then taught assertiveness strategies to assist them in managing risky sexual situations, such as when having sex with a noncompliant partner or when a partner has been drinking. All exercises modeled by the peer health educators were role-played by participants in several practice situations with the peer health educators providing corrective feedback.

The fourth session emphasized enhancing proper condom use skills and fostering positive norms toward consistent condom use. Condom use demonstrations with phallic replicas were modeled by peer health educators and subsequently role-played by participants. Norm-setting exercises focused on reinforcing the perception of consistent condom use as normative.

The fifth session emphasized development of cognitive coping skills, such

as sexual self-control, through cognitive rehearsal.^{22,23} During cognitive rehearsal, the peer health educators would describe a sexual scenario, often with a noncompliant sexual partner, and the women would apply the newly learned assertiveness strategies to solve the problem.

Participants in the HIV education condition received a single 2-hour HIV risk-reduction information session similar to that provided in the social skills intervention.

Participants in the delayed HIV education control condition did not receive any HIV information until they completed follow-up interviews. At that time, they received gender-based and culturally appropriate HIV education.

Monitoring the Intervention

The monitoring procedure consisted of two elements: logging the number and type of sessions participants received and obtaining anonymous participant ratings assessing the value of each social skills intervention session. Participants attended a median of four social skills intervention sessions. At the end of each session, participants completed a 10-item scale. Each scale item was rated using a 10-point Likert response format ranging from 1 (little value) to 10 (very valuable). The mean scale score was 96.0. Participant ratings did not differ significantly across the five intervention sessions.

Main Outcome Measures

Measures included in the baseline and 3-month follow-up interview were selected based on their relevance to previously identified constructs associated with the adoption and maintenance of consistent condom use, from the results of focus groups conducted among women in the target population, and from the theoretical models underlying the social skills intervention.

HIV Risk Behavior Knowledge.—A knowledge score was developed by summing correct responses to six binary response (true-false) items, with higher scores indicative of greater HIV risk-reduction knowledge. "High" and "low" HIV knowledge categories were determined based on a median split of scale scores. Internal consistency for the scale was 0.65.

Sexual Self-Control.—Sexual self-control was measured by a single item: "If a condom is not handy, I will have sex anyway." Participants disagreeing with the statement were categorized as having high sexual self-control, those agreeing were categorized as having low sexual self-control.

Sexual Assertiveness.—Sexual assertiveness was measured by a single item:

"Have you ever demanded that your regular sex partner use a condom?" Participants answering yes to the statement were categorized as having high sexual assertiveness, those answering no were categorized as having low sexual assertiveness.

Sexual Communication.—Sexual communication was measured by a single item: "Have you ever asked your regular sex partner to use a condom?" Participants answering yes to the statement were categorized as having high sexual communication, those answering no were categorized as having low sexual communication.

Partner Norms.—Partner norms were measured using the Interpersonal Impact subscale of the Condom Attitude Scale.²⁴ Each item was scored using a 4-point Likert scale ranging from strongly disagree (1) to strongly agree (4), with higher scores indicating greater impact on sex partners' adoption of safer sex norms. High and low interpersonal impact categories were determined based on a median split of scale scores. Cronbach's α for the scale was .76.

Condom Use Skills Scale.—Condom use skills were measured by an 11-item scale that assessed participants' ability to use condoms during sexual intercourse. Each item was scored using a 5-point Likert-scale, with higher scores indicative of poorer skills in using condoms. High and low condom use skills categories were determined based on a median split of scale scores. Cronbach's α for the scale was .84.

Consistent Condom Use.—Consistent condom use, the primary outcome, was defined as use of a condom during every episode of vaginal intercourse. Consistent condom use was calculated by dividing the number of occasions condoms were used during vaginal intercourse by the total number of episodes of vaginal intercourse reported in the 3-month follow-up period.

Statistical Analyses

Analyses were performed only on pre-specified hypotheses using an intention-to-treat protocol in which participants were analyzed in their original randomized conditions regardless of number of sessions attended.²⁵ Baseline differences between the three treatment conditions for continuous variables were assessed using analysis of variance (ANOVA), and differences for categorical variables were assessed using contingency tables analyses.²⁶ Intervention effects were evaluated using logistic regression models adjusting for corresponding baseline outcome variables.²⁷ Logistic regression was used because of the dichotomous nature of several outcome variables and the

markedly skewed distribution underlying scale scores. Consistent condom use was the primary outcome variable. Secondary outcome variables included HIV knowledge, sexual self-control, sexual assertiveness and communication, partner norms, and condom use skills. The primary predictor variable was treatment condition. Variables identified at baseline that approached statistical significance ($P \leq .10$) between treatment conditions and were theoretically important potential confounders were included in logistic regression models as covariates.²⁷ Model statistics computed included adjusted odds ratios (ORs) and corresponding 95% confidence intervals (CIs) to assess the significance and magnitude of the association between the treatment conditions and outcome variables.

Sample Size Determination

Sample size calculations were conducted based on our previous research with this population identifying approximately 25% of women as consistent condom users over a 3-month period. We projected an effect size for women randomized to the social skills intervention that would be meaningful in terms of reducing the risk for HIV acquisition (OR, 2.0). Setting α at .05 using a one-tail test (with power=0.80) required 46 participants in each treatment condition to detect the specified effect size.

RESULTS

A total of 128 African-American women 18 through 29 years of age (mean, 23.2 years; SD, 3.8 years) completed baseline interviews. The equivalence of sociodemographic variables (age, education, income, children, residence, and relationship length), sexual behavior in the past 3 months (frequency of vaginal intercourse, number of sex partners, and sexually transmitted disease history), alcohol use prior to sexual intercourse, and outcome variables (HIV knowledge, sexual self-control, condom use skills, communication skills, assertiveness skills, partner norms supportive of safer sex, and consistent condom use in the past 3 months) across the three treatment conditions was assessed at baseline and at follow-up. At baseline, participants in the social skills intervention condition were significantly more likely to be in a long-term relationship; 44.8 months compared with 21.4 months for the HIV education condition and 32.7 months for the delayed HIV education control condition ($F[2, 76]=2.98$; $P=.06$). Differences were also observed between treatment conditions with respect to income, with a larger proportion of the delayed HIV education control condition participants reporting incomes less than \$400 per month (82.5%) compared

Table 1.—Evaluation of Program Effects on Knowledge of the Human Immunodeficiency Virus (HIV), Coping Skills, Interpersonal Skills, Partner Norms, and Consistent Condom Use at 3-Month Follow-Up for the Social Skills Intervention Compared With the Delayed HIV Education Control Condition

Variable	Social Skills Intervention Condition		Delayed HIV Education Condition*		Adjusted Odds Ratio†	95% Confidence Interval	P
	Baseline	3-mo Follow-up	Baseline	3-mo Follow-up‡			
HIV knowledge, %							
High HIV knowledge	41.7	56.6	26.1	40.0	1.4	0.82-2.36	.22
Cognitive coping skills, %							
High sexual self-control	60.4	61.2	52.2	41.7	1.9	1.00-3.60	.05
Interpersonal skills, %							
High communication skills	80.4	89.4	86.4	65.2	4.1	1.67-10.0	.002
High assertiveness skills	56.3	61.2	39.1	37.5	1.8	1.01-3.27	.05
High condom use skills	47.9	51.2	43.5	35.0	1.3	0.63-2.51	.52
Partner norms, %							
Perceived partner norms supportive of safer sex	33.3	53.1	38.1	25.0	2.1	1.08-3.87	.03
Condom use behavior, %							
Consistent condom use	35.4	46.9	21.7	29.2	2.1	1.03-4.15	.04

*Delayed HIV education control condition is the referent for calculation of odds ratios.

†Baseline and follow-up percentages are unadjusted by covariates.

‡Adjusted by corresponding baseline variable, length of current relationship, and income level.

with participants in the social skills intervention (71.7%) and HIV education condition (60.0%) (χ^2 [df=2]=4.68; $P=.10$). At follow-up, length of relationship and income remained different across treatment conditions. Therefore, relationship length and income level were entered as covariates in logistic regression analyses.

Of the 128 participants completing baseline interviews, 100 (78.1%) completed 3-month follow-up interviews. Follow-up rates differed by treatment condition, with 48 (90.6%) of the 53 participants in the social skills intervention, 29 (82.9%) of the 35 participants in the HIV education condition, and 23 (57.5%) of the 40 participants in the delayed HIV education control condition completing 3-month follow-up interviews (χ^2 [df=2]=15.2; $P<.001$). Unavailability for follow-up (n=28) was attributable to relocation outside the Bayview-Hunter's Point community (n=23), incarceration/drug rehabilitation (n=3), and refusal to complete the follow-up interview (n=2). Additional analyses assessing attrition bias identified no differences on baseline variables across treatment conditions for participants unavailable for follow-up.

Table 1 summarizes the results of logistic regression analyses examining changes in outcome variables for the social skills intervention compared with the delayed HIV education control condition. Participants in the social skills intervention demonstrated increased consistent condom use (adjusted OR, 2.1; 95% CI, 1.03 to 4.15; $P=.04$), greater sexual self-control (adjusted OR, 1.9; 95% CI, 1.00 to 3.6; $P=.05$), greater sexual communication (adjusted OR, 4.1; 95% CI, 1.67 to 10.01; $P=.002$), greater sexual assertiveness (adjusted OR, 1.8; 95% CI, 1.01 to 3.27; $P=.05$), and increased partners' adoption of norms supporting consistent condom use (ad-

justed OR, 2.1; 95% CI, 1.08 to 3.87; $P=.03$). Dose-response effects within the social skills intervention were difficult to assess because of the high participation rate, as 80% of women completed four or more of the intervention sessions.

No statistically significant differences in outcome variables were observed between the HIV education condition relative to the delayed HIV education control condition (Table 2).

COMMENT

This study is the first randomized controlled trial of a community-based HIV sexual risk-reduction intervention for economically disadvantaged young adult African-American women. Women's self-reports indicate that significant changes were made in theoretically important areas of HIV prevention; interpersonal skills, cognitive coping skills such as sexual self-control, partner norms, and, most importantly, consistent condom use. The inference that the increase in consistent condom use is attributable to the social skills intervention is strengthened by concomitant favorable changes in theoretically important HIV preventive skills and norms.

One methodological characteristic of the present study that differentiates it from other randomized controlled behavior change interventions designed to enhance condom use is the classification of the outcome variable. Consistent condom use was selected as the primary outcome measure based on findings from prospective studies indicating that condoms, when used consistently, can provide a 70% to 100% reduction in the risk of HIV transmission.⁶ In particular, the most recent findings, from the European Study Group on Heterosexual Transmission of HIV,¹⁰ observed no seroconversions among couples who used condoms

consistently, while the seroconversion rate among inconsistent condom users was significantly higher (4.8 per 100 person-years). Moreover, predictions based on mathematical modeling suggest that, irrespective of the number of sexual partners and the prevalence of HIV among potential sex partners, consistent condom use can substantially reduce the risk of sexually transmitted HIV infection relative to no or half-time condom use.²⁴ Thus, as empirical evidence supports the clinical and public health significance of consistent condom use for preventing HIV infection, future behavior change interventions should assess consistent condom use as a primary outcome measure for evaluating program efficacy.

The effectiveness of this intervention may be attributed, in large part, to the focus on gender relations in which HIV sexual risk behaviors occur. In managing safer sex, women have to exercise influence over themselves as well as their sexual partners.¹⁸ However, few HIV prevention interventions have been based on theoretical models that address gender relations.^{16,19} The theory of gender and power, a gender-appropriate model useful for understanding relationship dynamics, provided a framework for developing and implementing the social skills intervention. In particular, the social skills intervention addressed how to successfully negotiate safer sex and foster favorable partner norms supportive of consistent condom use within the context of a heterosexual relationship where women are often in unequal positions of power relative to men.

This intervention's effectiveness may also have been the result of using African-American women peer health educators to implement the HIV social skills intervention. Peer health educators were used to implement the social skills in-

Table 2.—Evaluation of Program Effects on Knowledge of the Human Immunodeficiency Virus (HIV), Coping Skills, Interpersonal Skills, Partner Norms, and Consistent Condom Use at 3-Month Follow-up for the HIV Education Only Treatment Condition Compared With the Delayed HIV Education Control Condition

Variable	HIV Education Condition		Delayed HIV Education Condition*		Adjusted Odds Ratio†	95% Confidence Interval	P
	Baseline	3-mo Follow-up	Baseline	3-mo Follow-up‡			
HIV knowledge, %							
High HIV knowledge	48.3	48.6	26.1	40.0	0.9	0.54-1.76	.94
Cognitive coping skills, %							
High sexual self-control	55.2	48.3	52.2	41.7	0.9	0.42-1.74	.67
Interpersonal skills, %							
High communication skills	75.0	62.1	88.4	85.2	0.5	0.25-1.13	.10
High assertiveness skills	51.7	44.8	39.1	37.5	0.8	0.43-1.61	.58
High condom use skills	55.2	46.2	43.5	35.0	1.5	0.66-3.52	.28
Partner norms, %							
Perceived partner norms supportive of safer sex	39.3	48.3	38.1	25.0	1.1	0.56-2.28	.73
Condom use behavior, %							
Consistent condom use	20.7	37.9	21.7	29.2	1.1	0.55-2.40	.71

*Delayed HIV education control condition is the referent for calculation of odds ratios.

†Baseline and follow-up percentages are unadjusted by covariates.

‡Adjusted by corresponding baseline variable, length of current relationship, and income level.

tervention because they are perceived as a credible source of information, communicate in a manner that is easily understood, and serve as positive role models. Peer health educators are also more effective at facilitating the acquisition of social skills through modeling exercises that emphasized skills mastery, such as sexual communication and assertiveness, and fostering perceptions of consistent condom use as normative.

While demonstrating that young adult women can be taught skills to encourage their sex partners' consistent use of condoms and that several theoretically important mediators associated with the adoption of this HIV prevention strategy can be enhanced, no differences were observed for two other important mediators (condom use skills and HIV risk-reduction knowledge). Condom use skills may take longer for women to acquire and to feel confident in using. With respect to HIV risk-reduction knowledge, both the social skills intervention and the delayed HIV education control condition demonstrated high baseline HIV knowledge scores, suggesting that efforts to disseminate HIV information have been effective. Although differences were observed between the social skills intervention and delayed HIV education control condition, achieving statistical significance was difficult because of a ceiling effect.

A subsidiary analysis evaluating the efficacy of the HIV education condition relative to the delayed HIV education control condition identified no statistically significant differences in consistent condom use or theoretically important mediators of HIV preventive behavior. These findings corroborate previous research that suggests that providing HIV risk-reduction information, in and of itself, is not sufficient to motivate the adoption of preventive behaviors.⁴ In general, inter-

ventions that are theory driven, emphasize intrapersonal and interpersonal factors, provide skills training, and attempt to modify social norms have been more effective at promoting use of HIV prevention behaviors.²⁹⁻³¹

The present study is not without limitations. The external validity of the findings may be affected by the unavailability of participants for follow-up. However, neither participants unavailable for follow-up nor those remaining in the study cohort differed across treatment conditions on sociodemographic, psychosocial, or behavioral variables. This suggests that the study findings may be generalized to low socioeconomic, young adult African-American women residing in urban environments. However, the findings may not be applicable to African-American women with different sociodemographic or behavioral risk profiles, for example, women who are injection drug users. Evaluating this intervention with African-American women with different risk profiles may help establish its generalizability across risk groups.

One potential limitation is the lack of a placebo attention control condition. It is plausible that at least part of the observed intervention effect is attributable to the nonspecific special attention received by women assigned to the social skills intervention. Future interventions should include a placebo attention group in the study design to control for the effects of differential attention as a result of treatment assignment.

A further methodological concern is the reliability of self-reported outcome measures, particularly condom use. Since direct observation of sexual behavior is impractical, HIV prevention interventions have typically relied on participants' self-reports. Recent findings suggest that self-reported sexual behavior among African-

American women may be reliable. Young adult African-American women attending family planning clinics reported 2-month test-retest reliability for a variety of sexual behaviors, including condom use, as relatively high, ranging from 0.80 to 0.98.³² Similarly, findings from a study of predominantly African-American couples attending an inner-city sexually transmitted disease clinic indicate that women's self-reports of condom use were highly correlated with their sexual partners' reports of condom use.³³ However, as a method of validating self-reported condom use, future studies may consider monitoring biological changes that can be measured objectively, such as incident sexually transmitted diseases and pregnancy, that are specific for the occurrence of unprotected sexual intercourse.

