

Adult and Adolescent Spectrum of Disease Project in Michigan

Summary Report

1990-2003

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INTRODUCTION

The Adult and Adolescent Spectrum of Disease (ASD) project was a supplemental surveillance project sponsored by the Centers for Disease Control and Prevention (CDC) to learn more about the disease status of HIV-infected persons.¹ Health departments in eleven U.S. cities collected data for a period of 14 years, 1990-2003. The data from ASD formed the basis for the revision of the AIDS surveillance case definition in 1993 to include CD4⁺ T-cell count <200 cells/mm³ as an AIDS-defining event and to include three additional opportunistic illnesses as AIDS-defining.² In the following years, 1994-2003, ASD continued to track developments in the natural history of HIV infection, such as the improved health status of HIV-infected persons following introduction of more effective therapies for HIV and for opportunistic illnesses, the side-effects of these therapies, and the rise of liver disease in persons co-infected with HIV and hepatitis.

METHODS

Data Collection

ASD in Michigan collected data at two medical centers in Detroit. The medical records of HIV-infected persons were abstracted from the time the person first contacted one of the ASD sites for HIV care until they died or were lost to follow-up. Persons were enrolled if they were hospitalized or if they visited an outpatient clinic for HIV-related care in 1990-2002. Baseline forms were completed by abstracting data from the persons' medical records from the 12-month period preceding enrollment. The enrollment date was either the date the person was discharged from their initial hospitalization at an ASD site, or the date they first contacted the outpatient clinic for HIV-related care. If the person only contacted an emergency room for care, they were not enrolled. No new persons were enrolled in 2003.

After the person was enrolled, all their medical records at both ASD sites were reviewed at six-month intervals to collect their follow-up data. Each follow-up record contained data collected from six months of the person's medical records. If no data were found on the person for any six-month follow-up interval at either ASD site, they were assigned Unknown status for that interval. If the person's status was Unknown for three consecutive intervals, they were considered lost to follow-up as of the last date of the third Unknown interval. Follow-up continued until the persons died or were lost to follow-up. When a person who had been lost to follow-up was seen again for HIV care at one of the ASD sites, follow-up resumed and continued until the person died or was again lost to follow-up. At the termination of the ASD project, follow-up ended with each person's last follow-up interval in 2003.

The Facilities

A total of 5569 persons were enrolled in ASD over the course of the project, 1990-2002, 2052 (37%) at the Henry Ford Health System (HFH) and 3517 (63%) at the Detroit Medical Center (DMC). Persons for whom white or black race/ethnicity was recorded were distributed between the two sites as shown in this table.

Table 1
Distribution of Persons of Black and White Race Enrolled in ASD Between the Two Sites

	N	HFHS	DMC
White males	1173	69%	31%
Black males	2484	34%	66%
White females	192	26%	74%
Black females	1514	19%	81%
Overall	5363	37%	63%

Sampling of the Population

The population of HIV-infected persons contacting either of the ASD sites was sampled for inclusion in ASD. Males 20 years of age and older were sampled at a rate of 40% starting in 1993 at one site and in 1997 at the other. All females, and males 19 years of age and younger, were enrolled throughout the project period, at both sites. Baseline data on demographics and modes of HIV transmission were adjusted for the sampling scheme in effect at the time and place the persons were enrolled. For example, the number of males 20 years of age and older in any given demographic or mode category was weighted (multiplied) by 2.5 if they were enrolled when 40% sampling was in effect at the site where they were enrolled. The numbers of younger males, and all females, were given a weight of 1.

- The proportions of persons in each category of a demographic characteristic or of risk were calculated as follows: The weighted number of persons in each category was divided by the total of the weighted numbers of persons in all categories to provide the adjusted proportions. This procedure was repeated for each two-year time period.
- The N listed for each two-year period of demographic/HIV transmission mode data is the actual number of individuals enrolled (not the weighted total).

- The tests for linear trend over time were performed as follows: The adjusted proportions were multiplied by the original, unweighted total number of persons in the two-year time period to provide adjusted numbers of persons in each category of each demographic characteristic and of risk. The tests were performed for each category separately. For example, the adjusted numbers of persons of black race and the adjusted numbers of persons not of black race for the various two-year time periods were tested.

For the data on disease status at baseline, information from both the baseline record (12 months before enrollment) and the first follow-up record (six months following enrollment) were included. For the data on persons in follow-up care, the second and all subsequent follow-up records were used, covering the period from six months after enrollment onward. When analyses of events during follow-up are reported as the proportion of persons in care, a person is included if they had any data on care collected in any one of their follow-up records in the two-year period. Interval records with Unknown or Lost status were included only in the calculations of the proportions of persons in care that died or were lost to follow-up. All other calculations from follow-up data included only records in which patient contact was recorded.

Antiretroviral drug prescriptions

From 1998 onwards, each follow-up record allowed for recording all the different regimens the persons was prescribed during the six-month period. Regimens were categorized as HAART, ART (not HAART), or No ART (see Definitions). If any HAART regimen was recorded during the follow-up interval the record was categorized as HAART. If ART was recorded, but no HAART was recorded at any time during the interval, the record was categorized as ART (not HAART). A record was categorized as No ART only if no ART regimen was recorded at any time during the interval. For example, a follow-up record in which both a HAART regimen and a two-drug (not HAART) regimen were prescribed would have been categorized as having HAART prescribed. The proportion of six-month follow-up records in each of the three prescription categories was calculated. Conceptually, this procedure represents calculating the proportion of person-time during follow-up that fell into each prescription category. The proportions of persons in a two-year period used in many of the other figures and tables represents the number of events (diagnoses, etc.) per person two-year period, while the antiretroviral drug analysis represents the number of prescriptions per person six-month period.

Statistical analyses. Changes over time were tested using a Chi-square test for linear trend of proportions. Differences among race-sex groups were tested using a Chi-square test for equality of proportions.

BASELINE DATA

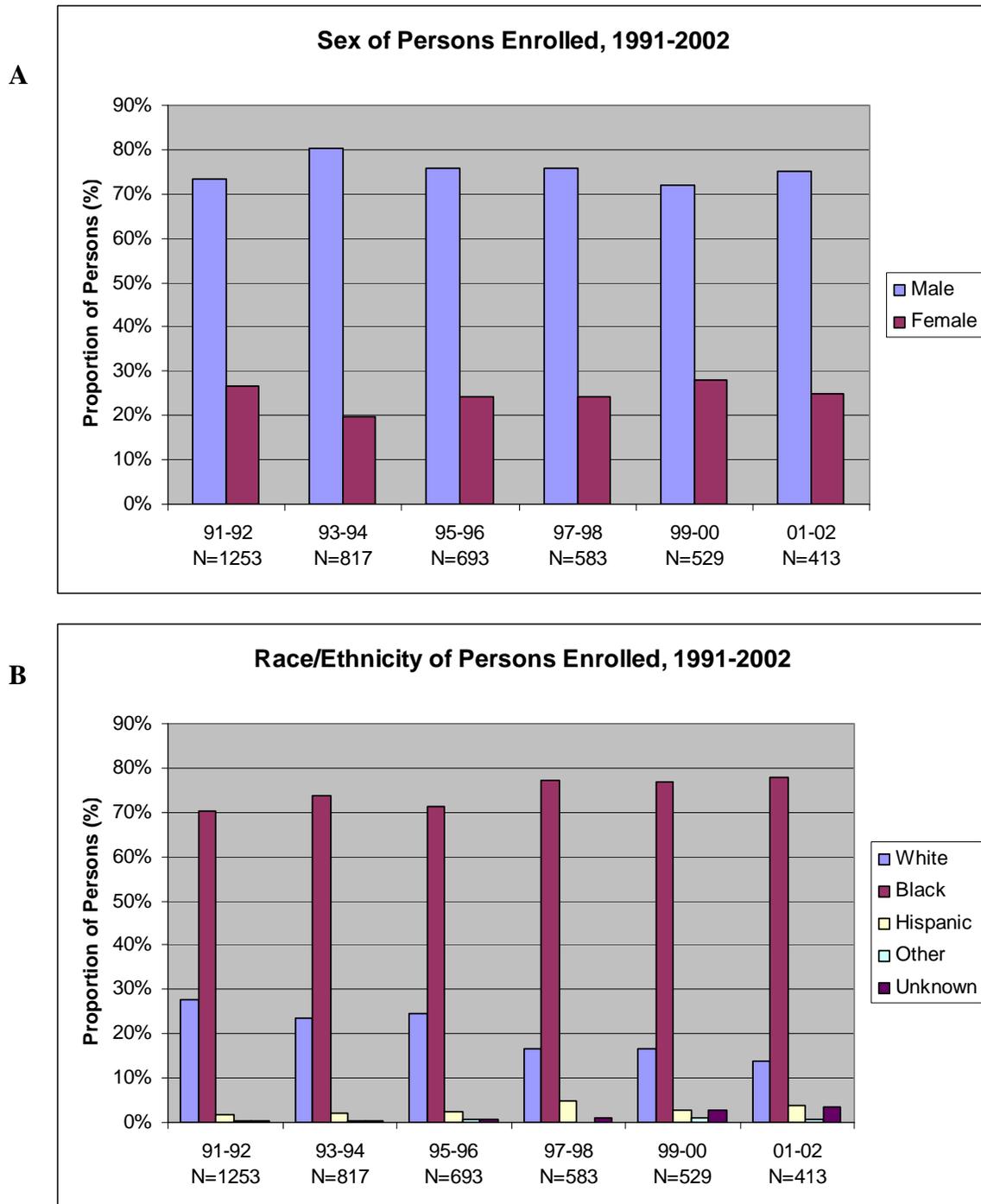
DEMOGRAPHICS AND MODE OF HIV TRANSMISSION

Figure 1

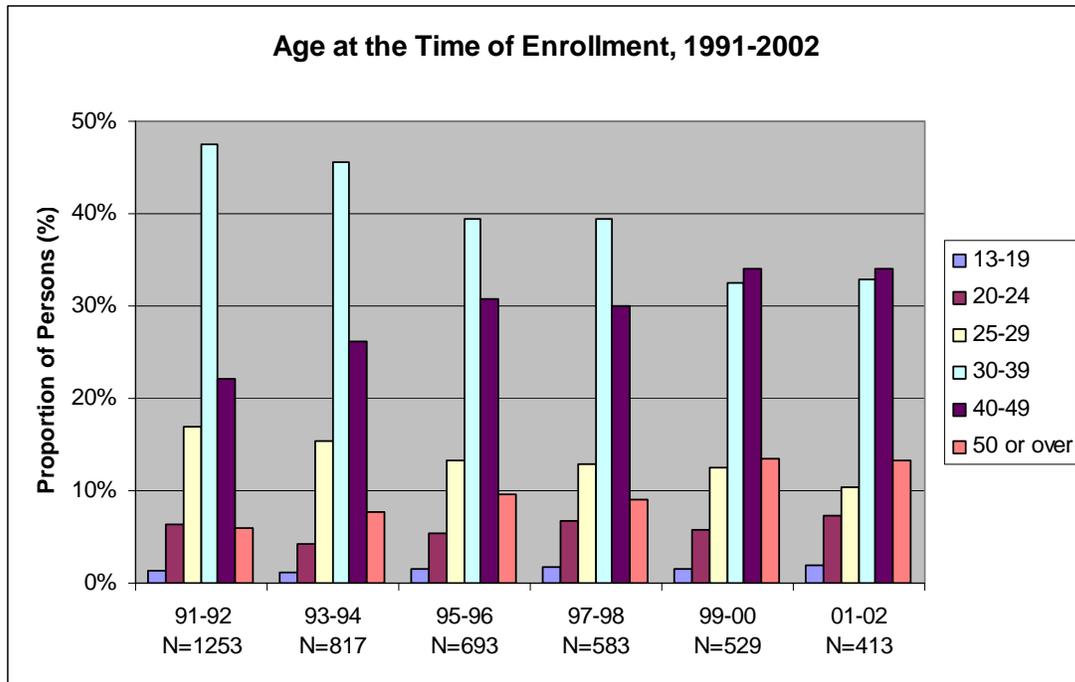
Demographics and Mode of HIV Transmission of Persons Enrolled in ASD, by Two-year Periods

A, Sex; B, Race/Ethnicity; C, Age; D, Modes HIV Transmission.