An additional methodological concern is the limited sample size. In most randomized clinical trials of limited size there is often some imbalance, even when stratifying for primary variables. In the present study, women in the social skills intervention reported being in longer relationships and having higher income levels. Though the analyses were adjusted for these variables, it is conceivable that statistical adjustment may not adequately control for these variables. Thus, the favorable treatment effects observed could be explained by these differences. However, the longer duration of relationships for women in the social skills intervention condition may mitigate against identifying a significant intervention effect. Recent findings from the present study and other studies indicate that length of relationship is inversely related to condom use. Specifically, the longer a woman is in a relationship, the less likely her partner is to use condoms and the more difficult it is to change condom use behavior.³⁴ Differences in income level between the so-

cial skills intervention and the delayed-HIV education control group, though less pronounced, conceivably could affect differences in treatment effects. Further studies may need to enroll larger sample sizes to assure equivalence across treatment conditions.

Finally, while not specifically a methodological limitation, the length of the study follow-up period (3 months), while useful for reducing attrition and obtaining more reliable self-report information,⁴⁵ limits inferences regarding maintenance of treatment effects. Long-term follow-up is essential since newly adopted HIV preventive behaviors must be enduring if they are to be meaningful. However, the high relocation rate observed in this study poses a formidable methodological obstacle to conducting long-term follow-up assessment.⁴⁶

CONCLUSION

Human immunodeficiency sexual risk-reduction interventions have been evaluated for a variety of populations^{16,37},

however, only a few studies have focused exclusively on women.³⁸⁻⁴¹ Of the studies evaluating changes in condom use, both are clinic based.^{42,43} Clinic-based studies may have limited relevance for women not seeking clinical services.

The present study represents the first evaluation of an intervention designed to increase consistent condom use among a community-recruited sample of women. The findings suggest that a culturally appropriate, gender-tailored intervention that emphasizes social skills training and attempts to modify partner norms may be effective at enhancing consistent condom use and psychosocial mediators associated with this HIV preventive behavior.

In the absence of an effective prophylactic vaccine or cure, interventions designed to enhance the use of HIV prevention behaviors are needed to avert further escalation of new infections, particularly among African-American women at high risk for sexually acquired HIV infection. Given the epidemiological significance of consistent condom use as an

effective strategy in preventing HIV infection, relative to any use of condoms during sexual intercourse,^{42,43} interventions that emphasize and assess the adoption of consistent condom use may have a greater public health impact on reducing HIV incidence. Ultimately, however, controlling the HIV epidemic among inner-city women is dependent not only on the development and evaluation of gender-tailored prevention interventions but also on how effectively these interventions can be translated into existing community prevention activities and how rapidly they can be disseminated to high-risk urban centers.

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Maintaining Low HIV Seroprevalence in Populations of Injecting Drug Users

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Objectives.—To describe prevention activities and risk behavior in cities where human immunodeficiency virus (HIV) was introduced into the local population of injecting drug users (IDUs), but where seroprevalence has nevertheless remained low (<5%) during at least 5 years.

Design and Setting.—A literature search identified five such cities: Glasgow, Scotland; Lund, Sweden; Sydney, New South Wales, Australia; Tacoma, Wash; and Toronto, Ontario. Case histories were prepared for each city, including data on prevention activities and current levels of risk behavior among IDUs.

Participants.—Injecting drug users recruited from both drug treatment and non-treatment settings in each city.

Interventions.—A variety of HIV prevention activities for IDUs had been implemented in each of the five cities.

Results.—There were three common prevention components present in all five cities: (1) implementation of prevention activities when HIV seroprevalence was still low, (2) provision of sterile injection equipment, and (3) community outreach to IDUs. Moderate levels of risk behavior continued with one third or more of the IDUs reporting recent unsafe injections.

Conclusions.—In low-seroprevalence areas, it appears possible to severely limit transmission of HIV among populations of IDUs, despite continuing risk behavior among a substantial proportion of the population. Pending further studies, the common prevention components (beginning early, community outreach, and access to sterile injection equipment) should be implemented wherever populations of IDUs are at risk for rapid spread of HIV.

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THE INJECTION of illicit psychoactive drugs has now been reported in 118 countries throughout the world, and human immunodeficiency virus (HIV) infection among injecting drug users (IDUs) has been reported in 80 countries.^{1,2} In some areas, the spread of HIV among IDUs due to the multiperson use of drug injection equipment has occurred extremely rapidly. In New York City, for example, HIV seroprevalence among IDUs increased from less than 10% to more than 50% in 5 years³; in Edinburgh, Scotland, HIV seroprevalence among IDUs increased from 0 to more than 40% in 1 year⁴; in Bangkok, Thailand, HIV seroprevalence among IDUs increased from 2% to more than 40% in 2 years⁵; and in the Indian state of Mani-

pur, HIV seroprevalence increased from 0 to approximately 50% in 1 year.⁶ HIV has spread rapidly among populations lacking awareness of acquired immunodeficiency syndrome (AIDS) as a local threat and having mechanisms such as "shooting galleries" or "dealer's works" that provided rapid and efficient mixing among large numbers of IDUs.⁷

In sharp contrast, however, there are also areas where HIV was introduced into the local population of IDUs, but where HIV seroprevalence among IDUs has remained low and stable for extended periods. We identified such areas and characterized their HIV prevention activities to determine methods that might prevent epidemic spread of HIV among IDUs.

METHODS

This article presents case histories of cities in which HIV has been introduced into a heterosexual IDU community, but where HIV seroprevalence has remained low and stable. Operationally, we defined "introduction of HIV" into a local population as an HIV seroprevalence rate of at least 1% and "stable low seroprevalence" as a seroprevalence rate of less than 5% with no increasing trend for at least 5 years. (For cities in which seroprevalence data were collected on an annual basis, we required six data points—6 years of data—since the first data point serves as the baseline from which stability is assessed.) The 5% HIV seroprevalence level was selected because it is well below the 10% level from which rapid, epidemic-scale increases in HIV seroprevalence among IDUs have frequently been observed.⁷ Because HIV seroprevalence is often higher among IDUs not in drug abuse treatment,^{8,9} we also required seroprevalence data from at least one nontreatment sample of

Table 1.—Characteristics of the Injecting Drug User (IDU) Populations in Five Cities*

City	Estimated IDUs, No.	City Population	Drugs Injected	Type of Drug Treatment, No.
Glasgow, Scotland	8500	700 000	Buprenorphine, heroin	Methadone, 1000 Detoxification, 100 Outpatient, 2500 Residential, 30
Lund, Sweden (Skåne province)	500 city (3000 province)	90 000	Amphetamine, heroin	Methadone, 60 Detoxification, 12 Residential, 8 Outpatient, 500
Sydney, New South Wales, Australia	7800	3 100 000	Heroin, amphetamine	Methadone, 6000 Detoxification, 200 Residential, 700 Outpatient, 900
Tacoma, Wash (Pierce County)	500 city (3000 county)	177 000	Heroin, cocaine	Methadone, 240 Detoxification, 12 Outpatient, 700
Toronto, Ontario	8000	635 000	Cocaine, heroin	Methadone, 200 Detoxification, 128 Residential, 329

*Number of IDUs in community estimated by capture/recapture in Glasgow; multiple methods in Lund and Sydney, and synthetic area analysis in Tacoma. Data on "drug treatment" include treatment provided to noninjecting drug users. City population is from the most recent census data for each city.

IDUs. Indeed, lack of data from nontreatment samples was the most common reason for excluding cities that, in other respects, showed possible stable low seroprevalence.

Several methods were used to identify geographic areas with stable low seroprevalence among IDUs. We searched published literature reviews,^{1,10,11} the abstracts of the most recent international conferences on AIDS (Florence, Italy, 1991; Amsterdam, the Netherlands, 1992; Berlin, Germany, 1993; and Yokohama, Japan, 1994), and computerized bibliographical databases. We also used unpublished seroprevalence studies and personal communications with other researchers in the field. The search was initiated in 1992 and conducted through the spring of 1995.

HIV Prevalence

Five cities were located that met our operational definition for stable low HIV seroprevalence: Glasgow, Scotland; Lund, Sweden; Sydney, New South Wales, Australia; Tacoma, Wash; and Toronto, Ontario. Serial cross-sectional seroprevalence data were available from studies conducted in Glasgow,¹²⁻¹⁴ Tacoma,¹⁵ and Toronto¹⁶ and from multiple studies in Sydney.¹⁷ The minimum sample size for determining seroprevalence for a given year in these studies was 95 subjects in each of the treatment and nontreatment samples.

In Lund and the surrounding Skåne province, there has been extensive voluntary HIV counseling and testing of IDUs, with individually coded reports for all HIV seropositives.^{18,19} Each positive case is investigated to determine where the person was living when the seroconversion occurred. In Skåne, all known IDUs are tested post mortem for HIV, and there have been no cases of

deceased HIV-positive IDUs who had not been previously reported.¹²⁻¹⁸

Risk Behavior Among IDUs

In each of these cities, persons who had injected illicit drugs within the previous 2 months were recruited both from drug abuse treatment programs and from at least one nontreatment setting. In all five cities, more than 95% of the IDUs approached agreed to participate. After informed consent was obtained, similar questionnaires covering demographic characteristics, drug use, and AIDS risk behavior were administered by trained interviewers. The questionnaire from the World Health Organization's Multi-Site Study of Drug Injecting and the Risk of HIV Infection² was used in Glasgow, Toronto, and Sydney, the European Community Multi-Site Study questionnaire²⁰ was used in Lund, and a questionnaire developed for a syringe-exchange evaluation study was used in Tacoma.²¹ A question on deliberate risk reduction ("Since hearing about AIDS, have you changed your behavior in order to avoid getting AIDS?") was included in the questionnaires used in all five cities. The interview data were collected between 1990 and 1993 in the different cities. Sample sizes were 919 for Glasgow, 112 for Lund, 424 for Sydney, 874 for Tacoma, and 582 for Toronto.

HIV Prevention Activities

Local experts (including some of the coauthors of this article) completed questionnaires describing the local drug-injection situation and the local AIDS prevention activities for IDUs. All these local experts have been conducting research on HIV infection among IDUs in their communities during the last 5 or more years. The descriptions of the local IDU situations included available

data on the size of the IDU population, availability of drug abuse treatment, and informed judgments on characteristics such as the geographic concentration of the IDU population, the quality of public transportation, police tactics, and access to health care for IDUs. The description of prevention activities included when prevention activities were first initiated (early prevention was defined as beginning when HIV seroprevalence was <5%) and the extent to which ready access to sterile injection equipment, community outreach, expansion of drug abuse treatment, bleach distribution, and HIV counseling and testing were used as prevention methods.

RESULTS

IDU Population in the Five Cities

Table 1 presents descriptive information about the local IDU population and health care for IDUs in each of the five cities. In the ratings by the local experts, the IDU population was somewhat concentrated in all cities except Lund, where it was highly concentrated; public transportation was good in all cities except Tacoma, where it was poor; police did not make it difficult to carry syringes in Glasgow, Lund, or Sydney, but made it somewhat difficult to carry syringes in Tacoma and Toronto. All cities except Tacoma have universal health insurance; discrimination against IDUs in health care settings was rated as moderate in Glasgow, Lund, and Sydney and severe in Tacoma and Toronto. These descriptions are as of early 1994 and thus reflect the historical impact of some HIV prevention efforts, such as expansion of drug abuse treatment programs.

The IDU population was relatively stable over time in these five cities. There were no major changes in the size of the IDU population; in particular, there were no increases in the numbers of new injectors and no appreciable immigration of IDUs from other areas. Street prices for injectable drugs remained fairly constant, and no new types of injectable drugs were introduced in any of the cities. The demographic and social characteristics of the IDU populations in these cities also did not change appreciably during the period of stable low seroprevalence.

Introduction of HIV into the IDU Population

How HIV was first introduced into a local population of IDUs usually cannot be known with certainty, but there is some evidence as to probable means of virus entry for these five cities. In Glasgow, HIV was probably introduced by travelers to and from Edinburgh (less

Table 2.—Stable Low Human Immunodeficiency Virus (HIV) Seroprevalence Among Injecting Drug Users (IDUs) in Five Cities*

City	No. of Studies	Subjects Tested, No.	Sites	Years	Seroprevalence, %
Glasgow, Scotland	7	2300	Hospital Outreach	1986 through 1992	3, 5, 4, 1, 2, 1, 1
Lund, Sweden	Continual	>80% at least once >80% more than once	Syringe exchange Drug treatment	1986 through 1992	<2 cumulative
Sydney, New South Wales, Australia	7	2700	Drug treatment Sexually transmitted disease clinics Outreach	1984 through 1991	Among heterosexual IDUs: 4, 5, 0.5, 1, 1, 3, 2, 4
Tacoma, Wash	7	1000	Drug treatment Syringe exchange Outreach	1988 through 1993	0.4, 3, 3, 4, 3, 4, 3
Toronto, Ontario	7	1300	Drug treatment Outreach Syringe exchange	1988 through 1993	Among heterosexual IDUs: 0, 2, 3, 3, 1, 3, 2

*Number of study subjects estimated by adding subjects from individual studies, reducing by one third for possible multiple participation, and rounding to the nearest 100. Seroprevalence results presented in order of first year of data collection in different studies in each city, except that there are data from two concurrent 1992 studies in Tacoma; Toronto results are from studies conducted in 1988, 1989, 1989 through 1990, 1991 through 1992, 1991 through 1992, 1992 through 1993, and 1992 through 1993; and Sydney results are from studies conducted in 1984 through 1988, 1985 through 1989, 1985, 1986 through 1988, 1986 through 1988, 1987, 1987 through 1991, and 1989 through 1990. In Glasgow, testing from 1986 through 1989 was done on a voluntary, named basis, and thus persons suspecting they were HIV-positive may have been more likely to volunteer; Glasgow data from 1990 through 1992 were collected as part of anonymous studies and may thus be less susceptible to volunteer bias. In Lund, there have been approximately 50 cases of HIV-seropositive IDUs who have moved into the province, and there have been eight local seroconversions. In Sydney, seroprevalence was notably higher among IDUs also reporting male-with-male sex, varying from 13% to 44% across different studies (see review by Kaldor et al¹⁷). For seroprevalence estimates in this table, IDUs reporting male-with-male sex were excluded in Sydney and Toronto, but were included in the other cities.

than 80 km away), where HIV seroprevalence among IDUs has been high since the mid 1980s.⁴ In Lund, HIV was almost certainly introduced by immigration of HIV-positive IDUs from other parts of Sweden and by travelers to and from nearby Copenhagen, Denmark.¹⁸ In Sydney,^{22,23} Tacoma,¹⁶ and Toronto,²⁴ HIV probably entered through IDUs who were initially infected through male-with-male sex, since these cities have substantially higher HIV seroprevalence rates among IDUs reporting male-with-male sex than among other IDUs.

HIV Prevalence Among IDUs

Seroprevalence studies in the five cities are presented in Table 2. In the four cities where seroprevalence was studied through serial cross-sectional designs (Glasgow, Sydney, Tacoma, and Toronto), the observed rates were all within narrow ranges, with no increasing trend over time in any city. In each of these five cities there were at least two studies of HIV prevalence among IDUs not in treatment. In Lund, where HIV counseling and testing of IDUs is conducted on a continual basis, the HIV infection level has remained low and stable.

HIV Prevention Activities

There have been a variety of HIV prevention efforts in each of the five cities.^{18,25-29} Only brief comparative summaries are provided herein.

The first two common characteristics across the five cities were that prevention efforts were initiated relatively early and included large-scale provision of sterile injection equipment. In Glasgow, both a syringe exchange and a program to sell sterile needles and syringes in pharmacies to IDUs were be-

gun in 1987. In Lund, a syringe-exchange program was begun in 1986. In Sydney, the law requiring prescriptions to purchase needles and syringes was repealed, and a program of both over-the-counter sales and syringe exchanges was begun in 1987—indeed, an educational campaign to “never share needles” was launched by the wife of the Australian prime minister in 1987. In Tacoma, a syringe-exchange program was begun in 1988. In Toronto, a street outreach and bleach distribution program for IDUs was begun in 1987, and a syringe-exchange program was initiated in 1989. As indicated in Table 2, seroprevalence was less than 5% among IDUs in each of these cities when these prevention efforts were initiated.