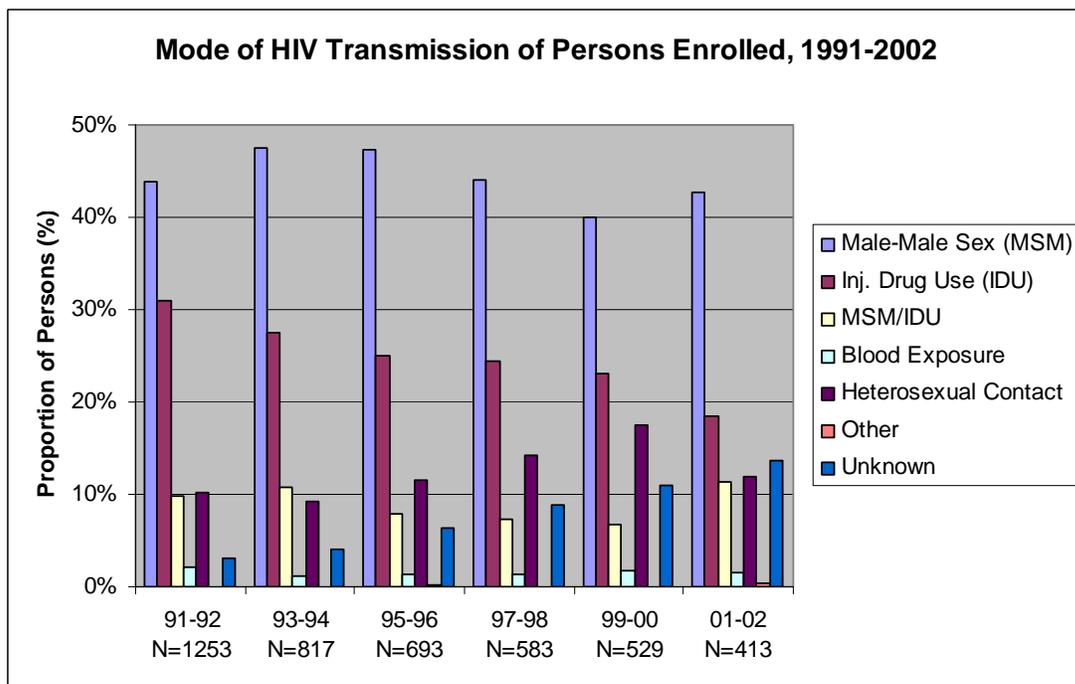
The proportions of patients were all adjusted for sampling, as described in the Methods section. All p-values were obtained from Chi-square tests for linear trends over time.



C



D



Sex. The distribution by sex did not have a linear trend over the time period, 1991-2002 ($p=0.54$).

Race/Ethnicity. The proportion newly enrolled persons who were white decreased over the time period, 1991-2002 ($p<0.001$), while there were increases in the proportions who were black

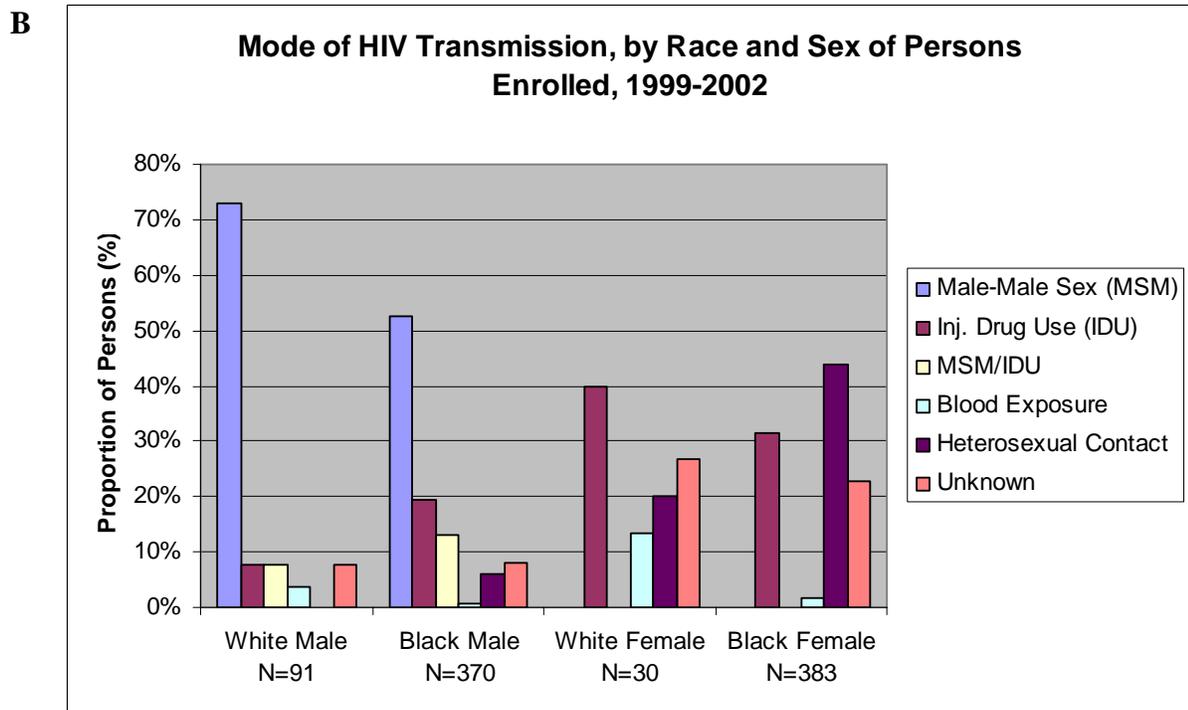
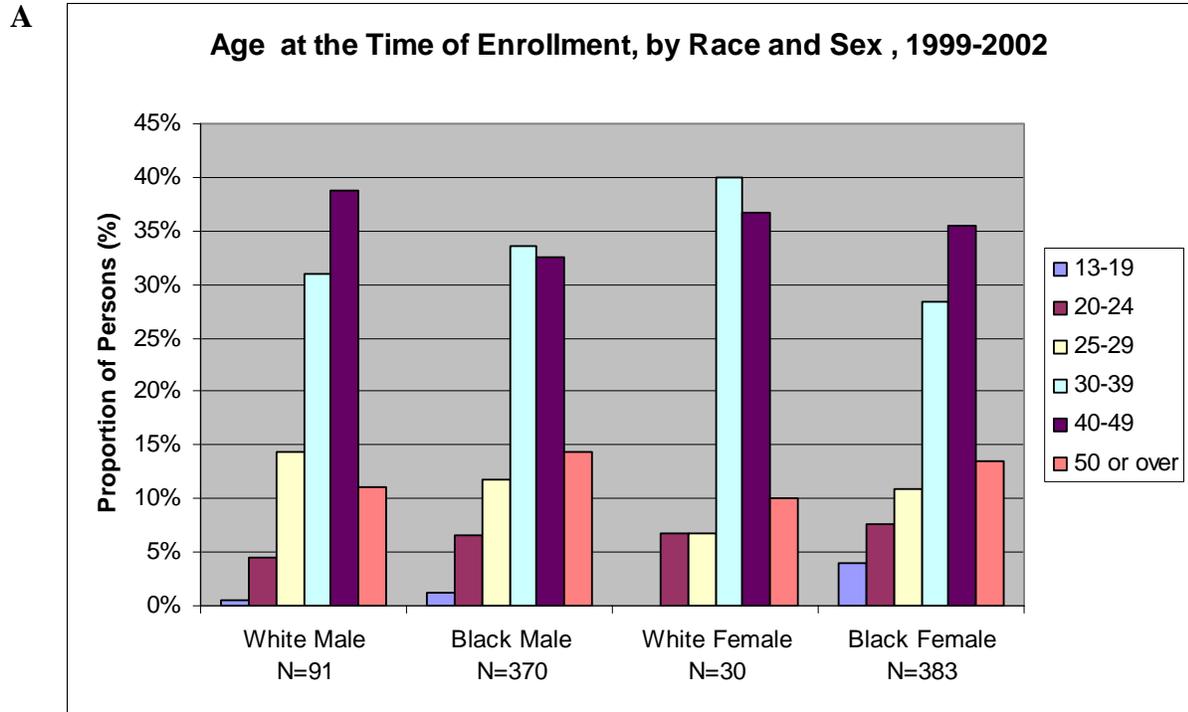
($p=0.0001$) and Hispanic ($p<0.0001$). The proportion with Unknown race/ethnicity also increased ($p<0.0001$), while the proportion of Other race/ethnicity groups (Asian, Pacific Islander, American Indian and Alaskan Native) was small ($<1\%$) and did not have a linear trend ($p=0.135$).

Age. The age distribution of persons newly enrolled in ASD shifted toward older age groups over the time period, 1991-2002. There were significant downward linear trends in the proportions with age 25-29 ($p=0.0001$) and 30-39 ($p<0.0001$), while there were significant upward linear trends in the proportions with age 40-49 (<0.0001) and over 50 ($p<0.0001$). There were not significant linear trends in the proportions with age 13-19 ($p=0.187$) or age 20-24 ($p=0.316$). However, the small numbers of persons in these latter two age groups limited the power to show a significant change.

Mode of HIV Transmission. The proportion of newly enrolled persons whose mode of HIV transmission was a history of injection drug use decreased ($p<0.0001$), while the proportion whose HIV infection was attributed to heterosexual contact increased ($p=0.0001$), over the time period, 1991-2002. The proportion of persons whose mode of HIV transmission was Unknown also increased ($p<0.0001$). The increase in the proportion infected by heterosexual contact may have increased even more than these data show, because many of those with Unknown mode were women who probably were infected heterosexually but did not meet the CDC definition of heterosexual transmission. (See Definitions.). There were not significant linear trends in the proportions whose HIV infection was attributed to Male-Male Sex ($p=0.127$), or Other modes ($p=0.057$).

Representativeness. These adjusted proportions reflected the characteristics of the population of persons who obtained HIV care at the ASD sites. With respect to demographics and modes of HIV transmission, the ASD population was representative of the population of HIV-positive persons in Southeast Michigan whose HIV diagnosis had been reported to HARS.

Figure 2
Age (A) and Modes of HIV Transmission (B) of Persons Who Were Enrolled in 1999-2002, by Race-sex Group



The age distributions were similar in all four race-sex groups ($p=0.84$). Analysis of the age distributions by sex and race separately also did not show any differences between groups ($p=0.57$ and 0.84 , respectively).

The distribution by mode of HIV transmission, in contrast, varied dramatically among the race-sex groups ($p<0.001$). The most frequent mode for both white and black males was male-male sex, while for white females it was injection drug use, and for black females heterosexual contact. The category, Other, is not shown because it was less than 1% for all four groups. Caution should be exercised in interpreting the data on white females because of their low number.

DISEASE STATUS AT THE TIME OF ENROLLMENT

Table 2
Hospitalization and Vital Status at the Time of Enrollment, by Two-year Periods

These proportions include events that occurred before the end of the first six-month follow-up interval, which was six months after the person was enrolled in ASD. For persons whose first contact with an ASD site was hospitalization, death would have been counted if it occurred during the initial hospitalization or within six months after the discharge from that initial hospitalization. For persons whose first contact with an ASD site was an outpatient visit, hospitalization or death would have been counted if it occurred within six months after the first outpatient visit.

Time Period	Proportion of Persons Newly Enrolled During the Time Period						p*
	91-92	93-94	95-96	97-98	99-00	01-02	
N	1253	816	691	583	529	413	
Hospitalized	55%	55%	56%	53%	53%	57%	0.69
Died	12%	13%	11%	7%	6%	5%	<0.0001

*Chi-square test for linear trend

The proportion of persons recently enrolled in ASD who were hospitalized was 55% overall and did not show a linear trend over the time period, 1991-2002. This finding suggested that the proportion of HIV-infected persons who entered medical care when they were sick was similar before and after HAART became available (1996). A factor that may have contributed to the proportion hospitalized at the time of enrollment in ASD was the fact that the ASD sites provided both primary and tertiary care.

The proportion of recently enrolled persons who died decreased by about half and did show a significant linear trend over the time period. This decrease reflected the introduction of HAART and other improvements in prevention of opportunistic illnesses.

Figure 3
Diagnosis of AIDS Among Newly Enrolled Persons, by Two-year Periods

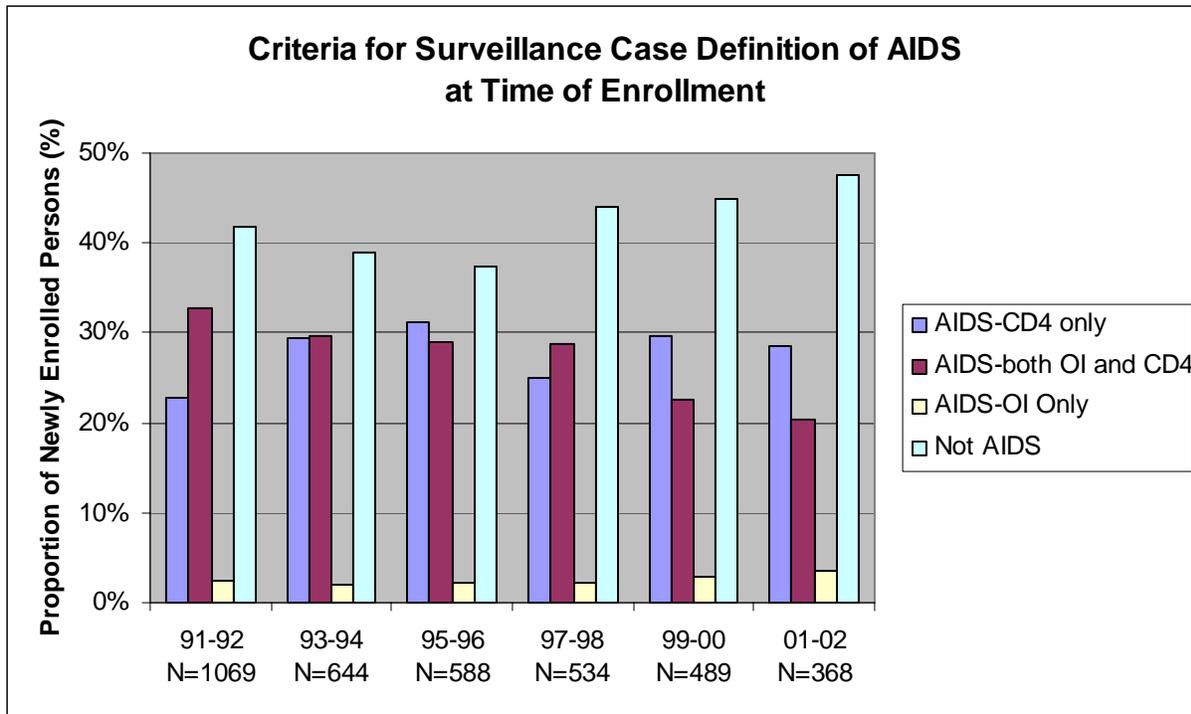
Persons were included only if a CD4⁺ T-cell count or percent was recorded during the baseline or the first six-month follow-up record. Overall, 14% of the newly enrolled persons were excluded on this basis, and it is unknown what proportion of them might have met the criteria for the surveillance case definition of AIDS. The data included CD4⁺ T-cell counts and percents that were recorded during this 18-month period and AIDS-defining illnesses (OI) that occurred at any time before the end of the first follow-up interval.

AIDS-CD4 Only: Diagnosis of AIDS based on a CD4⁺ T-cell count < 200 cells/mm³ or <14% of total lymphocytes, without diagnosis of an AIDS-defining illness.

AIDS-both OI and CD4: Diagnosis of AIDS for a person who has both a diagnosis of an AIDS-defining illness and a CD4⁺ T-cell count < 200 cells/mm³ or <14% of total lymphocytes.

AIDS-OI Only: Diagnosis of AIDS based on the diagnosis of an AIDS-defining illness when the CD4⁺ T-cell count data did not meet the criteria for the surveillance case definition of AIDS.

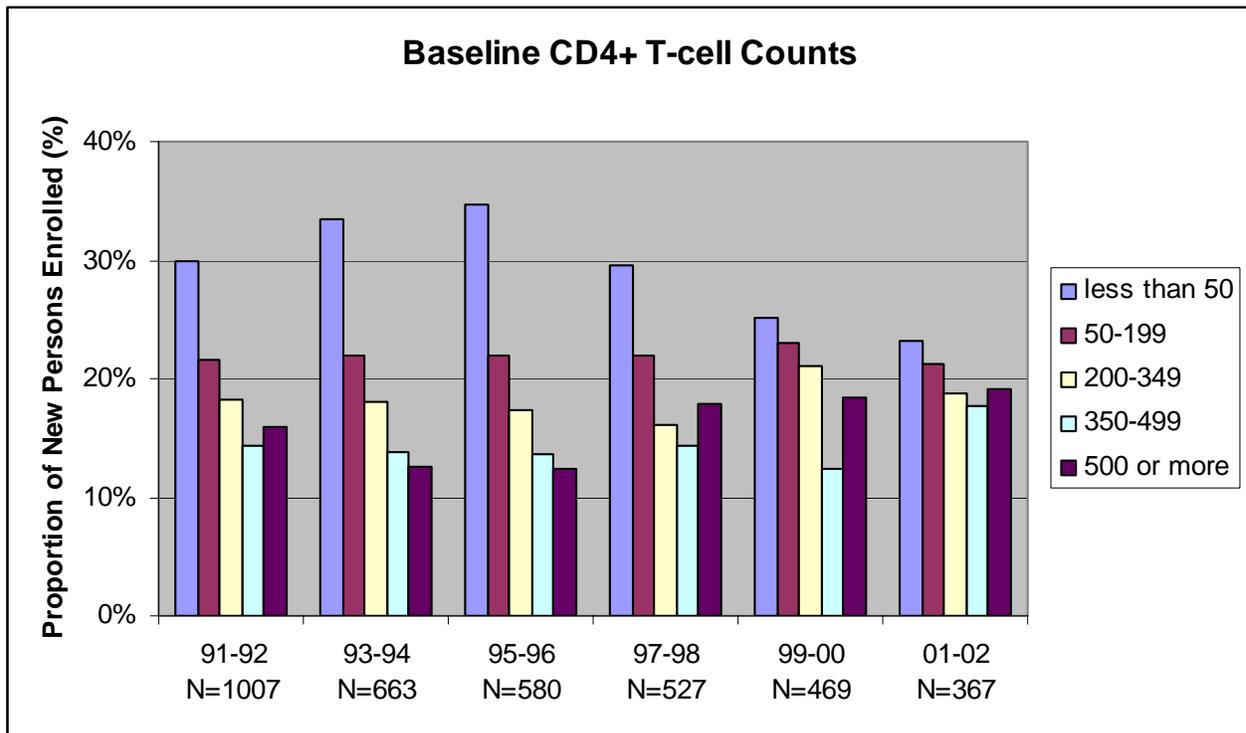
Not AIDS: The person's data did not meet the criteria for the surveillance case definition of AIDS.



Diagnosis of AIDS was made primarily on the basis of CD4⁺ T-cell data, and of these 40-60% (in the various time periods) also had a diagnosis of AIDS-defining illness. Only 3-5% of AIDS diagnoses were based on the occurrence of an AIDS-defining illness when the CD4⁺ T-cell data did not meet the criteria for the surveillance case definition of AIDS. There was a statistically significant decrease in the proportion of persons with a diagnosis of AIDS at the time of enrollment, from a high of 63% in 1998-1996 to a low of 52% in 2001-2002 (p=0.015).

Figure 4
Baseline CD4⁺ T-cell Counts of Newly Enrolled Persons, by Two-year Periods

Persons were included only if a CD4⁺ T-cell count was recorded for them in the baseline or the first six-month follow-up record, resulting in exclusion of 15% of the newly enrolled persons. The number of persons included in this analysis was less than in Figure 3 because the analysis in Figure 3 included persons who had a CD4⁺ T-cell percent recorded but not a count. This analysis included the lowest CD4⁺ T-cell count that was recorded during this 18-month period. Counts are expressed in cells/mm³.



The distribution of CD4⁺ T-cell counts varied with time (p=0.001). The most notable changes were that the proportion of persons coming to the ASD sites for HIV care with CD4⁺ T-cell counts <50 cells/mm³ decreased over time, while the proportions with CD4⁺ T-cell counts ≥350 cells/mm³ increased. It should be noted that these CD4⁺ T-cell counts reflect only disease status when persons first contacted an ASD site for HIV care. They do not necessarily reflect disease status at the time HIV infections were diagnosed or at the time persons first sought care.

Table 3
Hospitalization, Vital Status and AIDS Diagnosis at the Time of Enrollment, 1999-2002, by Race-sex Group

Persons were included in analysis of hospitalization and vital status, regardless of whether CD4⁺ cell data was recorded for them. For analysis of AIDS diagnosis, a CD4⁺ count or percent in the baseline record or the first follow-up record was required.

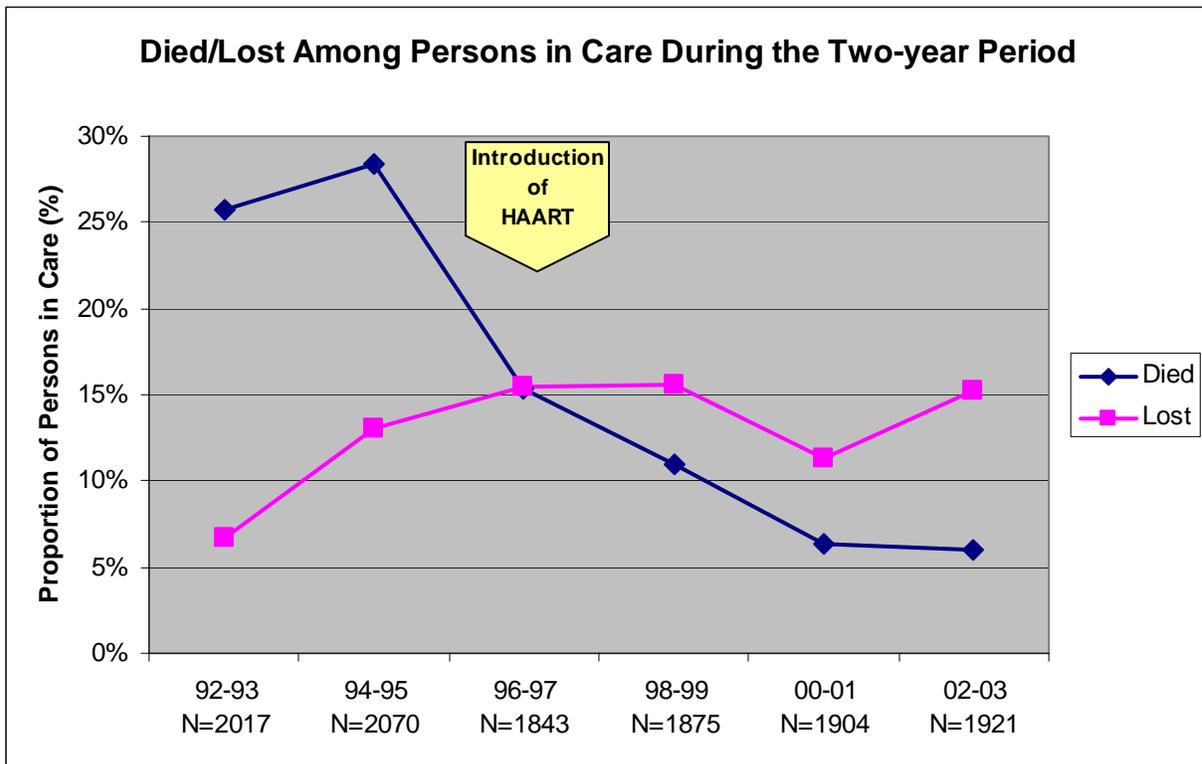
Hospitalization, Vital Status and AIDS Diagnosis at the Time of Enrollment, 1999-2002, by Race-sex Group					
	N and Proportion of Persons in the Race-sex Group				p
	White Male	Black Male	White Female	Black Female	
<i>N</i>	91	370	30	383	
Hospitalized	33%	55%	50%	59%	0.001
Died	3%	7%	3%	5%	0.33
<i>N</i>	84	337	28	345	
AIDS Diagnosis	49%	60%	50%	49%	0.025

The proportion hospitalized and proportion with an AIDS diagnosis varied significantly among the race-sex groups, but the proportion that died did not. The most striking differences were that hospitalization was less frequent among white males than among the other race-sex groups, and a higher proportion of black males had an AIDS diagnosis than the other race-sex groups. The higher proportion of black males that died suggested a difference, but the power to show a statistically significant difference was limited by the small number of deaths. Data are shown from 1999 –2002 to show more recent trends.