In each of the five cities, an estimated one fifth to one third of the IDUs are regular users of the local syringe exchanges. Moreover, many of these regular participants also exchange injection equipment on behalf of others who do not formally participate in the exchanges. The exchanges in Sydney, Tacoma, and Toronto do not limit the number of needles and syringes that can be exchanged at one visit, enhancing the likelihood that IDUs coming to the exchange will also provide sterile injection equipment to others. It was not possible to estimate the percentage of IDUs who regularly obtain sterile injection equipment from pharmacies in these five cities, but in the assessment of the local experts, legal pharmacy sales are also an important source of sterile injection equipment in all the cities except Lund. (There, it is illegal for pharmacies to sell equipment for injecting illicit drugs, and IDUs would have to take a half-hour ferry ride to Copenhagen to purchase injection equipment from a pharmacy.)

The third common characteristic of the prevention programs in the five cities was that they all involved community outreach to IDUs to disseminate AIDS information and risk-reduction supplies and to build trust between health care workers and IDUs. All outreach programs also provided referrals to other services, such as drug abuse treatment and HIV counseling and testing. Several outreach programs provided some services “on-site.” In Glasgow, outreach was conducted both in association with the original pharmacy sale program and with the expansion of the syringe-exchange program, and drop-in centers were established for female prostitutes (many of whom were IDUs).^{30,31} In Lund, health care workers went into the community to recruit participants for the syringe exchange.³² In Sydney, drug users’ groups were supported with government funding to advise on AIDS prevention efforts and to operate some of the services (including syringe exchanges).²⁷ In Tacoma, the syringe-exchange program was initiated in a high-drug-use area by a former staff person of a drug abuse treatment program who had good relationships with IDUs.²⁵ In Toronto, the outreach included an ambassador component, in which active drug users were trained to serve as outreach workers to their peers.²⁹ Moreover, in each of these cities, the information imparted by community outreach workers, and the resulting climates of trust, were further disseminated throughout the oral communication networks of IDUs themselves, thus reaching persons who were not in direct contact with the outreach workers.^{25,27,31}

Large-scale expansion of drug abuse treatment to prevent HIV infection among IDUs was used only in Sydney.

Table 3.—Prevention Components and Injecting Drug User (IDU) Responses to the Acquired Immunodeficiency Syndrome in Five Cities With Stable Low Human Immunodeficiency Virus (HIV) Seroprevalence

City	Began Early	Provided Sterile Equipment	Community Outreach	Greatly Expanded Drug Treatment	Bleach Distribution	Extensive HIV Testing	Self-reported Behavior Change Among IDUs	Residual Risk Behavior
Glasgow, Scotland	X	X	X				X	X
Lund, Sweden	X	X	X			X	X	X
Sydney, New South Wales, Australia	X	X	X	X	X		X	X
Tacoma, Wash	X	X	X		X		X	X
Toronto, Ontario	X	X	X		X		X	X

Expansion of methadone maintenance treatment was begun there in 1985 (when there were only 840 persons in methadone programs in New South Wales) and increased until 5829 persons (of an estimated 8000 IDUs) were in methadone treatment in 1991. In the other four cities, there has been modest (Glasgow, Lund, and Toronto) or no (Tacoma) expansion of drug abuse treatment. The community outreach efforts did, however, lead to increased demand for drug abuse treatment among IDUs in all five cities. In several cities, the outreach programs became important sources of referral to drug abuse treatment.

Distributing bleach for disinfecting injection equipment was an HIV prevention strategy used extensively in Sydney, Tacoma, and Toronto. In Sydney and Tacoma, bleach distribution was done primarily in conjunction with syringe exchanges, while Toronto began conducting a bleach distribution outreach program before initiating its syringe-exchange program.

Extensive voluntary HIV counseling and testing as a principal method of AIDS prevention was used only in Lund. The syringe-exchange and outreach program greatly increased the numbers of IDUs who received voluntary HIV counseling and testing. All the other cities provided some HIV counseling and testing to IDUs, often through referral from the outreach efforts and as part of research studies. (In Tacoma, some coordination difficulties occurred between the syringe-exchange or outreach program vs the local counseling or testing site, so that this city probably had the least amount of voluntary HIV counseling and testing among IDUs.)

The prevention activities for IDUs in these cities received substantial coverage in the local mass media. Even though some of the prevention activities—such as syringe exchanges—were controversial, the news coverage was generally favorable.

AIDS Risk Behavior Among IDUs

A full analysis of HIV risk behavior and behavior change among IDUs in these cities is beyond the scope of this

article, but two aspects are worth mentioning. First, large majorities of IDUs in each of the cities reported deliberate risk reduction in response to concern about AIDS. Eighty-four percent of subjects in Glasgow, 82% in Lund, 84% in Sydney, 73% in Tacoma, and 87% in Toronto reported that they had "changed their behavior in order to avoid getting AIDS." Reducing sharing of injection equipment was the most commonly mentioned specific behavior change.

Second, even with the high frequency of risk reduction among IDUs in these five cities, there was still a substantial percentage who reported at least some recent HIV risk behavior. Thirty-six percent of subjects in Glasgow, 58% in Lund, 41% in Sydney, and 46% in Toronto reported that they had "injected with needles or syringes that had been used by others" in the 6 months before the interview. In Tacoma, 30% reported that they had "injected with needles or syringes that had been used by others" in the month before the interview. (The wording of this question was the same in all cities, but with a different time frame in Tacoma.) The IDUs in these cities had clearly not eliminated HIV risk behaviors.

Space limitations and differences in the questionnaires preclude a more detailed comparison herein of the residual HIV risk behavior among IDUs in these cities. It does appear, however, that most of the residual risk behavior was confined within dyads or small groups of IDUs and thus the probability that an HIV-seronegative IDU would share injection equipment with an HIV-seropositive IDU would be low.

Table 3 summarizes the prevention activities and response to concerns about AIDS among IDUs in these five cities, which occurred while the IDU populations were basically stable, ie, without any notable increases in the size of the population, in-migration from other areas, frequencies of drugs injected, or types of drugs injected.

COMMENT

No search for areas of stable low HIV seroprevalence that attempts to include

all unpublished data is likely to be comprehensive. Nevertheless, the search conducted for this study was relatively extensive and, as far as we could determine, was biased neither toward any geographic region nor toward the presence or absence of any specific type of AIDS prevention programming. The most likely source of bias is that cities conducting sufficient research to determine stable low seroprevalence by our criteria are also more likely to be sufficiently concerned about HIV infection among IDUs to have implemented at least some type of prevention program.

Stable low HIV seroprevalence in a population of IDUs neither implies an absence of new HIV infections nor guarantees against all future outbreaks of HIV transmission in these cities. There have been reports of relapses to unsafe sexual behavior among gay men in San Francisco, Calif, despite the considerable HIV prevention activities there.³⁴⁻³⁶ In at least three of these five cities (Tacoma, Toronto, and Sydney), HIV seroprevalence is substantially higher among IDUs who also engage in male-with-male sex. Relapses in reducing sexual or injection risk among IDUs who also engage in male-with-male sex could, therefore, lead to increased HIV transmission for the IDU population as a whole. If an outbreak of increased HIV transmission should occur in a low-seroprevalence area, it will be important to ensure that the public health system can react quickly enough to contain such an outbreak.

The five case histories presented herein, however, demonstrate that rapid transmission of HIV is not inevitable among IDUs. Stable low HIV seroprevalence can be maintained even with a substantial proportion of IDUs still engaging in some injection risk behavior. This finding in itself has important policy implications. It clearly contradicts the opinion expressed by some public officials that the only way to prevent HIV infection among IDUs is to stop their drug injection.³⁷

There are also data indicating low and possibly stable HIV seroprevalence among IDUs in other cities in Australia.

lia,¹⁷ the United Kingdom,^{38,39} and New Zealand.⁴⁰ Preliminary analyses of blinded seroprevalence surveys collected through the Centers for Disease Control and Prevention at drug treatment programs suggest that low seroprevalence may also exist in a number of other US cities (S. Lehman, MD, oral communication, May 31, 1994). The major limitation in identifying other cities with stable low seroprevalence was the lack of data from nontreatment samples. Nonetheless, to the best of our knowledge, at least some of the three common prevention components identified herein had been implemented in all these other cities in which stable low seroprevalence may be occurring.

While it is important to demonstrate that stable low seroprevalence is possible among populations of IDUs, it is also important to consider whether the specific AIDS prevention components identified herein were responsible for the observed stable low seroprevalence. Did the prevention activities implemented in these cities prevent epidemics of HIV infection in the local IDU populations?

With full recognition of the limits of case histories, we believe that it is possible to outline the elements of a causal analysis and note the major limitations. First, the descriptions of the IDU populations and health care for IDUs in these five cities (Table 1) did not identify any obvious reason why HIV would not have spread rapidly in these cities in the absence of the prevention activities that were implemented.

Given the existing research literature on community outreach to IDUs^{41,42} and access to sterile injection equipment,^{10,18,19,26} it is plausible that these two components could help prevent rapid transmission of HIV in a population of IDUs. Mathematical analyses of HIV transmission would also suggest that initiating behavior change and risk reduction when HIV seroprevalence is low would also be effective in limiting HIV transmission.⁴³ Thus, it is possible to "rule in" these three components as potential causes of stable low HIV seroprevalence among IDUs.⁴⁴

The prevention activities that were undertaken in some of but not all these five cities might also have contributed to reducing HIV transmission among the local populations of IDUs. The media coverage of AIDS among IDUs in these cities—often focused on the local prevention programs—might also have contributed to awareness of AIDS and behavior change.

As noted in the "Results" section, large percentages of IDUs in each of these five cities reported behavior

change in response to AIDS. Other analyses of self-reported AIDS behavior change among IDUs—with the same question used herein—have shown that self-reported behavior change is associated with avoiding HIV infection among IDUs.⁴⁵⁻⁴⁷ This finding suggests that the self-reports of behavior change are valid and that these behavior changes substantially lessen the likelihood of becoming infected with HIV.

The related research literature thus suggests that the HIV prevention activities implemented in these five cities greatly limited HIV transmission in the local IDU populations.

We see at least two major difficulties in causal analyses of HIV prevention among populations of IDUs. First, any conclusions as to whether the common prevention components identified in this article are either necessary or sufficient to prevent high rates of HIV infection in populations of IDUs would require appropriate comparison populations of IDUs in which HIV seroprevalence exceeded 5% by some substantial margin. There are, unfortunately, many areas in which HIV infection rates have reached high levels.^{7,48} To the best of our knowledge, the three common prevention components identified herein—beginning early, ready access to sterile injection equipment, and community outreach—were not all implemented in any IDU population in which widespread transmission of HIV occurred. Developing rules for selecting appropriate comparison cities with prevention failures would, however, be a difficult task.

The second major difficulty concerns the differences in types and frequencies of HIV risk behavior among IDUs. The data presented herein show that it is possible to maintain stable low HIV seroprevalence in a population of IDUs with at least occasional injection risk behavior in a substantial proportion of the population. We do not yet have a good specification of the types and frequencies of risk behaviors that lead to rapid transmission (epidemics) of HIV among populations of IDUs. Rather than "the proportion of the population with any recent risk behavior," we would suggest that variables reflecting "rapid and efficient mixing" of persons engaging in risk behaviors or "high rates of unsafe partner change"⁴³ are likely to differentiate stable low seroprevalence from rapid increases in seroprevalence.

In conclusion, the data from these five cities show (1) the existence of stable low HIV seroprevalence among some populations of IDUs; (2) that low seroprevalence can be maintained despite at least occasional risky injections among a substantial percentage of IDUs in the

population; and (3) that stable low seroprevalence was associated with a distinct pattern of AIDS prevention programming, ie, beginning prevention efforts when seroprevalence was low, good access to sterile injection equipment, and community outreach with referrals to other services and development of trust between IDUs and health care workers.

The data presented herein would appear to be the strongest evidence to date that it is possible to prevent epidemics of HIV transmission in the very high-risk group of IDUs. Whether the three common prevention components identified herein are necessary or sufficient to avert rapid transmission of HIV among IDUs in other areas remains to be determined. A conceptual explanation of stable low seroprevalence will require additional understanding of the specific risk-behavior and population-mixing patterns associated with rapid transmission of HIV among populations of IDUs.

Despite the need for additional information and better theory, the potential consequences of permitting rapid transmission of HIV among IDUs are such that responsible public health policy would seem to require, at the least, using the common prevention components wherever possible.

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This article is dedicated to the memory of Kerstin Tunving, MD, who died in 1994.

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The HIV/AIDS Pandemic -- Why Continued Funding is Needed

■ *HIV/AIDS: A Continuing Public Health Crisis*

The pandemic of HIV infection and AIDS continues to grow -- more persons in every geographic area and age group are becoming infected every day. Unlike cancer and heart disease, AIDS is an **expanding** public health threat. Since 1987, AIDS has gone from being the 15th ranked cause of death to the 8th -- it is now the leading cause of death for persons between the ages of 25 and 44. Since the disease was identified less than two decades ago, AIDS has killed over a quarter of a million Americans.

- In the United States, one person dies from AIDS every 8 minutes.
- An estimated 1 in 300 Americans are infected with HIV, the virus that causes AIDS.
- The CDC reports that in 1994 alone there were over 80,000 newly diagnosed cases of AIDS.
- One in four new HIV infections occurs among Americans under the age of 20. One in two new infections occurs among people under 25.
- The World Health Organization (WHO) estimates that by the end of the century, 30 - 40 million people will have been infected with HIV worldwide.

■ *Economic Impact of the Epidemic*

Unlike other leading causes of death, AIDS is a disease that strikes people in the prime of life -- it disproportionately kills the younger people during their most productive years.

- AIDS is now the **leading cause of death** for Americans between the ages of 25 and 44.
- Deaths due to AIDS are disproportionately disruptive to society. Persons aged 25-44 constituted 54% of the U.S. civilian labor force in 1992.
- Premature deaths due to AIDS result in the loss of many productive years of life and deprive young children of their parents. In terms of years of potential life lost (YPLL), in 1994 AIDS ranked fourth among all leading causes of death:

Cancer	1,874 YPLL (in thousands)
Unintentional Injuries	1,796
Heart Diseases	1,324
HIV/AIDS	1,056

■ ***AIDS is not just an urban problem.***

AIDS cases have been reported in all 50 states, the District of Columbia, Puerto Rico, and the American territories. The HIV/AIDS pandemic is spreading in rural areas and the south -- these are areas that to date have been less affected by the pandemic.

- In 1994, 35 percent of new AIDS cases were reported in Southern states.
- While most cases are still reported from urban areas, the rate of reported AIDS cases in non-metropolitan areas is increasing faster than urban areas.
- In six counties of North Carolina, AIDS was reported to be the leading cause of death among residents aged 20-29 years.

■ ***AIDS is spreading rapidly among women and children.***

The proportion of cases among women has increased steadily during the past decade -- and the epidemic in children is closely associated with the epidemic in women.

- In 1994 alone, over 14,000 women were diagnosed with AIDS -- that's one quarter of the AIDS cases reported among women since 1981.
- As of 1993, 21,000 women have died from AIDS.
- Women now comprise 21 % of reported HIV-infection cases.
- In 1994 alone, over 1,000 new pediatric AIDS cases were reported -- an 8 % increase from the number reported in 1993.
- An estimated 80,000 American children will have been orphaned by AIDS by the end of this decade.

■ ***Spending for AIDS and Other Public Health Threats***

AIDS is an increasing public health threat. Since its discovery in 1981, AIDS has consistently risen in the rankings as a cause of death, while cancer and heart disease rates have been comparatively stable.

- Direct lifetime medical care after diagnosis for an HIV-infected person costs more than for patients with cancer or heart disease, specifically:

\$ 61,211 for Heart Disease*
\$ 25,000 to 84,000 for Cancer**
\$119,000 for HIV/AIDS***

*for 5 years of care after initial heart attack. Source: *American Journal of Cardiology*, 1990.

**depending on stage diagnosed -- early or late. Source: Swartz & Rollins, *Business and Health*, 1985, 85, 24-6.

***Source: *Journal of the American Medical Association*, July 28, 1993.

- Spending for AIDS research is not out of balance with other diseases. Within the Public Health Service (PHS), research funding for cancer exceeded research on HIV/AIDS. In FY 1995, the PHS is slated to spend:

\$2.0 billion for cancer research,
\$1.5 billion for HIV/AIDS research,
\$805 million for heart disease research.

- Overall HHS spending for research, treatment, prevention, and income supplements is significantly greater for cancer, and heart disease than for AIDS. In FY 1995 HHS is slated to spend:

\$38.0 billion for heart disease
\$17.5 billion for cancer
\$ 6.0 billion for AIDS

■ *AIDS Research -- Collateral Benefits*

The nation's investment in HIV-related research is providing important benefits for understanding and treating other diseases. For example:

- AIDS research has accelerated study of the human immune system. This basic immunologic information is being applied to research to better understand and treat many other diseases, such as cancer and autoimmune diseases, including systemic lupus erythematosus, type I diabetes mellitus, rheumatoid arthritis, and multiple sclerosis. AIDS research also contributes to the prevention of other infectious diseases.
- HIV research involving the blood/brain barrier has led to a better understanding of the mechanisms by which infectious agents spread into the nervous system. This research has valuable implications for research on Alzheimer's disease, dementia, multiple sclerosis, neuropsychological disorders, encephalitis, and meningitis.
- Before the AIDS epidemic, little investment was made in research to treat viral diseases. Studies to develop anti-HIV therapies has led to drug development against many other disease-causing viruses.
- Research on HIV-related wasting has provided important information for research on nutritional disorders, metabolic abnormalities and gastrointestinal dysfunctions.

Ability of Primary Care Physicians to Recognize Physical Findings Associated With HIV Infection

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Objective.—To assess the ability of primary care physicians to identify physical findings associated with human immunodeficiency virus (HIV) infection.

Design.—Standardized patient examination.

Participants.—A total of 134 general internists and family practitioners were randomly selected after stratifying by year of medical school graduation, specialty, and experience caring for patients with HIV infection.

Main Outcome Measures.—Recognition of physical findings of Kaposi's sarcoma, oral hairy leukoplakia, and diffuse lymphadenopathy.

Results.—Despite being directed by presenting histories to sites of prominent physical abnormalities, only 23 (25.8%) of 89 physicians evaluating a patient with Kaposi's sarcoma and 22 (22.7%) of 97 physicians evaluating a patient with oral hairy leukoplakia detected and correctly diagnosed the abnormalities. Twenty-three (17%) of 133 physicians detected diffuse lymphadenopathy in a patient complaining of fatigue, fever, and arthralgias. Physicians with the most experience treating patients with HIV infection more frequently identified oral hairy leukoplakia, but HIV experience did not influence identification of Kaposi's sarcoma or detection of lymphadenopathy. There were no differences between general internists and family practitioners or among physicians by year of medical school graduation in identifying the three physical findings associated with HIV infection.

Conclusions.—Primary care physicians may frequently miss important physical findings related to HIV infection during patient examinations.

(JAMA. 1995;274:1380-1382)

SEVERAL physical findings are strongly associated with human immunodeficiency virus (HIV) infection. Kaposi's sarcoma (KS), a rare tumor in individuals who are not HIV infected, is the most common tumor in patients who are HIV-positive,^{1,2} and the presence of KS strongly suggests HIV infection. Oral hairy leukoplakia (OHL) is also strongly associated with HIV infection.^{4,5} In a study of 155 patients with OHL, all were found to be HIV infected or at risk for HIV disease.⁶ Diffuse lymphadenopathy, although associated with many diseases, is a common finding in HIV-positive individuals.⁷ In some patients, these or other physical findings may be the initial manifestations of HIV infection in otherwise asymptomatic individuals. However, little is known about physicians' skills at identifying

physical findings commonly associated with HIV infection.

This study used standardized patients to assess the ability of primary care physicians to identify three common physical findings associated with HIV infection: KS, OHL, and diffuse lymphadenopathy. Standardized patients are individuals trained to enact a specific case presentation and to evaluate physicians' performance.^{8,9} Use of standardized patients permits assessment of physicians' skills while controlling the patient presentation.

Methods

As part of a larger study using standardized patients,¹⁰ physicians came to a university clinic and saw as many as 16 standardized patients during 1 day of testing. Standardized patients presented a variety of symptoms and physical findings. Each standardized patient received at least 25 hours of training concerning specific medical histories to present, providing consistent responses to questions from physicians, and evaluating physicians' performance in history-taking skills, physical

examination, and counseling using objective criteria. Individuals who had prominent physical findings were selected for the patient roles, and their presenting histories were designed to direct physicians to the anatomic areas where the physical findings were located. The patient with OHL told physicians that he had a sore throat and also had noticed white spots on his tongue. On oral examination, the patient had white adherent plaques located on the lateral aspect of his tongue (Figure 1). The patient with KS had lesions on his left ear (Figure 2) and right shoulder. He gave a history of a resolving left earache and a painful right shoulder. The KS lesion on his right shoulder was 1×2 cm, purple, and had sharp margins. The patient with diffuse lymphadenopathy presented with a history of persistent fatigue, fever, and arthralgias and described joint pain in his knees, elbows, and shoulders. He had enlarged lymph nodes greater than 1 cm in diameter in the posterior cervical chains, anterior cervical chains, preauricular and postauricular areas, and axillae bilaterally. All physical findings were evaluated and their presence was agreed on by three physicians with considerable clinical experience in management of patients with HIV infection.

Two standardized patients had cardiac murmurs related to aortic insufficiency, and performance of physicians in detecting these murmurs was evaluated as a comparison with detection of HIV-related findings. The standardized patient with lymphadenopathy had a diastolic murmur related to aortic insufficiency resulting from childhood rheumatic fever. A fourth patient without HIV infection also had a diastolic murmur due to aortic insufficiency and told physician-subjects that he had a resolving upper respiratory infection and pleuritic chest pain. Both patients with diastolic murmurs also had systolic murmurs. These patients were examined by cardiologists and general internists prior to the standardized patient examination, and the underlying causes of the murmurs were confirmed by echocardiography. Both murmurs were graded as being at least III/VI.

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Figure 1.—White, adherent plaques of oral hairy leukoplakia located on the lateral aspect of the tongue.



Figure 2.—Distinct, raised reddish-purple lesion of Kaposi's sarcoma on the superior aspect of the helix.

Physical signs were verified by a clinician weekly before the standardized patient sessions to ensure that the signs were present and stable. Because of illness and absences among the standardized patients, not all participating physicians saw all standardized patients.

Primary care physicians (general internists, family practitioners, and general practitioners) from Washington, Alaska, Montana, Idaho, and Oregon identified in the *American Medical Association Directory* were recruited by mail. Recruitment methods are documented elsewhere.¹¹ The study was presented to potential subjects as a continuing medical education course in conjunction with a research project to document primary care practice patterns and clinical skills. Physicians were informed that the standardized patients would present histories and physical findings related to a broad range of diseases. Human immunodeficiency virus infection was listed among diseases that might be presented to the physicians. Physicians were not informed that one focus of the study was identification of physical signs related to HIV infection. The study design was approved by the University of Washington Human Subjects Review Committee, and physicians gave informed consent for participation.

Entry criteria for physician-subjects included spending at least 50% of professional time providing primary care, graduation from medical school in 1967 or later, and specialty in internal medicine, family practice, or general practice. Power calculations indicated that study of 120 physicians would provide sufficient power to detect differences in performance on key variables across a large number of cases; a slightly larger number was selected to compensate for possible dropouts. Among 599 interested and eligible physicians, 134 were randomly selected to participate after stratifying by prior experience with HIV-positive patients, year of medical school graduation, and specialty in either internal medicine or family medicine.

For each patient, physicians had 20 min-

utes to perform a focused history and physical examination. For these cases, physicians spent a mean of 14 minutes (median, 15 minutes) with each patient. After evaluating each patient, the physicians answered written questions concerning the history and physical examination, diagnostic work-up, differential diagnosis, and management plan. These responses provided the information that would be available in an office record, but also prompted the physicians to list any physical abnormalities that they detected.

Detection of each physical finding by a physician was determined from the written information completed by physicians concerning physical examination findings pertinent in developing a diagnosis, other physical examination abnormalities, and important negative findings. Acceptable responses included any mention of presence of lesions for the KS and OHL cases and any mention of lymphadenopathy for the patient with fatigue, fever, and arthralgias. Correct diagnoses of KS and OHL were determined by responses to a question for each case concerning the most likely diagnostic considerations.

Group comparisons were performed by the experience of the physician treating patients with HIV infection, board-certified specialty, and year of medical school graduation. An overall variable that combined the physician's training and practice experience with treating HIV-infected patients was developed from measures related to medical school experience, residency experience, and self-reported practice-based experience. Physicians were divided into those with least experience ($n=57$), moderate experience ($n=47$), and most experience ($n=30$) with treating HIV-infected patients from the three sources. By board-certified specialty, there were 66 general internists and 60 family practitioners, with eight noncertified physicians excluded from these analyses. By medical school graduation year, 30 physicians graduated between 1967 and 1974, 58 graduated between 1975 and 1981, and 46 graduated

between 1982 and 1988.

Group comparisons were performed for the percentage of physicians who correctly identified each physical sign among all physicians seeing each patient. For KS and OHL, comparisons were performed of the percentage of physicians who correctly diagnosed the lesion. For the patient with lymphadenopathy, comparisons were performed of the percentage of physicians detecting any lymphadenopathy. For patients with diastolic murmurs, comparisons were made of the percentage of physicians who described a diastolic murmur or mentioned an aortic insufficiency murmur in the differential diagnosis.

The Mantel-Haenszel test for linear association¹² (χ^2 for trend) was used to compare performance in detecting or identifying each physical sign by the experience of the physicians treating HIV-infected patients and year of medical school graduation. The χ^2 analyses were used to assess performance by board-certified specialty. For all analyses, the α level for a significant difference was set at $P<.05$.

Results

Despite being directed by the presenting history to the lesion sites and despite prominent lesions, only 42 (47.2%) of the 89 physicians who saw the patient with KS noted the presence of any abnormality, and only 54 (55.7%) of the 97 physicians who saw the patient with OHL mentioned the mouth lesion as a physical examination abnormality (Table). Among the physicians who detected an abnormality, many did not provide the correct diagnosis (19 [45%] of the 42 physicians who noted the presence of lesion in the patient with KS and 32 [59%] of the 54 physicians who noted the presence of a mouth lesion in the patient with OHL). Thus, among all physicians seeing each patient with a lesion, approximately one quarter both detected and correctly identified the lesion (Table). Among physicians who detected but did not correctly identify these two abnormalities, the most frequent diagnosis for the patient with KS was a lesion of unknown etiology ($n=11$), and the most frequent diagnosis for the patient with OHL was oral candidiasis ($n=18$). Only 23 (17.3%) of the 133 physicians performing a physical examination on the patient with prominent diffuse lymphadenopathy mentioned lymphadenopathy when asked about physical examination abnormalities.

Eleven (46%) of the physicians with the most training and practice experience in treating patients with HIV infection correctly identified OHL compared with five physicians (16.7%) with moderate experience and six physicians (14%) of physicians with the least experience ($P=.007$). There were no sig-

Identification of Physical Findings Associated With Human Immunodeficiency Virus Infection

Standardized Patient's Physical Finding	Physicians Who Saw Standardized Patient, No.	Physicians Who Detected Abnormality, No. (%) ^a	Physicians Who Correctly Diagnosed Abnormality, No. (%) [†]
Kaposi's sarcoma	89	42 (47.2)	23 (25.8)
Oral hairy leukoplakia	97	54 (55.7)	22 (22.7)
Diffuse lymphadenopathy	133	23 (17.3)	Not applicable

^aDetection of abnormalities was assessed through physicians' responses to a written questionnaire completed after seeing each standardized patient concerning pertinent physical examination findings, including abnormalities and important negatives. Accepted responses included any mention of presence of skin or mucocutaneous lesions for the dermatologic cases and any mention of lymphadenopathy for the patient with fatigue and weight loss.

[†]Correct diagnosis of Kaposi's sarcoma and oral hairy leukoplakia were determined from physicians' responses to a written questionnaire completed after seeing each standardized patient concerning the most likely diagnostic considerations for each patient.

nificant differences in identifying OHL or KS by specialty or by medical school graduation year, and there were no differences by any of the physician variables in detecting lymphadenopathy.

For the patient with arthralgias and fatigue, 75 physicians (56.4%) described a diastolic murmur or aortic insufficiency murmur. Among 58 physicians who did not correctly identify this murmur, 25 (43%) described only a systolic murmur, 11 (19%) did not mention the murmur, and 22 (38%) mentioned the presence of an undifferentiated murmur or misidentified the murmur. A total of 77 physicians (57.5%) described a diastolic or aortic insufficiency murmur in the patient with pleuritic chest pain. Among the 57 physicians who did not correctly identify this murmur 25 (44%) described a systolic murmur, 12 (21%) did not mention a murmur, and 20 (35%) mentioned the presence of an unspecified murmur. Of the 133 physicians who evaluated both patients with diastolic murmur, 51 (38%) correctly identified both murmurs, 33 (25%) did not correctly identify either murmur, and 49 (37%) identified one of the murmurs correctly.

Seventy percent of the internists identified the murmur for the patient with arthralgias and fever compared with 44% of family practitioners ($P=.004$), and 70% of internists identified the murmur for the patient with pleuritic chest pain compared with 47% of family practitioners ($P=.009$). For the patient with pleuritic chest pain, 23 (77%) of 30 physicians who graduated medical school between 1967 and 1974 correctly identified the murmur compared with 29 (50%) of the 58 physicians who graduated between 1975 and 1981, and 25 (54.3%) of 46 physicians who graduated between 1982 and 1988 ($P<.05$).

Comment

Human immunodeficiency virus infection is a disease with cardinal physical findings, and early identification of HIV infection is important for directing treatment that can reduce morbidity. Yet there is ample evidence that preventable morbidity and mortality occur in individuals

with undiagnosed HIV infection, as evidenced by low CD4 cell counts at diagnosis,¹³ presentation of *Pneumocystis carinii* pneumonia at the time of HIV diagnosis,¹⁴ and hospital admissions for preventable conditions among patients with previously undiagnosed HIV.¹⁵ Inadequate history-taking skills associated with assessment of risk for HIV infection have been documented,¹⁶⁻¹⁸ but physicians' ability to identify physical signs associated with HIV disease had not been studied.

In this study, we examined primary care physicians' ability to recognize three common findings associated with HIV infection: KS, OHL, and diffuse lymphadenopathy. The physicians frequently missed the three HIV-related physical findings and did not make the associated diagnoses.

Among physicians who performed physical examinations on the patients with KS and OHL, approximately half did not detect the lesions as physical examination abnormalities, even though they were alerted by histories to the lesion sites. Among physicians who did describe the lesions, approximately half did not correctly diagnose the lesions based on physical examination. Among all physicians seeing these two patients, approximately three fourths did not correctly detect and identify each lesion. For the patient with diffuse prominent lymphadenopathy, few physicians (17%) detected the abnormality. In comparison, more physicians detected and correctly identified prominent diastolic murmurs. However, 40% or more of physicians either did not detect each murmur or incorrectly identified the type of murmur. These data indicate deficiencies in HIV-related physical diagnosis skills among primary care physicians and also suggest more general deficiencies at physical diagnosis.

Experience with HIV-infected patients appeared to influence the ability to recognize OHL, but not KS or lymphadenopathy. Given the small number of cases studied, however, the power to detect differences in performance based on training experience and other variables is low. Prior experience with HIV infection and other variables may have a greater im-

pact on performance than suggested by the limited number of cases in our study. This study is also limited by the voluntary nature of physician participation. Physicians who volunteer to participate in a study related to clinical skills may be more confident in their skills and perform better than physicians who do not volunteer. Therefore, the findings reported here may overestimate performance among practicing primary care physicians.

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The authors are grateful to David Spaich, MD, for his comments on the manuscript.

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ECONOMICS of the PUBLIC SECTOR

Second Edition

JOSEPH E. STIGLITZ

Princeton University



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AIDS AND GOVERNMENTAL LIABILITY

State and
Local Government
Guide to Legislation,
Legal Issues, and
Liability

Brenda T. Strama, Editor

Section of Urban, State and

Local Government Law

American Bar Association

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FACSIMILE TRANSMISSION

DATE: 6/2/95

FAX TO: Richard Sorien**ADDRESS:** White House Office of the National AIDS Policy
Coordinator**PHONE:****FAX:** 632-1096

FROM: Mitchell Goldstein
Office of Budget, ASMB,
Department of Health and Human Services**ADDRESS:** Room 503-H
Hubert H. Humphrey Building
200 Independence Avenue, S.W.
Washington, DC 20201**PHONE:** (202) 690-7846**FAX:** (202) 690-6896

PAGES FOLLOWING COVER PAGE: 40**SUBJECT:** HHS Briefing Materials on HIV/AIDS

MESSAGE:

Per your request to Don Poppke.