FOLLOW-UP DATA

Figure 5
Vital Status During Follow-up, by Two-year Periods

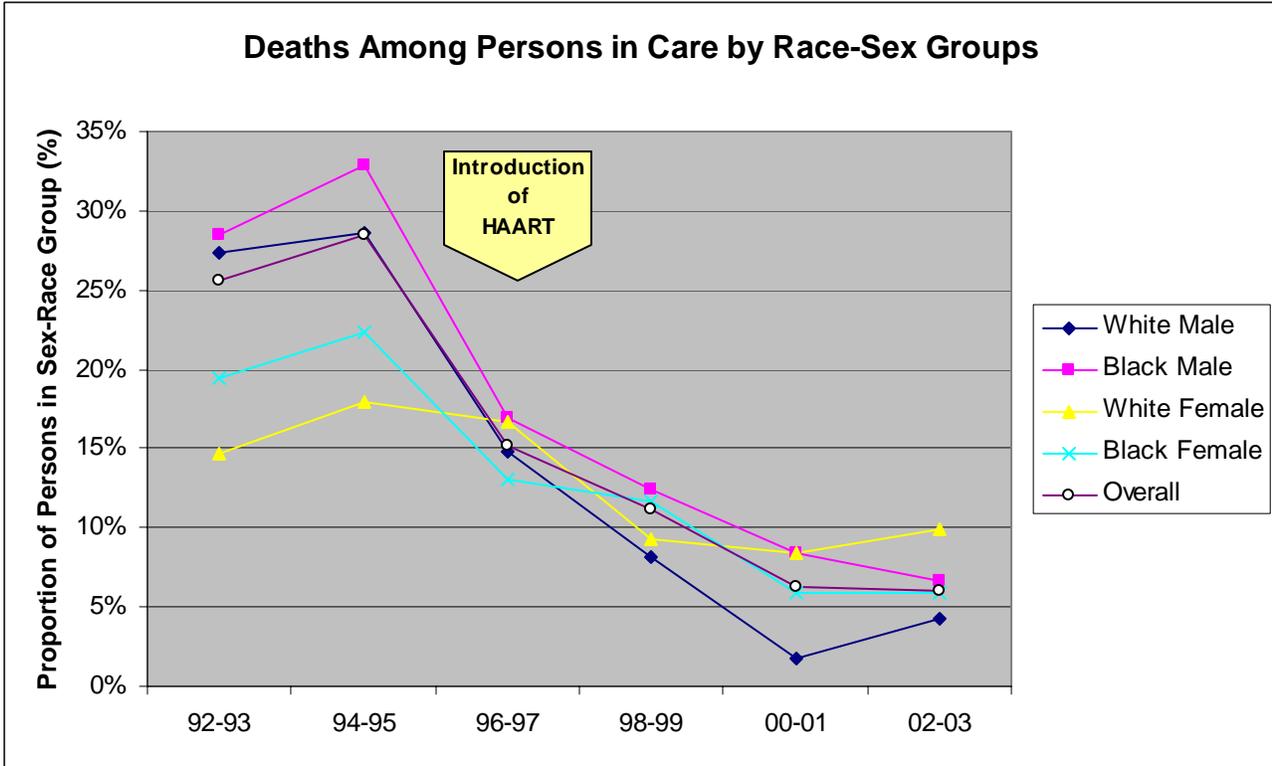
Persons were included if any follow-up record existed for them (from 6 months after enrollment onward) during any part of the two-year period. Records with Unknown and Lost-to-follow-up status were included. The vital status used for each person was that at the end of the last follow-up interval in the two-year period.



The proportion of persons who died decreased dramatically from 1994-1995 to 2002-2003, as prevention of opportunistic illnesses and treatment of HIV improved.

The increases in deaths and loss to follow-up during the first six years of the project reflected the fact that an increasing proportion of the persons had been in care for a longer time, and, most likely, had been infected with HIV for a longer time. In addition, according to the ASD protocol, it was not possible for a person to be considered lost to follow-up in less than 18 months after enrollment.

Figure 6
Deaths During Follow-up, by Race-sex Groups



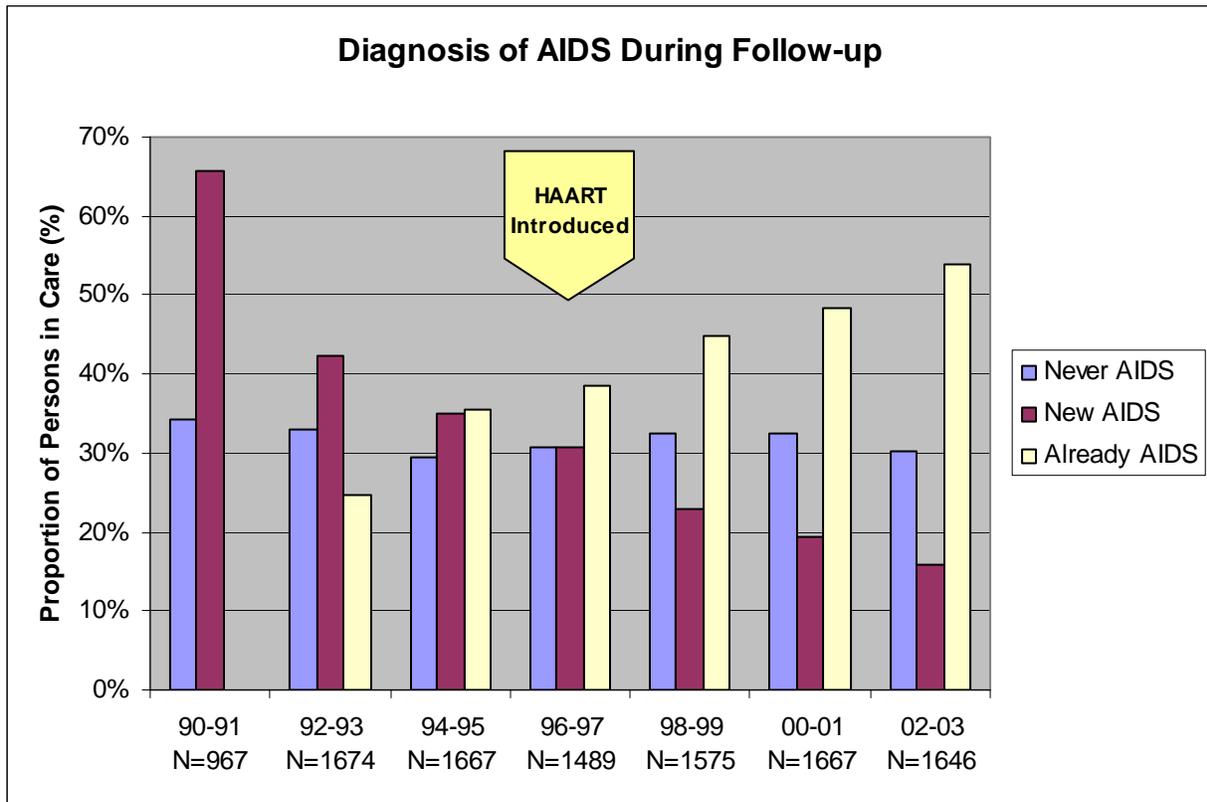
	Numbers of Persons in Each Race-Sex Group for Each Two-year Period				
	White Male	Black Male	White Female	Black Female	Overall
92-93	527	935	68	443	1973
94-95	514	908	78	523	2023
96-97	454	751	66	521	1792
98-99	394	759	75	582	1810
00-01	338	765	71	646	1820
02-03	325	751	71	678	1825

All four groups benefited from the improvements in prevention of opportunistic illnesses and HIV treatment, 1994-1995 through 2002-2003. During the first two periods, 92-93 and 94-95, the death rate was highest among black males, followed by white males, black females and white females, in that order ($p=0.001$ for 92-93; $p<0.001$ for 94-95). The differences between groups disappeared with the introduction of improved care in the subsequent periods ($p=0.29$ for 96-97; $p=0.15$ for 98-99; $p=0.26$ for 02-03), with the exception of 2000-2001 ($p<0.001$). The unusually low death rate for white males in 2000-2001 is unexplained.

Figure 7
AIDS Diagnoses During Follow-up

The proportions of persons in care during each two-year period who never had AIDS, who were newly diagnosed with AIDS, and who had previously had an AIDS diagnosis, according to the AIDS surveillance case definition criteria (See Definitions.).

Never AIDS: Persons who did not meet the AIDS criteria before or during the two-year period.
 New AIDS: Persons who met the AIDS criteria for the first time during the two-year period
 Already AIDS: Persons who had met the AIDS criteria before the beginning of the two-year period

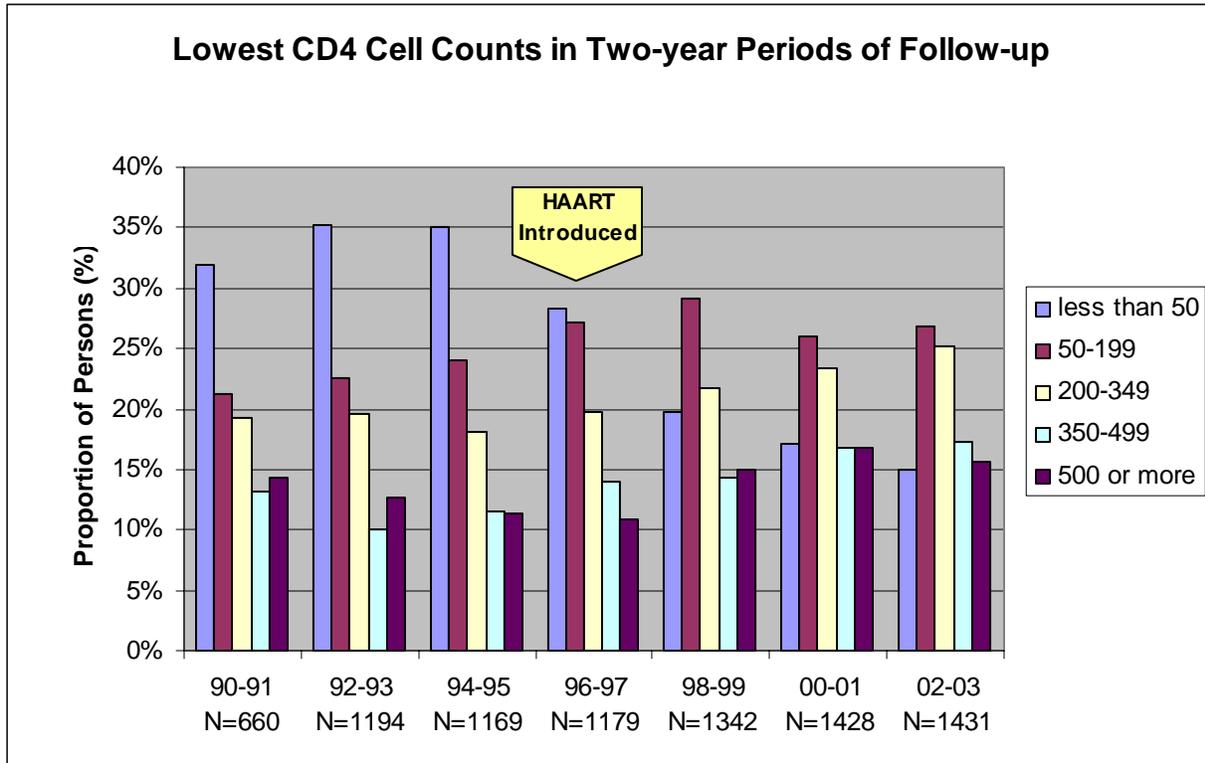


The relative proportions of persons in care in these categories changed over the project period ($p < 0.0001$) as a result of improvements in care.

1. Progression of HIV disease to AIDS among persons in care slowed. This change was reflected in the decreasing proportion of persons with a new diagnosis of AIDS at the end of the two-year period among those who did not have AIDS at the beginning of the period.
2. Life expectancy after persons met the AIDS criteria increased. This change caused the increase in the proportion that already had an AIDS diagnosis.

Figure 8
Lowest CD4⁺ T-cell Counts by Two-year Periods of Follow-up

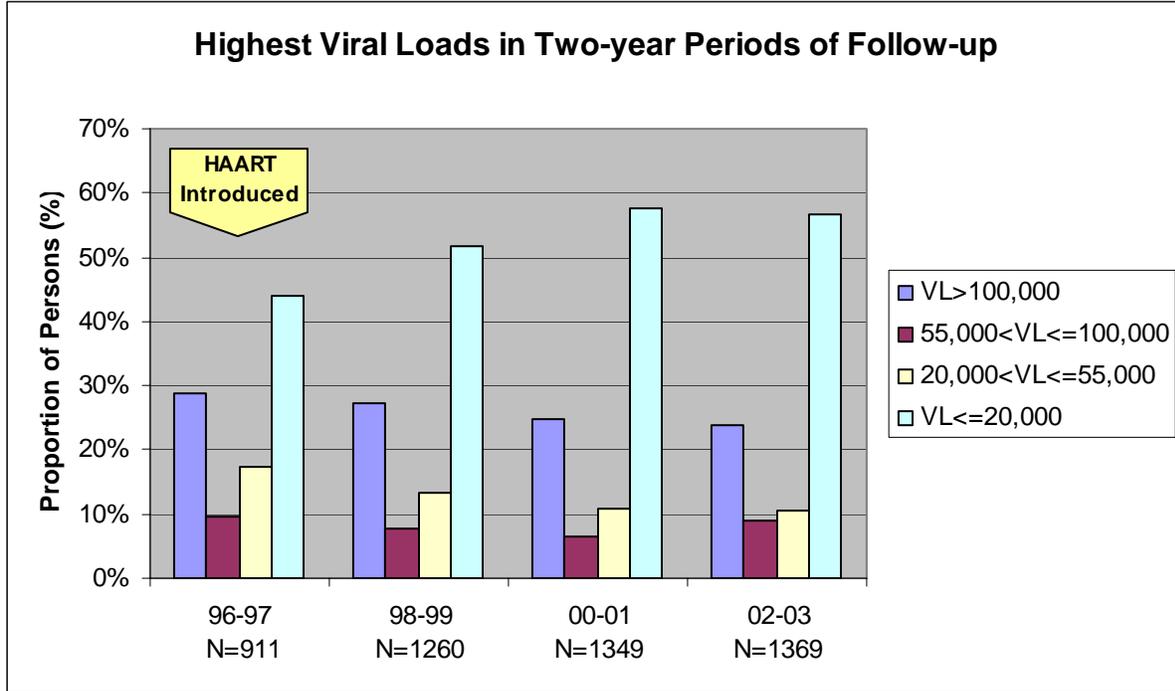
The persons included were those who received follow-up care and had at least one CD4⁺ T-cell count during the two-year period. The CD4⁺ T-cell count used for each person was their lowest during follow-up in the two-year period. Counts are expressed in cells/mm³.