HIV/AIDS

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HIV/AIDS - PHS**Budget Summary**

- ▶ 1996 AIDS spending for HHS totals nearly \$7 B, an increase of \$645 M (+11%) over 1995.
 - ▶ \$2.9 B in PHS, an increase of \$200 M (+7%)
 - ▶ \$3.7 B in Entitlement programs (Medicaid, Medicare, OASDI, SSI), an estimated increase of \$445 M (+14%).
- ▶ PHS: +\$200 M increase over 1995 level includes:
 - ▶ +\$91 M (+14%) for Ryan White Services.
 - ▶ +\$35 M (+6%) for CDC HIV/AIDS Prevention.
 - ▶ +\$73 M (+5%) for NIH Research on AIDS basic research and vaccine and therapeutic development.
 - ▶ +\$1 M (+1%) for FDA vaccine research.
- ▶ As the epidemic expands, we are seeing dramatic increases in entitlement spending. This may now be the best case for our investment in research and prevention.
 - ▶ From 1988 to 1996, discretionary spending rose from \$962 M to \$2.9 B (+198%). At the same time, entitlement spending increased from \$503 M to \$3.7 B (+640%).
 - ▶ In 1996 alone, we expect entitlement spending to grow by 14%, including a 23% increase in Social Security Disability payments alone.

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KEY INFORMATION:**HHS/HIV/AIDS Spending - by Agency**
(Dollars in Millions)

	1994	1995	1996	
			P.B.	+/- 95
PHS:				
FDA.....	\$72	\$73	\$74	+\$1
HRSA.....	608	661	752	+91
IHS.....	4	4	4	-
CDC.....	543	590	625	+35
NIH.....	1,297	1,335	1,408	+73
SAMHSA.....	28	25	25	--
AHCPR.....	11	11	11	--
OASH.....	5	4	4	--
Sub, PHS.....	\$2,568	\$2,703	\$2,903	+\$200
Entitlements:				
M'care/M'caid.....	1,990	2,240	2,490	+250
OASDI/SSI.....	840	1,005	1,200	+195
Sub, Entitlement	\$2,830	\$3,245	\$3,690	+445
Civil Rights.....	2	2	2	--
Total, HHS.....	\$5,400	\$5,950	\$6,595	+\$645

OTHER KEY INFORMATION:

► As of December 1993:

AIDS:

Cumulative Number of Cases	361,164
Adults/Adolescents	355,936
Children < 13 years old	5,228

Cases in 1993.....	106,949
Cases in 1992.....	47,572

Increase over 1992.....	+59,377
Percent Increase over 1992	+125%

HIV (Not AIDS):

Cumulative Number of Cases	55,649
Adults/Adolescents	54,854
Children < 13 years old	795

Cases in 1993.....	15,313
--------------------	--------

- Approximately 75% of all AIDS cases reported are for persons between 25 and 44 years of age. It is now the leading cause of death for all Americans, ages 25-44 years old (1993 data).

-- The Washington Post (2/3/95) reported that the spread of HIV is leveling off, HOWEVER, THE RATE IS STILL UNACCEPTABLY HIGH--40% OF ALL 441,528 AIDS CASES REPORTED SINCE 1981 WERE REPORTED IN 1993 AND 1994.

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- AIDS cases and annual rates per 100,000 population, by race/ethnicity/sex:

	Males		Females	
	Number	Rate	Number	Rate
White, not Hispanic.	43,987	57.3	4,103	5.0
Black, not Hispanic.	28,792	266.2	9,220	73.1
Hispanic.....	15,301	145.9	3,324	32.2
Asian/Pacific Islander	665	21.2	97	2.9
American Indian/ Alaska Native.....	281	41.3	55	7.7
TOTAL.....	89,165	87.5	16,824	15.4

Note: Figures are taken directly from the HIV/AIDS Surveillance Report--U.S. HIV and AIDS cases reported through December 1993, Year-end Edition, Vol. 5, No. 4.

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HIV As a Leading Cause of Death Projected to the Year 2000

	1992 Number	1992 Ranking	Projected		
			2000 Number	2000 Ranking	Percent Change
All Causes	2,175,613		2,339,166		
Heart Diseases	717,706	1	676,343	1	-6%
Cancer	520,578	2	594,006	2	14%
Stroke	143,769	3	141,051	3	-2%
COPD*	91,938	4	121,064	4	32%
Accidents	86,777	5	75,735	6	-13%
Pneumonia/Influenza	75,719	6	89,372	5	18%
Diabetes Mellitus	50,067	7	72,236	7	44%
HIV Infection	33,566	8	67,172	8	100%
Suicide	30,484	9	31,421	10	3%
Homicide	25,488	10	32,499	9	28%
Liver Disease/Cirrhosis	25,263	11	22,945	11	-9%

* Chronic Obstructive Pulmonary Diseases

- 1/ Year 2000 figures are projected by linear regression and do not take into account other factors—such as aging of the population and medical advances—which may raise rates for some causes of death and lower rates for others.
- 2/ Infant deaths are included in cause specific calculations.

Source: National Center for Health Statistics

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History of HIV Infection As a Leading Cause of Death

YEAR	Ranking as Cause of Death	Rate per 100,000 Population	Percentage of Total Deaths	Percent Change From Previous Year
1987	15	5.5	0.6	—
1988	15	6.8	0.8	20.0
1989	11	8.9	1.0	31.8
1990	10	10.1	1.2	12.6
1991	9	11.7	1.4	15.3
1992	8	13.2	1.5	11.5

The first year in which HIV infections appeared as a leading cause of death was 1987.

Data from the National Center for Health Statistics.

Monthly Vital Statistics Report Vol. 38, No. 5, Supplement, September 26, 1989.

Monthly Vital Statistics Report Vol. 39 No. 7, Supplement, November 28, 1990.

Monthly Vital Statistics Report Vol. 40, No. 8, Supplement, January 7, 1992.

Monthly Vital Statistics Report Vol. 41, No. 7, Supplement, January 7, 1993.

Monthly Vital Statistics Report Vol. 42, No. 2, Supplement, August 31, 1993.

Monthly Vital Statistics Report Vol. 43, No. 6, Supplement, December 8, 1994.

The population base for computing death rates changed from 1989 to 1990.

Death rates for 1987, 1988, and 1989 are based on population estimates based on the 1980 census counts. Death rates for 1990, 1991, and 1992 are based on population estimates based on the 1990 census counts.

Comparative Costs for Direct Medical Care

Cancer: \$25,000 - \$84,000 depending on stage diagnosed--
early vs. late.

Source: Swartz, R.M., and Rollins, P.M., Business and Health,
1985, 85, 24-26. Medstat, Ann Arbor, Michigan.

HIV/AIDS: \$119,000 Lifetime medical cost after diagnosis.

Source: Journal of the American Medical Association, July 28, 1993

Heart Disease: \$51,211 for 5 Years of Care after initial
heart attack (or death, whichever comes first).

Source: American Journal of Cardiology, 1990

Diabetes: \$11,157 annual per capita cost in 1992 dollars.

Source: Journal of Clinical Endocrinology and Metabolism, 1994
"Health Care Expenditures for Diabetes Mellitus", 1992
Rubin, Robert

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What Medical Procedures Cost

Problem	Cases	Yearly Deaths	Treatment	Per Patient
Heart Disease	7 million	500,000	284,000 Coronary Bypass Surgeries	\$30,000
Cancer	1 million	510,000	Lung Cancer, Cervical Cancer	\$29,000 \$28,000
Stroke	600,000	150,000	Hemiplegia, Rehabilitation	\$22,000
Injuries	2.3 million Hospitalizations	142,000	Quadriplegia, Hip Fracture, Severe Head Injury	\$570,000 \$40,000 \$310,000
AIDS	1-1.5 million HIV Infected	31,700	AIDS Treatment	\$75,000
Alcoholism	18.5 million	105,000	Liver Transplant	\$250,000
Drug Addiction	1-3 million (cocaine) 900,000 (IV drugs) 500,000 (heroin) 375,000 (drug-exposed infants)	NA	Care for Drug- Affected baby (5 years)	\$63,000

Source: American Family Physician, Dec. 1992

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HIV/AIDS

Total Federal Government Spending (by Agency)

(Dollars in millions)

HIV/AIDS	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996
HHS:											
Public Health Service.....	\$234	\$502	\$962	\$1,301	\$1,590	\$1,888	\$1,960	\$2,078	\$2,567	\$2,702	\$2,901
Medicaid (Federal Share).....	130	200	330	490	670	870	1,080	1,290	1,490	1,640	1,800
Medicare.....	5	15	30	55	110	180	280	385	500	600	690
Soc Security - DI.....	25	45	95	145	210	295	390	505	600	705	830
Soc Security - SSI.....	8	15	18	25	39	65	111	165	240	300	370
Office for Civil Rights.....	--	--	--	3	3	3	3	3	2	2	2
Subtotal, HHS.....	\$402	\$777	\$1,435	\$2,019	\$2,622	\$3,301	\$3,824	\$4,426	\$5,399	\$5,949	\$6,583
(Non-PHS: non-add).....	168	275	473	718	1,032	1,413	1,864	2,348	2,832	3,247	3,692
OTHER:											
Veterans Affairs Department.....	\$20	\$51	\$78	\$136	\$220	\$258	\$279	\$325	\$312	\$329	345
Defense Department.....	79	74	53	86	125	127	129	159	129	127	98
Agency for Internatl Development..	2	17	30	40	71	78	94	117	115	121	121
Justice/Bureau of Prisons.....	1	1	1	2	5	5	5	5	6	7	8
State Department.....	--	1	1	1	1	1	1	1	1	1	1
Labor Department.....	--	1	1	1	1	1	1	1	1	1	1
Education Department.....	--	--	1	--	--	--	--	--	--	--	--
Housing and Urban Development..	--	--	--	--	--	--	48	100	156	289	186
Ofc. Personnel Mgmt. - FEHB.....	3	4	7	12	21	34	58	98	108	119	132
Subtotal, Other.....	\$105	\$149	\$172	\$278	\$444	\$504	\$615	\$806	\$828	\$994	\$892
Total.....	\$507	\$926	\$1,607	\$2,297	\$3,066	\$3,805	\$4,439	\$5,232	\$6,227	\$6,943	\$7,485

AIDS/HIV

Total Federal Government Spending (by Function)

(Dollars in millions)

	1994					1995					1996				
	Research	Prevent.	Treatmt.	Income Support	Total	Research	Prevent.	Treatmt.	Income Support	Total	Research	Prevent.	Treatmt.	Income Support	Total
HHS:															
Public Health Service.....	\$1,508	\$445	\$613	—	\$2,567	\$1,548	\$481	\$664	—	\$2,702	\$1,621	\$528	\$754	—	\$2,901
Medicaid (Federal Share).....	—	—	1,480	—	1,480	—	—	1,840	—	1,840	—	—	1,800	—	1,800
Medicare.....	—	—	500	—	500	—	—	600	—	600	—	—	680	—	680
Soc Security - DI.....	—	—	—	600	600	—	—	—	705	705	—	—	—	830	830
Soc Security - SSI.....	—	—	—	240	240	—	—	—	300	300	—	—	—	370	370
Office for Civil Rights.....	—	2	—	—	2	—	2	—	—	2	—	2	—	—	2
Subtotal, HHS.....	\$1,508	\$447	\$2,603	\$840	\$5,389	\$1,548	\$493	\$2,904	\$1,005	\$5,949	\$1,621	\$528	\$3,244	\$1,200	\$6,593
(Non-PHS: non-add).....	0	2	1,000	840	2,832	0	2	2,240	1,005	3,247	0	2	2,490	1,200	3,692
OTHER:															
Veterans Affairs Department.....	\$6	\$31	\$275	—	\$312	\$6	\$31	\$292	—	\$329	\$7	\$31	\$307	—	\$345
Defense Department.....	47	22	60	—	129	41	13	73	—	127	10	14	74	—	98
Agency for Internatl Development.....	—	115	—	—	115	—	121	—	—	121	—	121	—	—	121
Justice/Bureau of Prisons.....	—	1	5	—	6	—	1	6	—	7	—	1	7	—	8
State Department.....	—	1	—	—	1	—	1	—	—	1	—	1	—	—	1
Labor Department.....	—	1	—	—	1	—	1	—	—	1	—	1	—	—	1
Education Department.....	—	—	—	—	0	—	—	—	—	0	—	—	—	—	0
Housing and Urban Development.....	—	—	—	156	156	—	—	—	289	289	—	—	—	186	186
Ofc. Personnel Mgmt. - FEHB.....	—	—	108	—	108	—	—	119	—	119	—	—	132	—	132
Subtotal, Other.....	\$53	\$171	\$448	\$156	\$828	\$47	\$168	\$490	\$289	\$994	\$17	\$169	\$520	\$186	\$892
TOTAL.....	\$1,561	\$618	\$3,051	\$996	\$6,227	\$1,595	\$661	\$3,394	\$1,294	\$6,943	\$1,638	\$697	\$3,765	\$1,386	\$7,485
Change from Previous Year.....	\$199	\$42	\$524	\$226	\$992	\$33	\$43	\$343	\$298	\$717	\$43	\$36	\$371	\$92	\$542
% Chg from Previous Year.....	15%	7%	21%	26%	19%	2%	7%	11%	30%	12%	3%	5%	11%	7%	8%

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**PUBLIC HEALTH SERVICE
HIV/AIDS FUNDING (by function)
(Dollars in thousands)**

3/1/95 17:09

	FY 1996				
	FY 1994	FY 1995	Pres. Budget		
			Pres. Bud.	+/- FY 95	% Chg.
I. Basic Science Research:					
A. Biomedical Research.....	\$297,738	\$322,016	\$343,889	\$21,873	7%
B. Neuroscience/Neuropsychic Research.....	48,440	50,482	52,734	2,252	4%
C. Behavioral Research.....	157,416	162,266	168,091	3,825	2%
D. Therapeutic Agents.....	464,575	479,608	496,289	16,681	3%
E. Vaccines.....	119,543	121,720	132,146	10,426	9%
F. Research Enhancement.....	<u>23,608</u>	<u>24,903</u>	<u>25,885</u>	<u>982</u>	<u>4%</u>
Subtotal, Basic Science Research.....	\$1,111,320	\$1,160,995	\$1,217,034	\$56,039	5%
II. Risk Assessment and Prevention:					
A. Surveillance.....	\$94,971	\$96,648	\$96,794	\$146	0%
B. Population-based Research— Natural History, Transmission, Risk Factors.....	214,698	202,635	218,462	15,827	8%
C. Info. & Education/Preventive Services:					
1. High Risk or Infected Persons.....	255,910	296,063	328,501	32,438	11%
2. Special Minority Initiatives.....	57,715	61,933	63,423	1,490	2%
3. School and College-aged Youth.....	48,477	48,433	48,453	20	0%
4. General Public and Special Programs.....	47,395	50,228	51,547	1,319	3%
5. Health Care Workers & Providers.....	21,188	20,690	20,583	-107	-1%
6. Prevention Capacity Enhancement.....	<u>11,752</u>	<u>11,740</u>	<u>11,740</u>	<u>0</u>	<u>0%</u>
Sub. Info. & Educ./Prev. Services.....	<u>442,437</u>	<u>489,087</u>	<u>524,247</u>	<u>35,160</u>	<u>7%</u>
Subtotal, Risk Assessment & Prevention.....	\$752,106	\$788,370	\$839,503	\$51,133	6%
III. Product Evaluation, Research, & Monitoring:					
A. Therapeutic Agents.....	\$25,115	\$25,235	\$25,536	\$301	1%
B. Vaccines.....	11,807	11,863	12,005	142	1%
C. Diagnostic Reagents & Test Kits.....	8,690	8,732	8,836	104	1%
D. Blood & Blood Products.....	17,375	17,458	17,667	209	1%
E. Medical Devices.....	<u>9,412</u>	<u>9,457</u>	<u>9,570</u>	<u>113</u>	<u>1%</u>
Subtotal, Product Eval., Res., & Monitoring.....	\$72,399	\$72,745	\$73,614	\$869	1%
IV. Clinical Health Services, Research & Delivery:					
A. Services:					
1. Drug Subsidy Programs.....	\$0	\$0	\$0	\$0	—
2. Other Services.....	<u>613,238</u>	<u>663,645</u>	<u>754,406</u>	<u>90,761</u>	<u>14%</u>
Subtotal, Services.....	\$613,238	\$663,645	\$754,406	\$90,761	14%
B. Pediatric Demonstrations.....	0	0	0	0	—
C. Construction (Extramural).....	0	0	0	0	—
D. Research.....	<u>14,750</u>	<u>14,603</u>	<u>14,865</u>	<u>262</u>	<u>2%</u>
Subtotal, Clin. Hlth Services, Res., Delivery.....	\$627,988	\$678,248	\$769,271	\$91,023	13%
V. PHS-Wide Activities:					
A. OASH/Natl AIDS Prog. Office.....	\$2,869	\$1,742	\$1,739	-\$3	0%
B. Contingency Fund.....	0	0	0	0	—
C. Construction (Intramural).....	0	0	0	0	—
Subtotal, PHS-Wide Activities.....	\$2,869	\$1,742	\$1,739	-\$3	0%
TOTAL, PHS HIV/AIDS.....	\$2,666,682	\$2,702,100	\$2,901,161	\$199,061	7%

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HIV/AIDS - PHS**Ryan White Reauthorization****QUESTION:**

The Ryan White Care Act expires at the end of FY 1995. What do you envision the reauthorization looking like?

ANSWER:

- ▶ We believe that the Ryan White CARE Act is a crucial element in fighting HIV/AIDS and have proposed to reauthorize this program.
 - The Ryan White program saves money. Community-based systems of care are cost effective. These systems reduce unnecessary emergency room use, delay or prevent the onset of opportunistic infections, and reduce hospital inpatient length of stay.
 - For example, the Ryan White legislation helps 42 communities which have been hardest hit by the epidemic develop and implement cost effective strategies for providing AIDS patients with care. Approximately 70 percent of all AIDS cases are in the Title I cities.
- ▶ Four principles govern our Ryan White reauthorization proposal:
 - Need to streamline wherever possible;
 - Need to increase accountability for service delivery and quality of care;
 - Need to increase diverse community representation in planning and priority setting; and,
 - Need to increase focus on planning, coordination, and technical assistance.
- ▶ Considerable discussion has occurred on whether the funding formulas for Titles I and II should be changed to achieve a more "equitable distribution." We support any revisions that meet the following criteria:
 - Retain the current Title structure;
 - Move towards a funding formula for Title I based on people living with AIDS rather than cumulative cases;
 - Use data that are current, uniform, valid, and publicly available nationwide; and,
 - Contain a transition clause from current formulas to help prevent rapid and potentially catastrophic disruptions in current service levels in areas.

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KEY INFORMATION:

- On February 22, Dr. Lee testified before the Senate Labor Committee outlining the Department's position on reauthorization of Ryan White.

Ryan White Budget Authority

(in millions)

	<u>FY 1993</u>	<u>FY 1994</u>	<u>FY 1995</u>	<u>FY 1996</u>	<u>+/-</u>
Title I (Cities)	\$184.8	\$325.5	356.5	\$407.0	+\$50.5
Title II (States)	115.3	183.9	198.1	221.9	+23.8
Title III (CHCs)	48.0	48.0	52.3	62.6	+10.3
Title IV					
(Pediatric)	--	22.0	26.0	32.0	+6.0
Total	\$348.1	\$579.4	\$633.0	\$723.5	+\$90.5

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HIV/AIDS - PHS

Ryan White Funding

QUESTION:

How much have you requested for Ryan White in FY 1996?

ANSWER:

- ▶ Since the Clinton Administration came to office in 1993, funding for Ryan White has more than doubled -- from \$348 million to \$723 million.
- ▶ We are seeking a total of \$723.5 million for Ryan White activities, an increase of \$90.5 million, or 14 percent, over the FY 1995 level. This level provides:
 - Emergency Relief for Cities (Title I): A total of \$407 million (+\$50.5 M, +14%) for cities with a high incidence of HIV infection (more than 2,000 cases).
 - The request will maintain the formula grant for the 42 cities receiving funding in FY 1995 at their current funding level, while funding any additional cities * (10 to 14 additional cities are expected to qualify).
 - State Comprehensive Care Delivery (Title II): A total of \$221.9 million (+\$23.8 M, +12%) for formula-based State grants States to assist in providing systems for home- and community-based services for HIV-infected patients.
 - More than 260 consortia are planning and delivering HIV/related outpatient services.
 - Early Intervention Services (CHCs) (Title IIIb): A total of \$62.6 million (+\$10.3 M, +20%) for the primary care of populations at risk of HIV/AIDS, principally delivered through community and migrant health centers.
 - Services will be provided to 125,200 individuals (+20,500) who are infected with HIV or are at-risk for HIV infection through 150 primary care grantees (+10).
 - Demonstration Grants for Research and Services for Pediatric Patients (Title IV): A total of \$32 million (+\$6 M, +23%) to develop models of comprehensive systems of care, linked to research, for children, adolescents, women, and families.
 - Title IV projects have developed comprehensive care systems in more than 80 communities.

* Requires legislative change. See "Ryan White - Title I Funding."

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KEY INFORMATION:

Ryan White Budget Authority

(in millions)

	<u>FY 1993</u>	<u>FY 1994</u>	<u>FY 1995</u>	<u>FY 1996</u>	<u>+/-</u>
Title I (Cities)	\$184.8	\$325.5	356.5	\$407.0	+\$50.5
Title II (States)	115.3	183.9	198.1	221.9	+23.8
Title III (CHCs)	48.0	48.0	52.3	62.6	+10.3
Title IV (Pediatric)	--	22.0	26.0	32.0	+6.0
Total	\$348.1	\$579.4	\$633.0	\$723.5	+\$90.5

ADDITIONAL BACKGROUND:

- Title I: Formula Grants to Cities - Supports "emergency relief" for cities with high HIV infection incidence (> 2,000 AIDS cases).

- Funds can be used to pay for outpatient and ambulatory care and support services, and inpatient case management services designed to prevent unnecessary hospitalizations.

- 8 additional cities qualified for funds in 1995:

-- Austin, TX	-- Portland, OR
-- Caguas, PR	-- San Antonio, TX
-- Dutchess County, NY	-- Santa Rosa-Petaluma, CA
-- Jacksonville, FL	-- Vineland-Millville, NJ

- An additional 10 to 14 cities are anticipated to qualify for funds in 1996. The following 14 cities may qualify:

-- Aquadilla, PR	-- Middlesex, NJ
-- Atlantic City, NJ	-- Minneapolis, MN
-- Cleveland, OH	-- Naples, FL
-- Fort Pierce, FL	-- Sacramento, CA
-- Fort Worth, TX	-- San Jose, CA
-- Hartford, CT	-- Savannah, GA
-- Mayaguez, PR	-- Trenton, NJ

- Title II: Formula Grants to All States - Supports HIV "comprehensive care" to help operate HIV service delivery consortia; provide home- and community-based care; continue life-insurance coverage for infected persons; and provide for life-sustaining HIV/AIDS treatments.

- Funds from this formula grant are distributed to all States, proportional to their number of AIDS cases, population, and per capita income.

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- ▶ Title III (Part II): Discretionary Grants - Supports "early intervention services" to deliver primary care services to populations at risk of HIV/AIDS, principally through community and migrant health centers.
- ▶ Title IV: Discretionary Grants: Develops models of comprehensive systems of care, linked to research, for children, adolescents, women, and families. This Title also authorizes expenditure for certain activities related to blood banks and emergency response employees.
- Title IV was first funded in FY 1994. The level appropriated, \$22 million, included \$21 million previously available for the Pediatric AIDS Health Care Demonstration Grant program.

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HIV/AIDS - PHS**Ryan White Title I Funding****QUESTION:**

How many additional Title I cities do you anticipate in FY 1996, and does your request ensure that no city currently receiving funding would receive a decrease between FY 1994 and FY 1996?

ANSWER:

- ▶ We are seeking a total of \$407 million for Ryan White Title I--Emergency Relief for Cities, an increase of \$50.5 million (+14%) over the FY 1995 level.
 - This level is more than double the funding available for Title I when President Clinton came into office in FY 1993.
- ▶ In order to maintain the 42 cities receiving funding in FY 1995 at their current funding level for the formula portion of Title I and fund the additional cities (10-14 cities) expected to qualify for funding in FY 1996, a change in the way funds are distributed is required!
 - The President's budget contains appropriations language allowing funds available under the discretionary portion of Title I to be used to ensure that no FY 1995 grantee receives less in its formula grant in FY 1996 than it did in FY 1995.

KEY INFORMATION:

Ryan White Budget Authority
(in millions)

	<u>FY 1993</u>	<u>FY 1994</u>	<u>FY 1995</u>	<u>FY 1996</u>	<u>+/-</u>
Title I (Cities)	\$184.8	\$325.5	\$356.5	\$407.0	+\$50.5
Title II (States)	115.3	183.9	198.1	221.9	+23.8
Title III (CHCs)	48.0	48.0	52.3	62.6	+10.3
Title IV					
(Pediatric)	--	22.0	26.0	32.0	+6.0
Total	\$348.1	\$579.4	\$633.0	\$723.5	+\$90.5

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ADDITIONAL BACKGROUND:

- ▶ Under current law, Title I funds are allocated 50 percent to formula grants and 50 percent through discretionary grants to the cities. The proposed appropriations language would require, in cases where a specific city would receive less in its formula grant in FY 1996 than in FY 1995, funds to be taken from the discretionary 50 percent to increase the FY 1996 formula grant to the FY 1995 level.
 - ▶ During the FY 1995 budget process, the Senate raised concerns on how Title I eligibility is determined. The Senate was concerned with the proliferation of small cities (populations less than 500,000) that qualified under the per capita incidence rate of not less than 0.0025. Cities with populations under 500,000 are not identified by name in CDC's HIV/AIDS Surveillance Report.
 - The final outcome was all 4 cities that met the incidence rate, even those with populations under 500,000, were funded in FY 1995.
 - ▶ Title I: Formula Grants to Cities - Supports "emergency relief" for cities with high HIV infection incidence (> 2,000 AIDS cases or per capita incidence is not less than 0.0025).
 - Funds can be used to pay for outpatient and ambulatory care and support services, and inpatient case management services designed to prevent unnecessary hospitalizations.
 - 25 cities qualified for funds in 1993:

-- Anaheim	-- Jersey City	-- Philadelphia
-- Atlanta	-- Los Angeles	-- Ponce, PR
-- Baltimore	-- Miami	-- San Diego
-- Boston	-- Nassau/Suffolk, NY	-- San Francisco
-- Chicago	-- New Orleans	-- San Juan
-- Dallas	-- Newark	-- Seattle
-- Detroit	-- New York	-- Tampa
-- Ft. Lauderdale	-- Oakland	-- Washington
-- Houston		
-
- An additional 9 cities qualified for funds in 1994:

-- West Palm Beach, FL	-- Kansas City, MO/KS
-- Denver	-- New Haven/Bridgeport, CT
-- Orlando	-- Phoenix, AZ
-- Riverside/San Bernadino, CA	-- St. Louis, MO/IL
-- Bergen/Passaic, NJ	
-

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- An additional 8 cities qualified for funds in 1995:

-- Austin, TX	-- Portland, OR
-- Caguas, PR	-- San Antonio, TX
-- Dutchess County, NY	-- Santa Rosa-Petaluma, CA
-- Jacksonville, FL	-- Vineland-Millville, NJ

- An additional 10 to 14 cities are anticipated to qualify for funds in 1996. The following 14 cities may qualify:

-- Aquadilla, PR	-- Middlesex, NJ
-- Atlantic City, NJ	-- Minneapolis, MN
-- Cleveland, OH	-- Naples, FL
-- Fort Pierce, FL	-- Sacramento, CA
-- Fort Worth, TX	-- San Jose, CA
-- Hartford, CT	-- Savannah, GA
-- Mayaguez, PR	-- Trenton, NJ

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HIV/AIDS - PHS

Needle Exchange

QUESTION:

Despite the suggestions of some of your own AIDS experts, why are you continuing to support the prohibition on needle exchange that exists in the General Provisions of your Appropriations Act? What is the Department's policy toward needle exchange programs?

ANSWER:

- ▶ Currently, the 1996 budget reflects no change in the previous policy -- that is, we are still not ready at this time to drop the prohibition on directly supporting needle exchange programs with Federal funds. I do not envision a change to this policy in the near future.
- Section 506 of the General Provisions of the 1995 Labor-HHS Appropriations Act prohibits us from using Federal funds to support programs that distribute sterile needles for injecting any illegal drug, unless the Surgeon General determines that such programs are both a) effective in preventing the spread of HIV and b) do not encourage illegal drug use.
- ▶ The PHS has indicated that they are not aware of any conclusive evidence or study that has proven needle exchange programs to be both effective at preventing the spread of AIDS and discouraging illegal drug use.
- Such evidence is necessary to meet the criteria required by the statutory prohibition before we could consider recommending a change in the current policy.
- A recently reported review by CDC of a needle exchange program in San Francisco found its effectiveness to be "inconclusive."
- ▶ We encourage further evaluations of State- or locally-financed programs to help us find a conclusive answer to this very difficult issue that has strong advocates for both sides.

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ADDITIONAL INFORMATION:

- ▶ While we are not funding any direct needle exchange programs, we are financing evaluations of such efforts.
- The Centers for Disease Control and Prevention (CDC) expects to spend about \$3.4 million in both 1995 and 1996 for evaluations of street and community-based outreach efforts to prevent HIV infection among IV drug users, which may include State or locally-financed needle exchanges projects.
- As directed by Section 706 of the 1992 ADAMHA Reorganization Act (P.L. 92-321), the National Institute on Drug Abuse (NIDA) spent \$1 million in 1993 as a one-time expenditure for a study by the National Academy of Sciences/Institute of Medicine on the effectiveness of needle exchange and bleach distribution programs. (The report of this study is currently undergoing peer review.) NIDA also spent another \$1 million in both 1993 and 1994 to support several other research projects to study needle exchange programs.
- ▶ Congressional Prohibitions on Federal Funding for Needle Exchange Programs:
 - Section 506 of the General Provisions of the FY 1995 Labor-HHS Appropriations Act (P.L. 103-333) states:

"Notwithstanding any other provision of this Act, no funds appropriated under this Act shall be used to carry out any program of distributing sterile needles for the hypodermic injection of any illegal drug unless the Surgeon General of the United States determines that such programs are effective in preventing the spread of HIV and do not encourage the use of illegal drugs, except that such funds may be used for such purposes in furtherance of demonstrations or studies authorized in the ADAMHA Reorganization Act (Public Law 102-321)."
 - Similar language has appeared in the Labor-HHS Appropriations Acts in FYs 1990, 1991, 1993, 1994, and 1995 (though not in FY 1992); in the Ryan White Comprehensive AIDS Resources Emergency Act of 1990; and in several other health-related authorizations in 1988 and 1992.

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► State Laws:

- 44 States and the District of Columbia place criminal penalties on the possession and distribution of needles and syringes (drug paraphernalia laws).
- 10 States and the District of Columbia prohibit the sale of needles and syringes without a medical prescription (needle prescription laws).

► Needle Exchange Programs in Existence:

- Currently, there are approximately 77 known needle exchange programs were in operation in 23 different U.S. cities or counties. Beginning with the Tacoma, Washington program, all of these programs came into existence since 1988.
 - At the end of 1992, GAO had reported the existence of 32 known needle exchange programs in operation in 27 different U.S. cities or counties.

AIDS.NDL/(2-28-95)

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HIV/AIDS - PHS**Recent Accomplishments in NIH AIDS Research****QUESTION:**

What specific advances have recently been made by the NIH against HIV/AIDS?

ANSWER:

► NIH has continued to make important strides in our understanding of HIV disease and AIDS, and in better ways to prevent and treat the disease. Recent major accomplishments resulting from NIH funding include:

● Pediatric AIDS:

- Last year, an NIH-sponsored clinical trial (ACTG 076) demonstrated that AZT dramatically reduced the rate of transmission of HIV-infection from mother to infant when administered to the mother during pregnancy and labor and to the infant after birth.
- Two new tests have been developed recently that greatly improve the detection of HIV infection in newborns. These tests demonstrate that it is possible to distinguish between the maternal antibodies to HIV and those of the child.

● Basic Research:

- An important new rapid test has been developed to monitor the amount of HIV in a patient's bloodstream, a procedure that, in the future, may help clinicians decide when to give anti-HIV therapy and also gauge its effectiveness. The test, called the branched DNA assay for HIV-1 infection, also may help investigators determine more quickly if experimental HIV therapies are effective.

● Treatment:

- Scientific advances against opportunistic infections have been among our greatest successes in AIDS research thus far. People with HIV infection are now living twice as long as they did a decade ago. For example, new therapeutic regimens have recently been developed to treat cytomegalovirus (CMV) retinitis, which causes blindness; CMV infection of the intestines; *Mycobacterium avium* complex (MAC); and *Pneumocystis carinii* pneumonia (PCP).