The proportion that had a count less than 50 cells/mm³ decreased as HIV treatment and prevention of opportunistic illnesses improved, from 1994-1995 to 2002-2003. The persons with a CD4⁺ T-cell count less than 200 cells/mm³ included those that refused treatment, or whose HIV infection was resistant to treatment. In addition, those whose CD4⁺ T-cell counts may have previously improved with treatment, but decreased again as a result of treatment failure during the two-year period, might have had CD4⁺ T-cell counts in this range.

Figure 9
Highest Viral Load Measurements by Two-year Periods of Follow-up

The persons included were those who received any follow-up care and had at least one viral load measurement during the two-year period. The viral load measurement used for each person was their highest during follow-up in the two-year period.



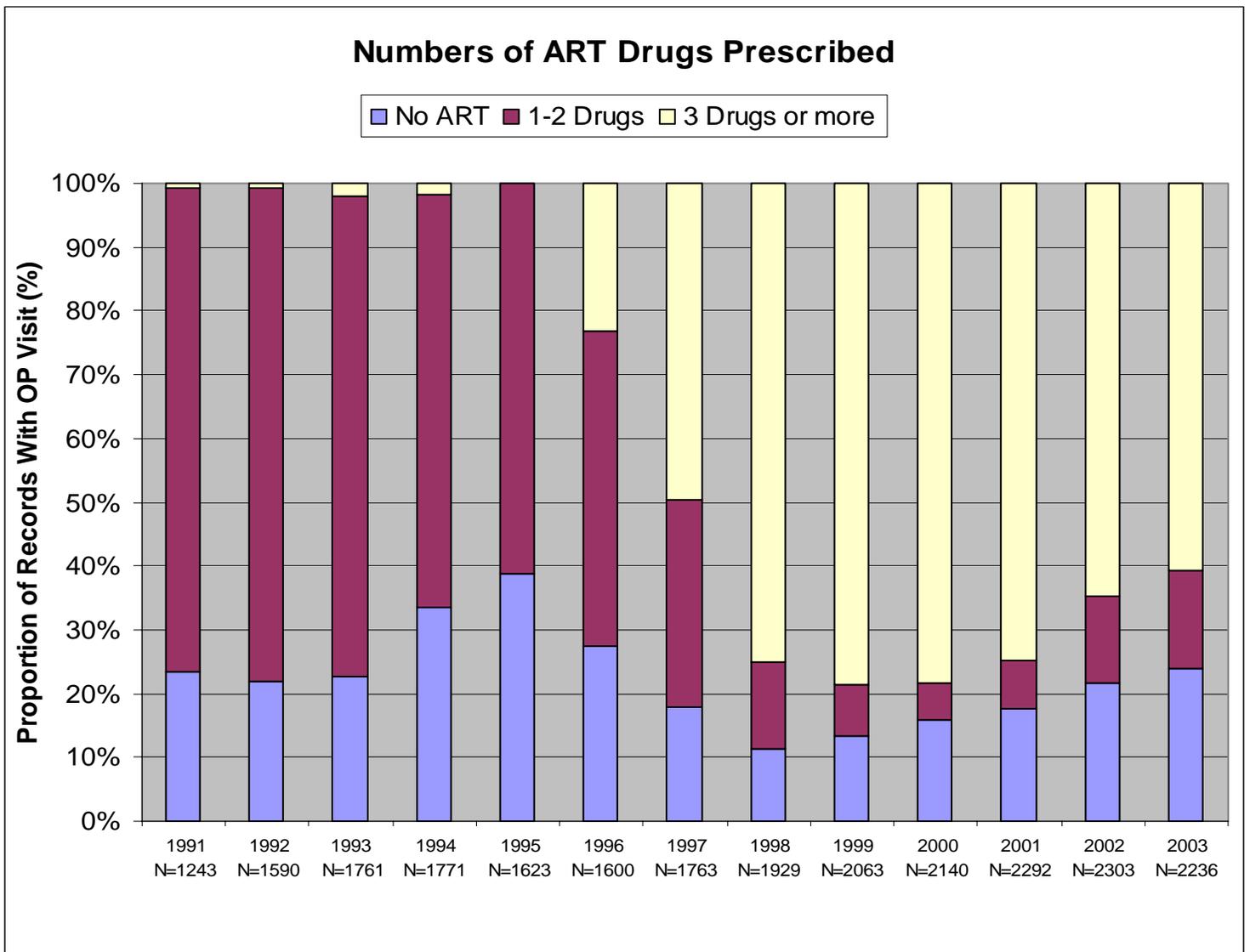
The proportion whose highest measurement in the two-year period was $\leq 20,000$ copies/ml increased between 1996-1997 and 2002-2003 ($p < 0.001$), while the proportion with a viral load $> 100,000$ copies/ml decreased ($p = 0.003$). In contrast to the $CD4^+$ T-cell counts, viral load measurements were not available for the pre-HAART years. Measuring viral loads only became a routine part of HIV care at about the same time HAART was introduced. Forty percent of the persons in care had at least one viral load measurement in 1996, 80% in 1997, and 80-90% in subsequent years.

Figure 10
Antiretroviral Regimens Prescribed During Follow-up Intervals with an Outpatient Visit

This analysis was based on follow-up records, with each person contributing up to two records to a single year, or up to 4 records to a two-year period. The records included were those in which the person had at least one outpatient visit recorded. The CD4⁺ T-cell counts are expressed in cells/mm³.

- A. The proportion of follow-up records with an outpatient visit recorded in which no ART drugs, one or two ART drugs, or three or more ART drugs were prescribed, by year.
- B. The proportion of follow-up records with an outpatient visit recorded in which the three types of ART regimens were prescribed, by two-year period and category of lowest CD4⁺ T-cell count for the person at any time in follow-up.

A



B

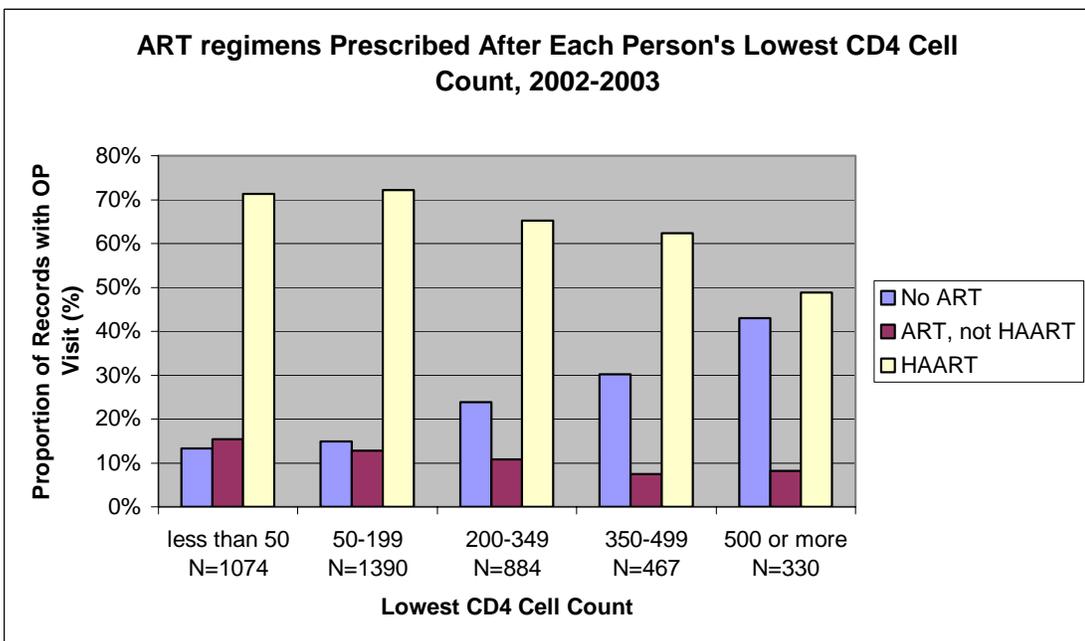
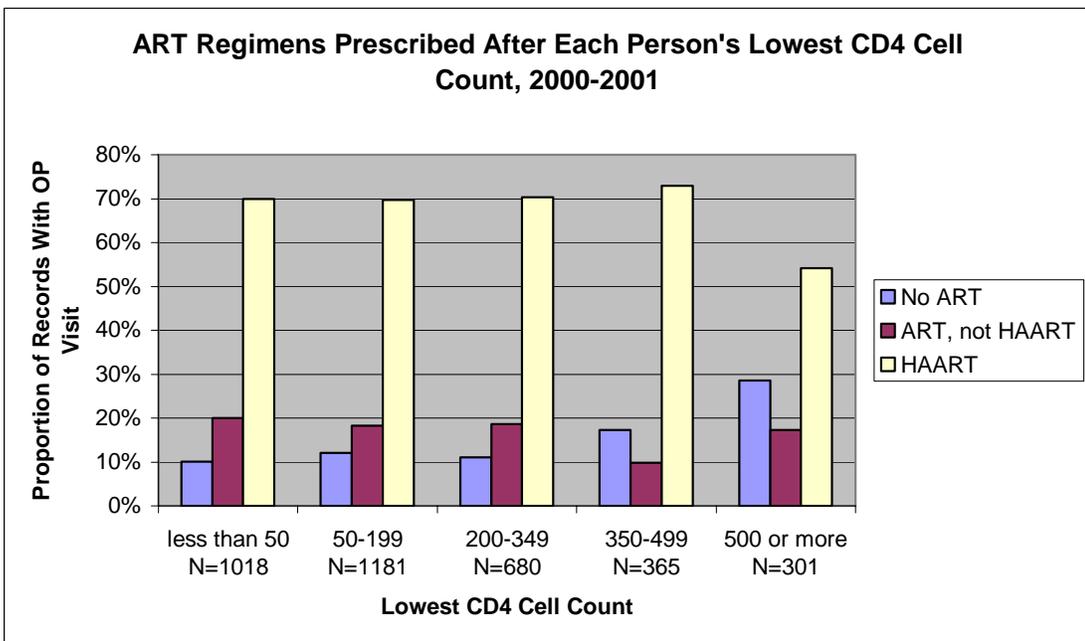
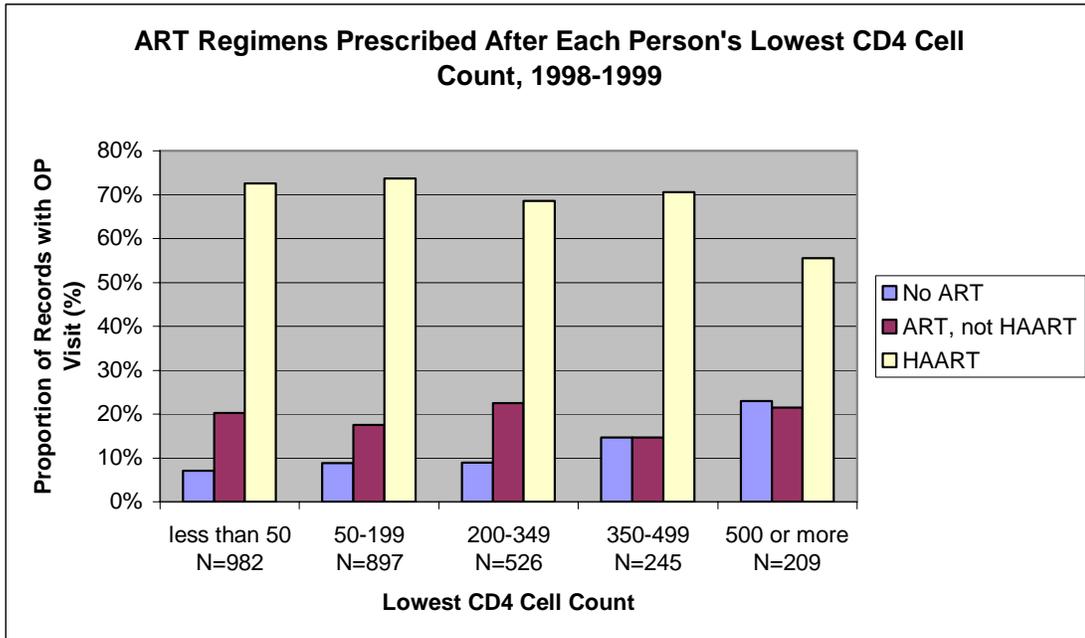


Figure 10 A shows the total number of different antiretroviral drugs that were prescribed in a six-month follow-up interval, without regard to which were prescribed simultaneously as part of a treatment regimen. The numbers of antiretroviral drugs prescribed increased during the time period 1996-1998, corresponding to the introduction of highly active combination antiretroviral therapy (HAART). After 1998 the proportion of patients that were not prescribed antiretroviral therapy (ART) began to increase again. Over the years 1998-2003, the Public Health Service guidelines for initiating antiretroviral therapy evolved, generally decreasing the CD4 cell count at which starting treatment was recommended. To examine whether these changes may have been responsible for the increase in the proportion of patients not receiving ART, we investigated the relationship between CD4⁺ T-cell counts and ART regimens prescribed.