- Treatment: (continued)

- In the area of drug development and testing, more than 72,000 potential agents for treatment were screened by the NIH Preclinical AIDS Drug Screening Program, from which six new compounds, which demonstrated anti-HIV activity, have been approved for Phase I clinical studies to determine safety.
- NIH clinical trials to date have evaluated approximately 100 therapeutic agents in trials involving more than 45,000 HIV-infected individuals. Several promising HIV protease inhibitors, a new class of drugs which attack a different target within the virus, are slated to begin phase III efficacy trials in the near future.
- The application of gene therapy to AIDS was advanced with the approval of 5 AIDS protocols by the NIH Recombinant DNA Advisory Committee. Findings from the studies will produce viable molecular tools to inactivate the virus or augment portions of the immune response.

- Vaccines:

- Preparations are well underway for large-scale clinical trials of vaccine candidates that may be identified. Presently, NIH is evaluating 13 vaccine candidates in small preliminary trials.

- ▶ Women and Minorities:

- Women with AIDS are a critical research focus for the NIH. The Women's Interagency HIV Study (WIHS) has been initiated as a prospective study of the clinical course of the infection, designed to identify the nature and rate of HIV disease progression in women. The study will also identify and characterize clinical manifestations of HIV specific to women.
- NIH policy now requires that women and members of minority groups and their subpopulations be included in all NIH supported biomedical and behavioral research involving human subjects.

AIDSACCO.96/(1-31-95)

AIDS Science Advances

The HIV Nucleocapsid Protein: A New Target for anti-HIV Drug Development.

The nucleocapsid protein p7 is essential for packaging HIV RNA genomes into viral particles. It contains "zinc finger" regions that serve as the site for the protease-induced cleavage events essential for such packaging. The nucleocapsid protein may provide an especially attractive molecular target for drug discovery since, for structural reasons, the development of resistance is likely to be relatively difficult. A 4-C-nitroso compound has been identified in a cell-based drug screening assay as a potent inhibitor of HIV-1 replication. Analysis of mechanism has shown that this compound disrupts the function of p7. This agent has particular promise as a therapeutic and also may yield insight into the late stage of the viral life cycle.

HIV-1 Infected Long-term Non-Progressors Provide Important Insight Into How the Virus May be Controlled

NIH-supported scientists have recently shown that a subset of HIV-1 infected individuals may survive for more than ten years with no impairment of their immune systems and no evidence of disease. An analysis of these individuals has revealed that they show intact lymph node architecture, further confirming their control of the virus. Viral titers are usually very low and some individuals appear to have been infected with a virus that has little or no pathogenicity. Others harbor viruses capable of infecting CD4+ T cells but they also have CD8+ T cells that markedly inhibit this infectious process. This work strongly suggests that it is possible to mount an immune response that, while failing to eliminate the virus, protects against the induction of disease. An important element of this protective immunity appears to be heightened activity of CD8+ T cells. Further analysis of these individuals promises to give deeper insight into the nature of protective immunity and into strategies through which it may be induced in others.

The Use of a Class of Potent anti-HIV Drugs, the Protease-Inhibitors, Gives Critical Information on Viral Dynamics in HIV-Infected Individuals.

The HIV-1 protease is one of three crucial enzymes required for viral replication. It is responsible for post-translational cleavage of two poly-proteins necessary for viral assembly. Accordingly, inhibitors of the protease have the potential to powerfully block HIV-1 replication. Several HIV-1 protease inhibitors have now been developed and are entering efficacy trials. The use of these inhibitors has also given novel insights into the dynamics of viral production and destruction in infected individuals. Treatment with protease inhibitors causes a rapid fall in viral burden in the plasma, with an apparent half-life of ~2 days. The data have shown that the vast majority of plasma virus is

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derived from recently-infected cells and that viral load is largely a function of viral production. It has been calculated that very large numbers of HIV are produced each day, with the mean value being approximately 1 billion virions per day. This rapid rate of production and short viral half-life also explains why viral resistance may develop very rapidly. This information will be of critical value in designing strategies for control of the virus.

Three-Dimensional Structure of HIV-1 Integrase Provides Critical Information in the Design of Potential anti-HIV-1 Drugs.

The enzyme that catalyzes the integration of HIV-1 pro-viral DNA into a host chromosome is critical in the life cycle of the virus. This enzyme is the third of the major HIV-1 enzymes to receive attention as a potential target for drug discovery and development. An impediment to progress toward this goal was the lack of understanding of the structure of the enzyme and thus of potential agents that might inhibit its catalytic activity. Recently, NIH scientists have solved the three-dimensional structure of the integrase by X-ray crystallographic methods. The structure that has been obtained revealed a striking resemblance between the catalytic site of integrase and that of a family of enzymes, designated polynucleotide transferases. The active site in the crystal fragment has two acidic amino acid residues that are highly conserved among other retroviral integrases and polynucleotide transferases. It appears likely that these acidic residues are crucial for catalysis and that they interact with magnesium, an essential co-factor of the enzyme. In parallel, other scientists have identified a protein, In1, that binds to HIV-1 integrase and stimulates its DNA joining activity. These insights should be of great value in efforts to develop a new class of anti-retroviral agents. If such agents can be developed, they will offer the promise of multi-drug combinations that would appear to offer the best hope for long-term drug control of viral replication.

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HIV/AIDS - PHS**AIDS Drug Development Task Force****QUESTION:**

Last year, you announced the formation of a new National Task Force on AIDS Drug Development. What has the Task Force accomplished during its first year?

ANSWER:

- ▶ In the past year, the full Task Force met four times to explore the complex issues of AIDS drug discovery, drug development, and the related interactions between the public and private sectors. The Task Force just recently sent 17 specific recommendations to the Department.
- The Assistant Secretary for Health has asked the National AIDS Policy Office to evaluate the Task Force's recommendations and report back to him by June 1, 1995.
- ▶ Thus far, the following recommendations from the Task Force have already been implemented:
 - NIH's Office of AIDS Research initiated a thorough review of the NIH AIDS drug discovery and screening programs, seeking to eliminate any ineffective components and expanding, as necessary, those found to be more effective.
 - A computerized database of NIH-funded research was recently established online to promote early communication of basic and applied clinical research results that may be relevant to HIV/AIDS drug development efforts.
 - NIH recently held workshops to examine the problems of developing animal models for use in AIDS research, and to develop wider collaboration and sharing in the use of drug screening assays.
 - Processes for reviewing gene therapy protocols at NIH and FDA were consolidated and streamlined while protecting scientific and ethical integrity of the process, eliminating duplication and saving time.
 - The Patent and Trademark Office (PTO) published new guidelines for reviewing patent applications to allow standards of utility to be established by scientific experts in the field. The Patent Office will now accept laboratory evidence of the effectiveness of drugs, rather than requiring more stringent and long-term clinical data.

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- ▶ The Department is also working now to implement recommendations dealing with women and minorities in clinical trials, pediatric drug development, and other obstacles to developing safe and effective therapies for HIV/AIDS.

ADDITIONAL INFORMATION:

- ▶ The National Task Force on AIDS Drug Development was chartered by the Secretary in November 1993 to expedite the search for new therapies against HIV infection and its associated malignancies and opportunistic infections, and to identify and remove obstacles to AIDS drug discovery and development. Members were appointed in February 1994.
- ▶ Chaired by the Assistant Secretary for Health, Dr. Philip Lee, the Task Force includes 18 members from academia, industry, community and government. The Director of NIH and the Commissioner of FDA also serve as members.
- ▶ The second phase of the Task Force's work will address more directly obstacles faced by private industry in the discovery and development of AIDS drugs by examining possible incentives and disincentives to private investment in AIDS drug development, examining models for heightened collaboration between private companies and between the private and public sectors, and exploring novel molecular targets for drug discovery.
- ▶ Membership of National Task Force on AIDS Drug Development:
(see next page)

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Members of National Task Force on AIDS Drug Development

- Moises Agosto
Research & Treatment Advocacy Manager
National Minority AIDS Council
Washington, D.C.
- Arthur Ammann, M.D.
Director, Ariel Project
Pediatric AIDS Foundation
Novato, California
- Stephen K. Carter, M.D.
Senior Vice President, Worldwide
Clinical Research and Development
Bristol-Myers Squibb
Princeton, New Jersey
- Ben Cheng
Information and Advocacy Associate
Project Inform
San Francisco, California
- Deborah J. Cotton, M.D., M.P.H.
Assistant Professor of Medicine
Harvard Medical School
Boston, Massachusetts
- Mindy Fullilove, Ph.D.
Research Psychiatrist, HIV Center
N.Y. State Psychiatric Institute
New York, New York
- David Ho, M.D.
Director
Aaron Diamond AIDS Research Center
New York, New York
- Daniel Hoth, M.D.
Senior Vice President
Cell Genesys
Foster City, California
- David A. Kessler, M.D.
Commissioner
Food and Drug Administration
Washington, D.C.
- Philip R. Lee, M.D.
Assistant Secretary for Health
Public Health Service, DHHS
Washington, D.C.
- Theresa McGovern
Director
HIV Law Project
New York, New York
- Charles Nelson
Laboratory Technician III
Morehouse School of Medicine
Atlanta, Georgia
- G. Kirk Raab
CEO
Genetech
San Francisco, California
- Robert Schooley, M.D.
Director, Colorado ACTU
University of Colorado
Denver, Colorado
- Edward Scolnick, M.D.
President
Merck Research Laboratories
Rahway, New Jersey
- Peter Staley
Founding Director
Treatment Action Group
New York, New York
- Harold Varmus
Director
National Institutes of Health
Bethesda, Maryland
- Flossie Wong-Staal, Ph.D.
Professor of Medicine and
Biology
University of California
San Diego, California

AIDSTASK.96/(1-30-95)

HIV/AIDS - PHS**Female Barriers/Topical Microbicides****QUESTION:**

What does your 1996 budget include for research on female barriers and topical microbicides for the prevention of sexually transmitted diseases (STDs), such as HIV/AIDS?

ANSWER:

- ▶ We recognize the importance of developing methods which women can use independently of their partners to protect themselves from STDs.
- ▶ In 1996, NIH plans to spend about \$22 million for research on female barriers and topical microbicides, a 3.5% (+\$0.7 M) increase over 1995. However, this follows a year in which NIH is nearly doubling (+71%) its investment in this field of research, from \$12 million in 1994 to \$21 million in 1995.
- ▶ NIH, especially the National Institute of Allergy and Infectious Diseases (NIAID), is continuing to support basic research on the molecular basis of the HIV and STD infection process. Such research provides the foundation for developing effective strategies to interfere with host/pathogen interactions using chemical barriers.
- ▶ NIH is also funding research on developing new diagnostic tests that are rapid, inexpensive, and easy to use. These tests will enable clinical research on microbicides to proceed rapidly and contribute significantly to reducing the costs of clinical evaluations of STDs.
- ▶ International sites that provide immediate access to populations with high rates of HIV infection and STDs have been established to be used in the evaluation of currently available chemical barriers and new microbicides.

NIH Funding for Female Barriers/Topical Microbicides Research
(Program Level in millions)

	<u>1993</u>	<u>1994</u>	<u>1995</u>	<u>1996</u>	<u>Chg.</u>
Barriers/Top. Microbic.	\$9.2	\$12.3	\$21.0	\$21.8	+\$0.7
(* Chg. Prior Year)...		+33.5%	+71.2%	+3.5%	

HIV/AIDS - PHS**AIDS versus Cancer Spending****QUESTION:**

How does spending for HIV/AIDS compare to spending for cancer, heart disease and diabetes? Do you believe that our spending on HIV/AIDS research is out of balance given that other diseases affect more people and take more lives?

ANSWER:**Relative Spending Figures:**

- ▶ Within just the Public Health Service (PHS), research spending only on cancer is still far more than for any other single disease. In 1996, we expect to spend \$2.1 billion for cancer research; \$1.6 billion for HIV/AIDS research; and \$830 million for heart disease research.
- ▶ However, in terms of PHS spending for research, prevention, and treatment combined, more funds are devoted to HIV/AIDS than to any other single disease, due primarily to our unique support of Ryan White HIV/AIDS treatment services. In 1996, PHS expects to spend \$2.9 billion on HIV/AIDS research, prevention, and treatment; \$2.5 billion in total for cancer; and \$834 million in total for heart disease.

Balance Between Diseases:

- ▶ I do not believe that research on HIV/AIDS is "out-of-balance" with other diseases. Such comparisons can be a bit misleading.
- ▶ HIV/AIDS was discovered just a little more than a decade ago, and it is already the number one leading cause of death for men between the ages of 25-44 and the second leading cause of death for all Americans in that age group.
- ▶ There are significant differences between HIV/AIDS and other diseases.
 - HIV/AIDS is infectious; heart disease and cancer are not.
 - HIV/AIDS strikes a younger population, leading to more years of productive life lost.
 - The changing demographics of the HIV/AIDS epidemic is skewing more and more to individuals in lower economic brackets; consequently, more and more persons with AIDS will need to rely on the public sector to finance the cost of their health care.
 - The total cost of treating a case of HIV is \$85,000;
 - 7,000 children a year are born to HIV infected women.

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- ▶ The most important reason such comparisons between diseases are not always appropriate is the nature of scientific inquiry itself. When we talk about basic science research, we really need to get away from looking at our expenditures in "boxes."
- Many times, breakthroughs occur in areas totally unrelated to the "label" we place on the basic research project.
- This "spin-off" effect is unpredictable, and I expect that our work in HIV/AIDS will have pay-offs even beyond our expectations in other fields.
- The spin-offs from our investment in AIDS are already reaping returns for other areas -- for example, our investment has lead to a greater understanding of viruses and enhanced our understanding of other immune compromising disorders.

ADDITIONAL INFORMATION:

(Dollars in millions)

PHS Only				
	1996			
	HIV/AIDS	Cancer	Heart D.	Diabetes
Research..	\$1,621	\$2,116	\$830	\$313
Treatment..	755	--	--	--
Prevention	525	395	4	27
Income Sup	--	--	--	--
Total....	\$2,901	\$2,491	\$834	\$340

	1995			
	HIV/AIDS	Cancer	Heart D.	Diabetes
Research..	\$1,548	\$2,049	\$805	\$304
Treatment..	664	--	--	--
Prevention	490	335	4	27
Income Sup	--	--	--	--
Total....	\$2,702	\$2,384	\$809	\$331

	1994			
	HIV/AIDS	Cancer	Heart D.	Diabetes
Research..	\$1,508	\$2,005	\$781	\$295
Treatment..	614	--	--	--
Prevention	444	258	4	25
Income Sup	--	--	--	--
Total....	\$2,566	\$2,263	\$785	\$320

	1993			
	HIV/AIDS	Cancer	Heart D.	Diabetes
Research..	\$1,285	\$1,954	\$755	\$287
Treatment..	397	--	--	--
Prevention	395	186	4	16
Income Sup	--	--	--	--
Total....	\$2,077	\$2,140	\$759	\$303

Total HHS (PHS + Entitlements)				
	1996			
	HIV/AIDS	Cancer	Heart D.	Diabetes
Research..	\$1,621	\$2,116	\$830	\$313
Treatment..	3,245	15,175	33,760	n/a
Prevention	528	395	4	27
Income Sup	1,205	1,616	7,130	n/a
Total....	\$6,599	\$19,302	\$41,724	n/a

	1995			
	HIV/AIDS	Cancer	Heart D.	Diabetes
Research..	\$1,548	\$2,049	\$805	\$304
Treatment..	2,904	13,625	30,645	n/a
Prevention	493	335	4	27
Income Sup	1,015	1,495	6,577	n/a
Total....	\$5,960	\$17,504	\$38,031	n/a

	1994			
	HIV/AIDS	Cancer	Heart D.	Diabetes
Research..	\$1,508	\$2,005	\$781	\$295
Treatment..	2,604	11,995	27,190	n/a
Prevention	447	258	4	25
Income Sup	835	1,380	6,054	n/a
Total....	\$5,394	\$15,638	\$34,029	n/a

	1993			
	HIV/AIDS	Cancer	Heart D.	Diabetes
Research..	\$1,285	\$1,954	\$755	\$287
Treatment..	2,072	10,095	23,095	n/a
Prevention	398	186	4	16
Income Sup	670	1,246	5,478	n/a
Total....	\$4,425	\$13,481	\$29,332	n/a

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HIV/AIDS - PHS**Use of HHS Funds for White House AIDS Office****QUESTION:**

Have any funds appropriated to HHS been used to support the operation of the White House AIDS Office?

ANSWER:

- ▶ As you know, in our FY 1995 request, we sought a total of \$2.9 million for the National AIDS Program Office and states our intention to use some of these funds to "providing support ... to the National AIDS Policy Coordinator (i.e., the White House AIDS Office)."
- ▶ In addition, to make sure that Congress was fully aware of our planned use of the final appropriation, we wrote (11/18/94) to the ranking minority and majority members of both the House and Senate Appropriations Subcommittees to advise them that we planned to use \$350 thousand to support certain activities of the National AIDS Policy Coordinator (e.g., rent, travel, supplies)
 - Letter to the Subcommittees is attached.
- ▶ On 2/7/95 we received a letter from Chairman Porter which stated that "The Subcommittee does not approve your proposal ... to support the National AIDS Coordinator in the White House."
 - Letter from Chairman Porter is attached.
- ▶ By the time we received the letter, \$54 thousand had already been obligated.
 - We took immediate action once we received the 2/7/95 letter and stopped all further obligations for the National AIDS Policy Coordinator.

KEY INFORMATION:

(dollars in thousands)

	<u>FY 1994</u>	<u>FY 1995</u>	<u>FY 1996</u>
NAPO Support for White House AIDS Office.....	\$153.5	\$53.7	\$0.0

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THE SECRETARY OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20201

NOV 18 1994

The Honorable Neal Smith
Chairman Subcommittee on
Labor, Health and Human Services,
Education and Related Agencies
Committee on Appropriations
House of Representatives
Washington, D.C. 20515

Dear Mr. Chairman:

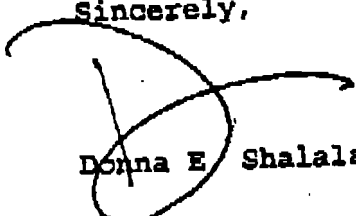
I am writing to inform you of our plans to use \$350,000 of FY 1995 funds appropriated for the National AIDS Program Office to partially support the National AIDS Policy Coordinator (NAPC). These funds were included within the appropriation account for the Office of the Assistant Secretary for Health.

I am fully aware that in your deliberations on the budget for this Office, a concern about the level of resources needed for directing and coordinating HIV/AIDS activities emerged. The Conference agreement specifies that \$1,750,000 is available for these purposes. As noted in our justification to the Committees, funding was requested to provide support to both the Assistant Secretary and the NAPC.

The \$350,000 identified for NAPC will be used to cover such expenses as rental of office space, communications, travel, supplies and equipment, and other support and contractual services. During FY 1995 the NAPC has been asked by the President to establish a new Interdepartmental Task Force on AIDS to ensure that HIV related activities of all Federal agencies are better coordinated and that inconsistencies in strategies and duplication of effort are eliminated.

I appreciate the Committee's continued interest in, and support of, this Department's response to the HIV/AIDS epidemic.

Sincerely,


Donna E. Shalala

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Congress of the United States
House of Representatives
Committee on Appropriations
Washington, DC 20515-6015
February 7, 1995

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 JAMES W. DYER
 TELEPHONE
 (202) 225-2771

Honorable Donna E. Shalala
 Secretary
 Department of Health and Human Services
 Washington, DC 20201

Dear Madam Secretary:

This letter is in response to your reprogramming letters of November 18, 1994 that were addressed to the Chairman of this Subcommittee in the last session of Congress. I apologize for the delay in responding. As you know, there has been a great deal of activity here during the past month.

The Subcommittee does not approve your proposal to utilize \$350,000 in the National AIDS Program Office to partially support the National AIDS Coordinator in the White House. In addition, the Subcommittee does not approve your proposal to utilize \$400,000 from funds appropriated under the Crime Bill to partially support the Ounce of Prevention Council.

Sincerely,

John Edward Porter, Chairman
 Subcommittee on Labor, Health
 and Human Services, Education
 and Related Agencies

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HIV/AIDS - PHS**Pediatric AIDS****QUESTION:**

How much does your 1996 budget include for pediatric AIDS?

ANSWER:

- ▶ In total, we expect to spend \$269 million on PHS's pediatric AIDS activities in 1996, an increase of \$15 million (+6%) over the 1995 level.
 - AIDS cases in women are one of the fastest growing segments of the AIDS population in the U.S., representing about 16% of all new non-pediatric cases reported in 1993. Women now comprise 21% of reported HIV-infection cases.
 - As more women have become HIV-infected, there has been a corresponding increase in the number of pediatric AIDS cases. AIDS is currently the 7th leading cause of death among children aged 1-4 years, and among the top five in some major urban areas.
- ▶ We recently released guidelines recommending that doctors counsel all pregnant women--4 million a year--about voluntary testing for HIV. Each year approximately 7 thousand HIV-infected women give birth and 2 thousand of them will pass the deadly virus on to their unborn babies. AZT drug treatment will reduce the risk of HIV transmission to their babies by two-thirds--and we believe that mothers should be informed in order that make that choice.
- ▶ 1996 President's budget includes increases of:
 - +\$9 M (+5%) to expand NIH pediatric AIDS research to a total level of \$184 M. This represents 13% of NIH's AIDS resources.
 - +\$6 M (+23%) to expand pediatric AIDS research trials in HRSA through Title IV of the Ryan White Act to a total level of \$32 M.

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Pediatric AIDS Expenditures (\$ in millions)				
	1993	1994	1995	+/-94
Ryan White Title IV..	\$22	\$26	\$32	+\$6
CDC Surveys/Prev.....	48	48	48	--
NIH Research.....	169	175	184	+9
SAMHSA Outreach/Educ.	4	3	3	--
AHCPR Research.....	2	2	2	--
Total.....	\$245	\$254	\$269	+\$15

ADDITIONAL INFORMATION:

► Pediatric AIDS Data (Final as of 12-31-93) :

- 5,228 total pediatric AIDS cases reported to CDC since 1981, including 2,819 deaths.

- Of the total pediatric AIDS cases, 959 (18%) were reported in 1993, representing a 23% increase over the cases reported in the same period in 1992.

► Pediatric AIDS Cases--

1992.....	781
1993.....	959
1994.....	na

HIV:► Live Births to Women with HIV--

	<u>Births</u>
1991.....	7,000
1992.....	7,000
1993.....	6,600
1994.....	na

(From Survey of Child-bearing women. Not uniform across States.)

- Transmission of HIV to child -- 17%-25% of children are born HIV-infected.
- Transmission of HIV to child with AZT Treatment Regimen -- 8%-9% of children will be born HIV-infected.

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► Potential Cost of Recommendation to Counsel and Test All
Pregnant Women--

Approx. for All Women -- \$246 M

- > CDC average cost for counseling and testing session: \$60
- > One birth cohort is approximately 4.1 M children

(Does not account for multiple births--simply 4.1 M x \$60.00)

Of this, Medicaid Pregnant Women-- \$84 M

States' Share..... \$34 M (40%)

- > CDC average cost for counseling and testing session: \$60
- > Medicaid pregnant women..... 1.4 M (1993)

(Does not account for multiple births--simply 1.4 M x \$60.00)

PUBLIC HEALTH SERVICE

Pediatric AIDS (Birth to 18)

(Dollars in thousands)

	FY 1994 Enacted	FY 1995 Enacted	FY 1996 Pres. Budget	Change/ FY 1995 \$	Change/ FY 1995 %
HRSA:					
Ryan White Title IV.....	\$22,000	\$26,000	\$32,000	\$6,000	23%
CDC:					
Perinatal Infections.....	\$8,646	\$8,637	\$8,637	\$0	0%
Childbearing Studies.....	13,440	13,426	13,426	0	0%
Mothers and Infants.....	<u>25,776</u>	<u>25,750</u>	<u>25,750</u>	<u>0</u>	<u>0%</u>
Subtotal, CDC.....	\$47,862	\$47,813	\$47,813	\$0	0%
NIH:					
Cancer.....	\$10,677	\$10,724	\$10,906	\$182	2%
Heart, Lung & Blood.....	17,668	17,831	18,616	784	4%
Neurological Disorders & Stroke.....	1,870	1,878	1,895	17	1%
Allergy & Infectious Diseases.....	65,979	67,892	72,441	4,549	7%
Child Health & Development.....	44,087	45,900	47,500	1,600	3%
Research Resources.....	7,224	7,687	8,077	390	5%
Human Genome Research.....	0	601	650	49	8%
Dental Research.....	2,041	2,041	2,139	98	5%
Diabetes/Digestive/Kidney.....	1,109	1,150	1,200	50	4%
Fogarty International Center.....	643	729	776	47	6%
Drug Abuse.....	2,794	3,500	4,000	500	14%
Alcohol Abuse/Alcoholism.....	2,821	2,825	2,825	0	0%
Mental Health.....	<u>12,416</u>	<u>12,734</u>	<u>13,344</u>	<u>610</u>	<u>5%</u>
Subtotal, NIH.....	\$169,329	\$175,492	\$184,368	\$8,876	5%
SAMHSA:					
Mental Health Demo/Training Cluster..	\$0	\$0	\$697	\$697	na
AIDS Training.....	179	179	0	-179	-100%
AIDS Demonstrations.....	559	554	0	-554	-100%
Substance Abuse/Training Cluster.....	0	0	2,475	2,475	na
AIDS Linkage Program.....	1,174	1,161	0	-1,161	-100%
AIDS Outreach Programs.....	<u>1,788</u>	<u>1,275</u>	<u>0</u>	<u>-1,275</u>	<u>-100%</u>
Subtotal, SAMHSA.....	\$3,700	\$3,169	\$3,172	\$3	0%
AHCPR.....	\$1,700	\$1,400	\$1,446	\$48	3%
TOTAL, Public Health Service.....	\$244,591	\$253,874	\$268,799	\$14,925	6%

HIV/AIDS - PHS

AIDS Policy Coordinator -- Role

QUESTION:

What is the role of the White House National AIDS Policy Coordinator (NAPC) in the National AIDS Policy Office? Why is there a need for this function when HHS has a National AIDS Program Office (NAPO)?

ANSWER:

NAPC:

- ▶ The National AIDS Policy Coordinator, Patsy Fleming, is an employee of the White House and provides direct counsel to the President on the issue of HIV/AIDS.
- ▶ The role of the AIDS Policy Coordinator is to provide high visibility to the public health issue of HIV/AIDS and to provide a public voice for the President both in the U.S. and abroad on this critical topic.
- ▶ The AIDS Policy Coordinator is responsible for directing AIDS policy government-wide. As such, she takes charge, for the President, of:
 - Broad policy direction on HIV/AIDS including -- housing, conditions of employment, civil rights, immigration, health insurance coverage, access to health care, science, public health education and outreach.
 - Interdepartmental communication and coordination of at least 10 agencies -- HHS, HUD, VA, DoD, AID, DoJ, State, Labor, Education, and OPM.
 - Direct input into the budget process of all Departments; setting priorities for HIV/AIDS program funding.
- ▶ This past year, the NAPC convened an Interdepartmental Task Force on AIDS--with representatives from all Departments on the Domestic Policy Counsel--and will publish a National Plan this summer.

NAPO:

- ▶ The scope of the PHS National AIDS Program Office (NAPO) is much narrower. NAPO supports the Assistant Secretary for Health as principal convener of forums incorporating representation from HHS's major agencies and staff offices on issues pertaining to HHS programs.

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- ▶ The budget for NAPO has been scaled back dramatically over the last several years, with many of the activities supported by NAPO being assigned to the NAFC or PHS agencies.
- ▶ Activities still performed by NAPO:
 - Provides coordination and leadership on behalf of the Assistant Secretary for Health, among the PHS agencies;
 - Staffs the HHS Coordinating Group on HIV/AIDS, the only forum for PHS and Departmental representatives to meet regularly to address critical issues;
 - Serves as the primary liaison for the Department and the Assistant Secretary for external groups, professional associations, and private organizations.
- ▶ Both Offices maintain a unique direct link so that HIV/AIDS problems are well coordinated through the Executive branch.

KEY INFORMATION:

- ▶ Examples of budget liaison role includes:
 - DoD: In December 1994, DoD had decided to rescind funds which had been budgeted for HIV/AIDS research. The National AIDS Policy Coordinator intervened and the funds were restored. The President sent a letter to the Pentagon emphasizing the high priority of AIDS research for the White House.
 - HUD: OMB had intended to "block grant" the Housing Opportunities for People with AIDS (HOPA) program. The National AIDS Policy Coordinator and Secretary of HUD persuaded the OMB Coordinator not to consolidate this program into a formula grant to States.
- ▶ Current staff of the White House National AIDS Policy Office:

White House Staff.....	2
HHS Representative.....	1
Presidential Management Intern..	1
Volunteers.....	2
Total Staff.....	6
- Eventually, it is expected that Departments government-wide will supply agency representatives to the National AIDS Policy Office with special expertise in this area as needed.

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- On February 7, Mr. Porter (Chairman, House Appropriations) denied our request to allocate \$350 thousand from the PHS National AIDS Program Office to the White House National AIDS Policy Office. Alternative means are being sought to finance the Office.

-- Our FY 1995 request included:

- \$350,000 in NAPO to support NAPC activities.
- Congress did not specifically deny this use until January 7, 1995.
- At that point, we ceased further support of NAPC activities, although by that time \$54,000 had already been obligated to NAPC.

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HIV/AIDS - PHS

AIDS "Spin-Offs" - Fact Sheet

The Nation's investment in HIV/AIDS-related research is providing important benefits for understanding and treating other diseases. For example:

- ▶ AIDS research has accelerated study of the human immune system. This basic immunologic information is being applied to research to better understand and treat many other diseases, such as cancer and autoimmune diseases, including systemic lupus erythematosus, type I diabetes mellitus, rheumatoid arthritis, and multiple sclerosis. AIDS research also contributes to the prevention of other infectious diseases, such as other STDs.
- ▶ HIV research involving the blood/brain barrier has led to a better understanding of the mechanisms by which infectious agents spread into the nervous system. This has valuable implications for research on Alzheimer's disease, dementia, multiple sclerosis, neuropsychological disorders, encephalitis, and meningitis.
- ▶ HIV research has accelerated development of highly specialized computer imaging techniques to solve the three dimensional structure of key components of viruses. These structures can then be utilized to design therapeutic agents to attack the virus and develop potential vaccines against HIV infection and other diseases.
- ▶ Before the AIDS epidemic, little investment was made in research to treat viral diseases. Instead, drugs were developed to treat the symptoms of the disease, while the body's immune system fought the virus. AIDS has brought attention to the need to develop anti-viral therapies. Studies to develop anti-HIV therapy have led to the possibility of drug development against many other viruses.
- ▶ Research on HIV-related wasting syndrome has provided important information for research on nutritional disorders, metabolic abnormalities, and gastrointestinal dysfunctions.
- ▶ The national HIV research effort has brought about unprecedented cooperation among Federal, university, and pharmaceutical industry scientists in the development of potential therapeutic agents and vaccines. This is an important model for other diseases.
- ▶ HIV research has resulted in new approaches for designing and conducting clinical trials, and for recruiting and enrolling patients in these studies. These models can be applied to clinical trials for other diseases.

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HIV/AIDS - PHS**HIV/AIDS Cases Rising****QUESTION:**

It has been recently reported that 40% of all AIDS cases have been reported in the past 2 years -- 1993 and 1994. Yet, on February 3, CDC (MMWR) reported that AIDS cases are dropping. Can you explain why you are reporting the facts differently?

ANSWER:

- ▶ Yes, 42% of all AIDS cases reported to date were reported in 1993 and 1994 (187,309 of 441,528 total cases). This is a true statement. The operative word is "reported."
 - ◆ Because of a new definition of AIDS, many cases reported in 1993 were based on the new definition. In previous years, some of these cases would not have been called AIDS--for example, women who are HIV positive and have invasive cervical cancer.
 - ◆ The 1993 numbers also reflect some "catch-up"--in other words, some individuals who were reported in 1993 would have been reported earlier had the new definition been in effect.
- ▶ AIDS cases are not dropping. As reported in the MMWR article you cite, using the "pre-1993" definition, AIDS cases are increasing by approximately 3% per year, both in 1993 and 1994.
 - ◆ The rate of increase in 1992 was 5% -- slightly higher.
- ▶ The number of new HIV/AIDS cases reported more than doubled in 1993 largely because of a new, broader definition which took effect on January 1, 1993.
 - ◆ The new definition was expanded to include individuals with severe HIV-related disease -- severe immunosuppression (total lymphocytes<14%), pulmonary tuberculosis, recurrent pneumonia, or invasive cervical cancer.
- ▶ Simply looking at the table included in the CDC MMWR (2/3/95) article may be misleading -- new cases in 1994 appear to be dropping from 106,618 to 80,691 (-24%) compared to 1993. However, the lead narrative paragraph of the article states that AIDS cases are still on the rise by 3% per year.