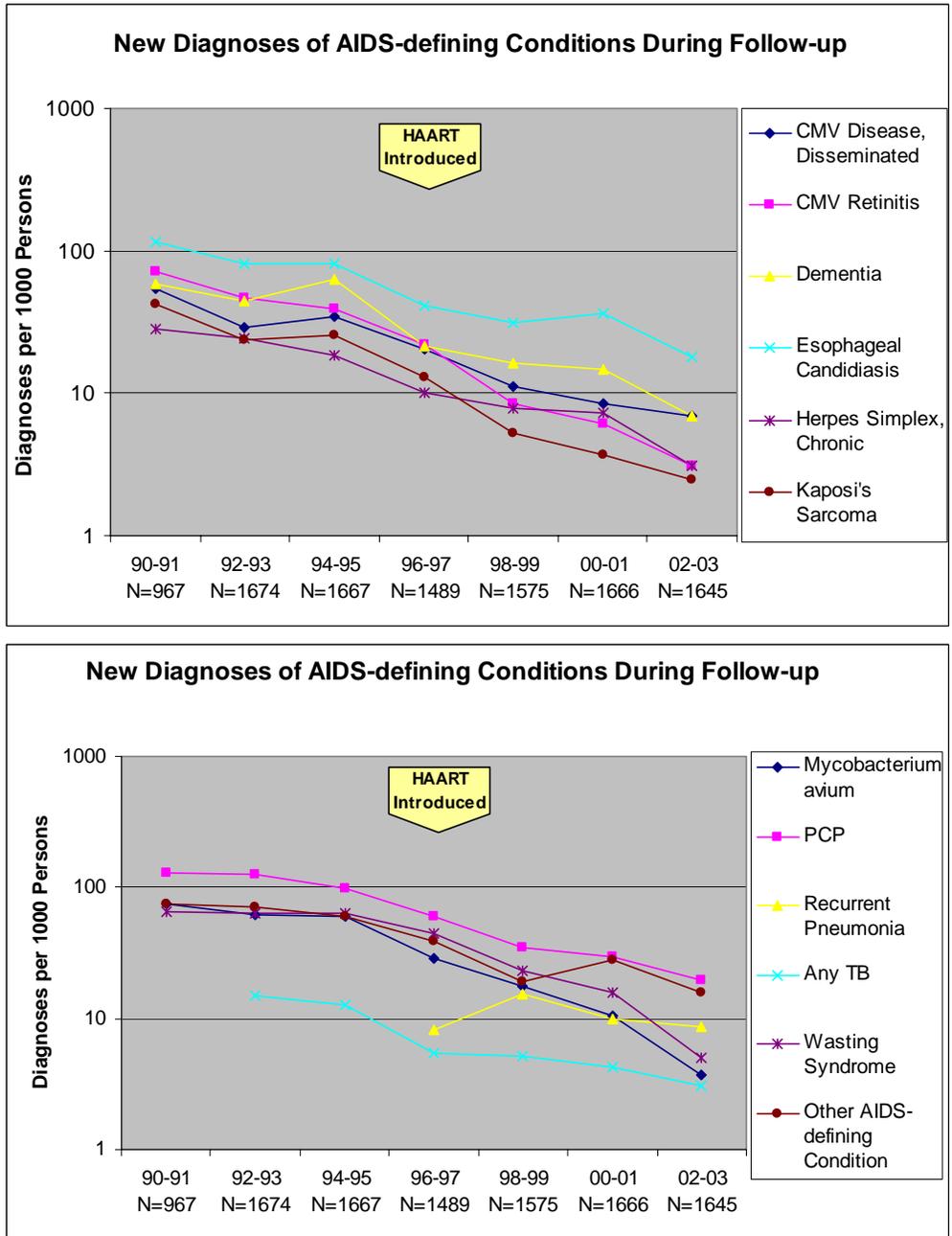
Figure 10 B shows the prescription of antiretroviral regimens, starting in 1998, with a separate graph for each two-year time period. The follow-up records included in this analysis for each person were the record with the lowest CD4⁺ T-cell count at any time in their ASD follow-up and all the subsequent records. For each category of lowest CD4⁺ T-cell count, the distribution of records in the two-year period among the various types of regimens is shown. The types of regimens were HAART, ART that does not meet the definition of HAART, and No ART (See Definitions.).

The higher the lowest CD4⁺ T-cell count was, the higher was the proportion of subsequent records without ART prescription. In addition, the proportion of records without ART prescription increased over the years, 1998-2003, especially in the higher categories of lowest CD4⁺ T-cell counts.

These observations reflect the Public Health Service guidelines for initiating antiretroviral therapy, which are based primarily on CD4⁺ T-cell counts. The lower the CD4⁺ T-cell count, the stronger the recommendation that HAART be prescribed. Over the years 1998-2003, it was shown that HAART did not provide significant benefit for persons with CD4⁺ T-cell counts of 500 cells/mm³ or more, and the benefit for persons with CD4⁺ T-cell counts of 200-349 cells/mm³, and especially 350-499 cells/mm³, was less than the benefit for persons with CD4⁺ T-cell counts less than 200 cells/mm³. Accordingly, the recommendations evolved, decreasing the CD4⁺ T-cell count at which starting HAART was strongly recommended and increasing the range of discretion left to the physician and the patient.

Figure 11
New Diagnoses of the Most Frequent AIDS-defining Conditions (OI) Among Persons in Follow-up Care, by Two-year Periods

The number of persons with a first diagnosis of each condition was counted and divided by the number of persons who were in follow-up care during the two-year period and had not previously had a diagnosis of the condition.



The frequencies of all these conditions decreased over the ASD project period, 1990-2003, and in most cases the rank order of their frequencies was similar throughout the project period.

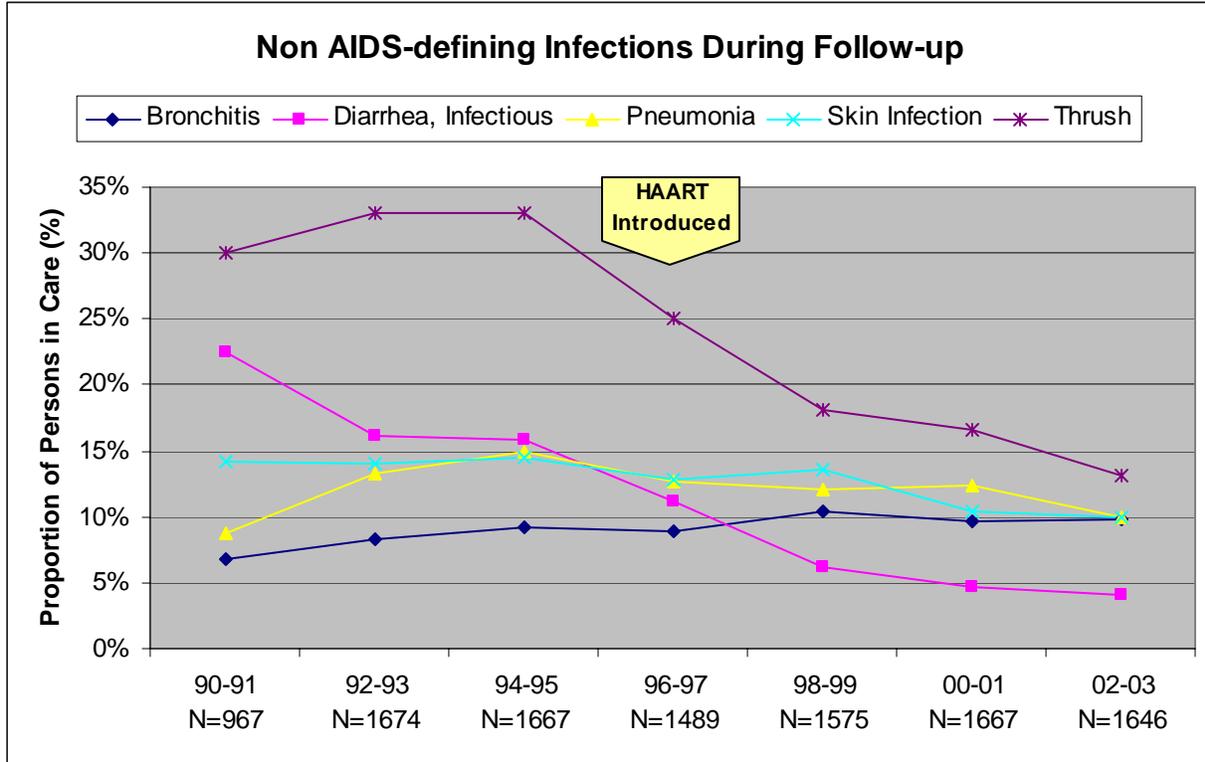
Table 4
Diagnoses of the Less Frequent AIDS-defining Conditions (OI) Among Persons in Follow-up Care

This table shows the frequencies of the AIDS-defining conditions not shown in Figure 12, among the 4488 persons with one or more follow-up records during the project period, 1990-2003.

AIDS-Defining Condition	Number of Diagnoses	Proportion of Persons
Burkitt's Lymphoma	4	0.09%
Candidiasis, Bronchi or Lungs	13	0.29%
Carcinoma, Invasive Cervical	2	0.04%
Coccidiomycosis, Extrapulmonary	9	0.20%
Cryptococcosis, Extrapulmonary	106	2.36%
Cryptosporidiosis, Chronic Intestinal	38	0.85%
Histoplasmosis, Extrapulmonary	13	0.29%
Immunoblastic Lymphoma	38	0.85%
Isosporiasis	1	0.02%
Mycobacterium, Other, Disseminated	41	0.91%
Primary Brain Lymphoma	67	1.49%
Progressive Multifocal Leukoencephalopathy	72	1.60%
Recurrent Salmonella Septicemia	3	0.07%
Toxoplamsosis of Brain	97	2.16%

The frequencies of these AIDS-defining conditions were lower than any of the conditions shown in Figure 12. Only four were diagnosed in more than one percent of the persons who received any follow-up care. In rank order of frequency (highest to lowest), these were extrapulmonary cryptococcosis, toxoplasmosis of the brain, progressive multifocal leukoencephalopathy, and primary brain lymphoma.

Figure 12
The Five Most Common Non AIDS-defining Infections



Thrush was the most common non AIDS-defining infection throughout the project period. Like the AIDS-defining conditions, thrush became much less frequent after the introduction of HAART, decreasing by more than half.

The frequency of infectious diarrhea followed a similar time course. In 2002-2003, it was less than one fourth the frequency in 1990-1991. Infectious diarrhea included intestinal cryptosporidiosis of less than one-month duration (not AIDS-defining), as well as other types of infections.

In contrast, the frequencies of bronchitis, pneumonia and skin infections remained relatively stable throughout the ASD project period. These diagnoses were recorded for 7-15% of the persons in care in each two-year period.

These observations suggested that thrush and infectious diarrhea might have been opportunistic illnesses, while the frequencies of bronchitis, pneumonia and skin infections were less influenced by the HIV-induced damage to the immune system.

Table 5
Characteristics of HIV/Hepatitis Co-Infected Persons in Follow-up Care, 2001-2003

Hepatitis A (HAV), Hepatitis B (HBV), or Hepatitis C (HCV) co-infection is defined as diagnosis of HAV, HBV (acute or chronic) or HCV, recorded in ASD at any time in the past and through 2003. Age is the age as of the last care recorded in 2001-2003. HAV and HBV Vaccination include vaccinations recorded in ASD at any time in the past and through 2003.

Modes of HIV transmission are defined under Definitions.

	All (n=1790)	HAV Co-infected (n=64)	HBV Co-infected (n=207)	HCV Co-infected (n=353)
Sex			*	*
Male	58%	66%	68%	50%
Female	42%	34%	32%	50%
Race				*
White	20%	30%	17%	13%
Black	75%	67%	80%	83%
Others	5%	3%	2%	4%
Age				*
<20	1%	0%	0%	0%
20-29	10%	11%	5%	3%
30-39	27%	14%	29%	9%
40-49	38%	39%	38%	43%
>=50	24%	36%	28%	44%
Modes of HIV Transmission			*	*
MSM	38%	45%	45%	10%
IDU	30%	34%	41%	78%
Blood Exposure	2%	5%	1%	5%
High-Risk Heterosexual	21%	8%	8%	6%
Presumed Heterosexual	8%	8%	3%	1%
Unknown/Others	1%	0%	<1%	0%
HAV Vaccination	14%	5%*	13%	23%*
HBV Vaccination	21%	24%	4%*	14%*

*Proportions significantly different from the proportions among all the persons in care, $p < 0.05$ in Chi square test comparing the distribution of co-infected patients among the categories of the demographic, vaccination or transmission risk factor to the distribution of all the persons in care.

Hepatitis C (HCV) was the most common hepatitis co-infection among HIV-infected persons. Of the 1790 persons in care in 2001-2003, 353 (20%) had a diagnosis of HCV at some time during ASD follow-up, while 207 (12%) had a diagnosis of hepatitis B (HBV), and 64 (4%) of hepatitis A (HAV). The true rates of co-infection with HBV, and particularly with HCV, may be higher than these estimates because HBV and HCV infections are frequently asymptomatic, and

routine, universal testing of HIV-infected persons for HBV- and HCV-infection was being phased in during the period, 2001-2003.

This table shows the profiles of demographics and modes of HIV transmission for all the persons in care and for the populations co-infected with HAV, HBV and HCV. Of persons co-infected with HCV, higher proportions were female and black, compared to the proportions among all persons in care, and a higher proportion were over 40 years of age. The predominance of blood transfer as the transmission mode for HCV was reflected in the higher proportions of HCV-co-infected persons who had a history of drug injection or other blood contact recorded as their HIV transmission mode. In contrast, the demographic and HIV transmission mode profiles of persons co-infected with HAV (predominantly oral-fecal transmission) did not differ significantly from the profiles of all the persons in care. Among persons co-infected with HBV, the only significant differences were that higher proportions were male and had MSM or drug injection recorded as their HIV transmission mode, reflecting the transmission modes for HBV (sexual contact and blood transfer).

The proportions of persons in care who were vaccinated against HAV and HBV were lower among persons co-infected with the respective viruses. These differences may reflect a higher rate of infection among unvaccinated persons.

The impact of HCV co-infection on the health of HIV-infected persons is increasing. The numbers of new HCV cases in the U.S. increased in the 1970's and 1980's, and dropped precipitously in the early 1990's.³ These changes created a cohort of HCV-infected persons in the population, and the aging of this cohort is expected to lead to an increase in the number of persons with HCV-related late stage liver disease through at least 2015.⁴ HIV-infected persons will be impacted even more than the general population, because HIV/HCV co-infected persons have a higher risk of liver disease than persons infected with HCV alone.⁵ Planning for the care of HIV-infected persons will need to take into account the increasing numbers of HIV-HCV co-infected persons who are expected to develop late stage liver disease over the next decade or more. Liver disease associated with HCV and HBV infection is already one of the leading non-AIDS related causes of death among HIV-infected persons.⁶

Table 6
Primary Malignant Neoplasms, non AIDS-defining

This table shows the numbers of primary neoplasms diagnosed among persons with one or more follow-up records during the project period, 1990-2003, and the proportion of persons with the diagnosis. N-all was used for all neoplasms except the genitourinary, female and male, for which the sex-specific N's were used. N-all=4488, N-females=1423, and N-males=3065. This list includes only sites of neoplasms that are not AIDS defining.

Site of Neoplasm	Number of Diagnoses	Proportion of Persons
Lymphoma	62	1.38%
Genitourinary, female	44	3.09%
Lung	32	0.71%
Skin	21	0.47%
Breast	19	0.42%
Other	15	0.33%
Brain/Other CNS	14	0.31%
Anorectal	11	0.25%
Liver/Gall bladder	10	0.22%
Oral cavity/pharynx	8	0.18%
Intestine/colon	6	0.13%
Respiratory, Upper	6	0.13%
Bone	4	0.09%
Esophagus	4	0.09%
Endocrine	3	0.07%
Genitourinary, male	3	0.10%
Myeloma	3	0.07%
Stomach	3	0.07%
Renal (kidney, bladder)	2	0.04%
Respiratory, Lower	2	0.04%
Heart/Mediastinum	1	0.02%
Leukemia	0	0.00%

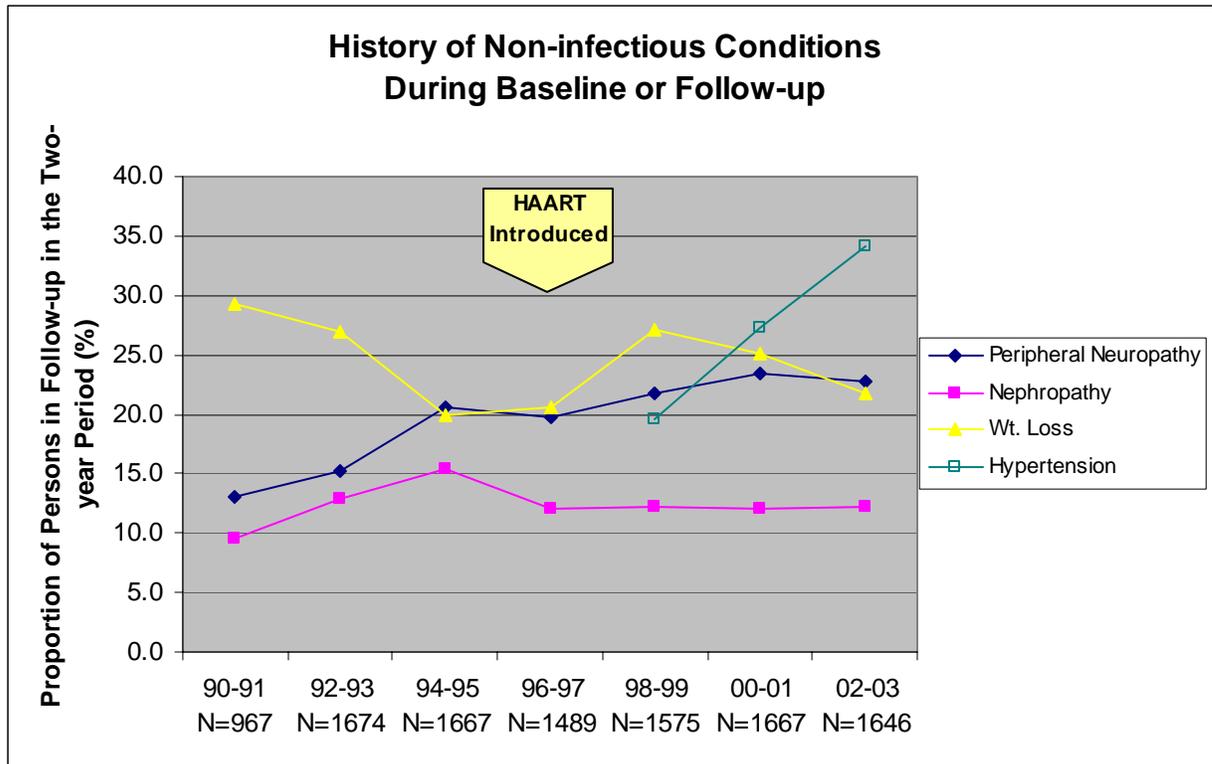
The frequencies of these neoplasms were very low. All but lymphoma and female genitourinary were diagnosed in less than 1% of the persons followed during the ASD project period, 1990-2003. Consequently, it was not possible to draw any conclusions about how the numbers of diagnoses of non AIDS-defining neoplasms may have varied with time.

Figure 13
Non-infectious Conditions, Diagnosed at Any Time in ASD, Baseline or Follow-up

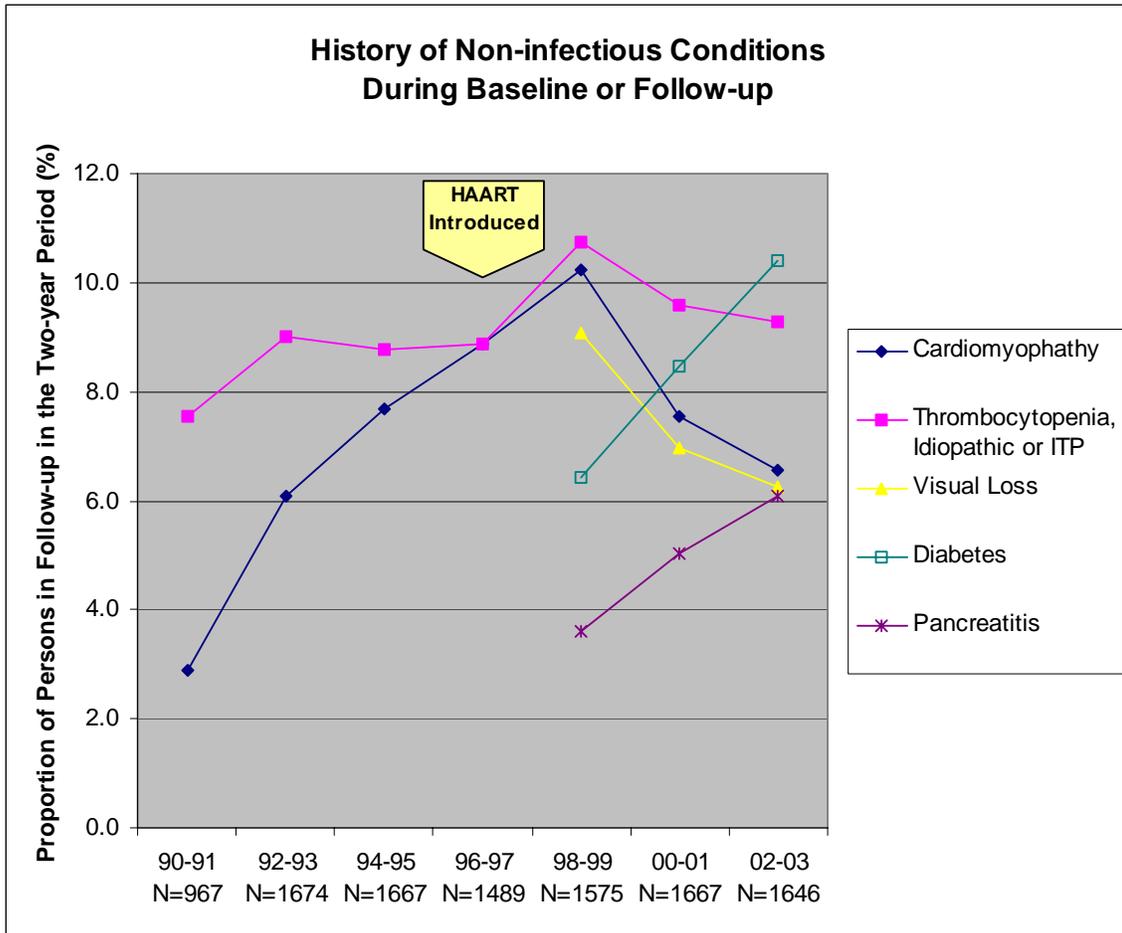
These figures show the proportions of persons with follow-up data recorded during the two-year period who had had a history of the condition at any time, recorded in their baseline or follow-up records through the two-year period.

A, the four most frequent non-infectious conditions; B, the five next most frequent non-infectious conditions; C, pregnancy (N=number of females).

A

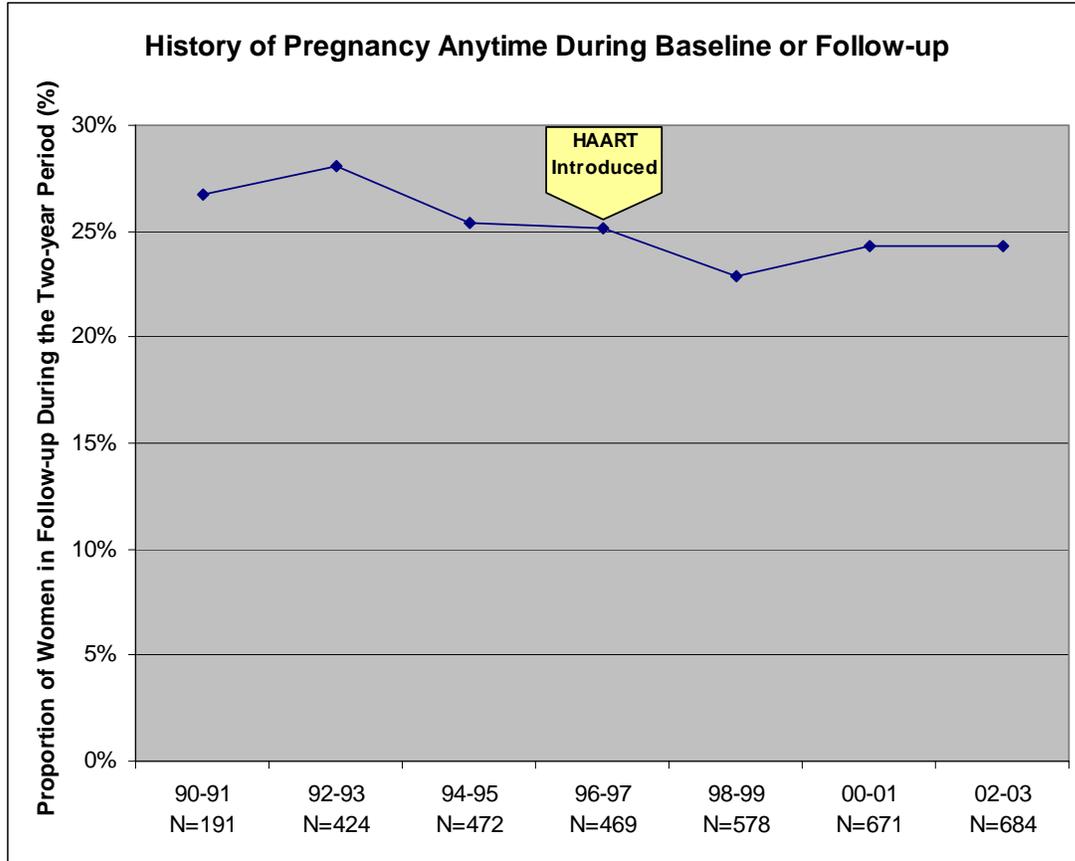


B



HIV infection and antiretroviral therapy both may influence the frequencies of the conditions in Figure 13 A and B. The conditions for which data collection was started in 1998 were added because their frequencies were expected to change with the use of HAART. However, a detailed analysis of these changes is beyond the scope of this report.

C



About a quarter of the women in care in any two-year period were pregnant during that two-year period or had been pregnant earlier in their history of receiving care for HIV at an ASD site.

Table 7
Other Conditions and Procedures Anytime in ASD, Baseline or Follow-up

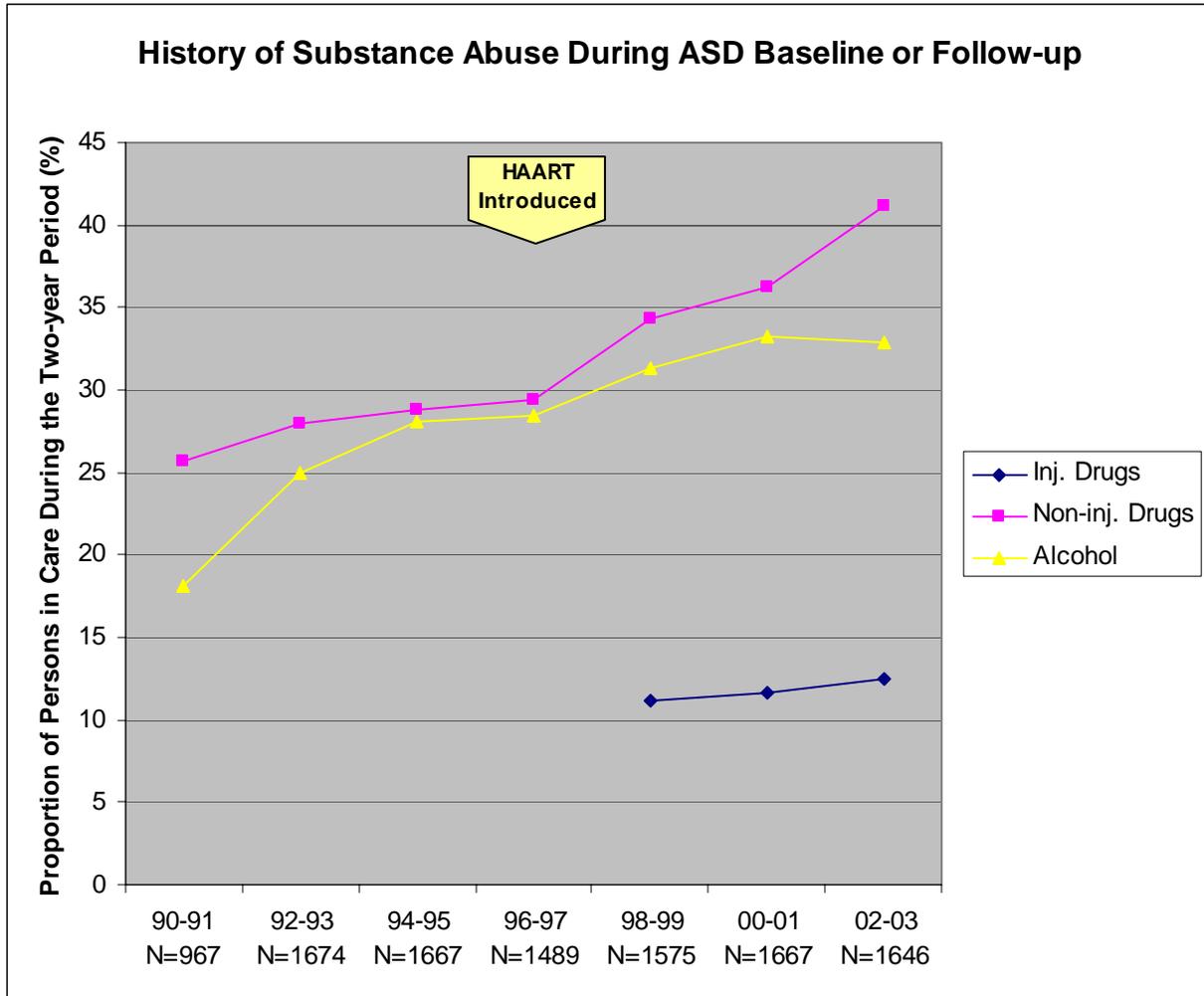
This table shows the proportion of persons with follow-up data recorded who had the listed condition or procedure at any time in their medical records reviewed for ASD, including baseline and follow-up intervals. Data on the conditions in the upper part of the table were collected throughout the project period, while collection of data on the conditions and procedures in the lower part of the table was initiated in 1998.

Other Conditions and Procedures Collected 1990-2003 (N=4489)		
Condition	Number of Persons	Proportion of Persons in Care
Acute HIV	36	0.8%
Hepatitis, Non-infectious, Drug-induced	176	3.9%
Cranial Neuropathy	114	2.5%
Other Conditions and Procedures Collected 1998-2003 (N=2426)		
Condition	Number of Persons	Proportion of Persons in Care
Dialysis	105	4.3%
Guillain-Barre Syndrome	1	< 0.1%
Myelopathy	12	0.5%
Nephrolithiasis	46	1.9%
Rape or Other Sexual Abuse	12	0.5%
Stroke	28	1.2%
Suicide Attempt	70	2.9%

All of these conditions and procedures are infrequent, occurring in less than 5% of all the persons who had any follow-up care at an ASD site.

Figure 14
Substance Abuse, Diagnosed at Any Time in ASD, Baseline or Follow-up

This figure shows the proportions of persons with follow-up data recorded during the two-year period that had had a history of the particular substance abuse at any time, during the two-year period or before.

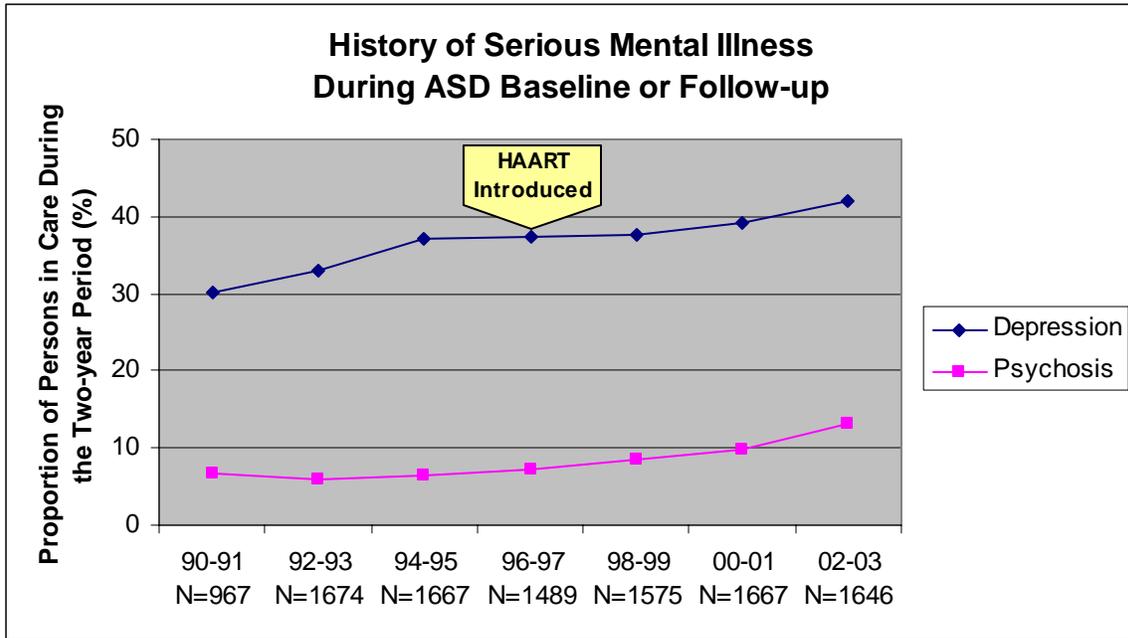


The proportions of persons in follow-up who had a history of abusing non-injection drugs or alcohol during the time of their care at an ASD site increased steadily through the project period. On the other hand, current use of injection drugs was only recorded starting with 1998 data, and the proportion of persons in follow-up who had a history of current injection drug use during the time of their care at an ASD site was comparatively constant from 1998 onward.

The proportion of persons in follow-up who abused alcohol or non-injection drugs was much higher than the proportion using injection drugs.

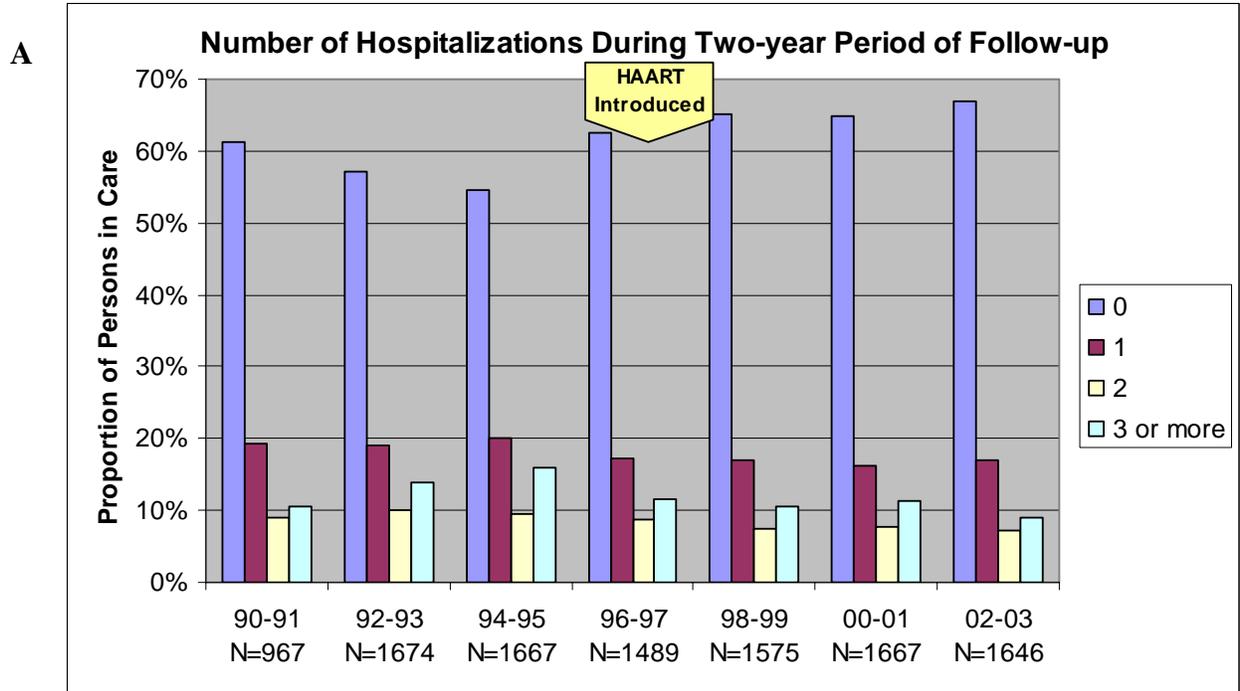
Figure 15
Serious Mental Illness, Diagnosed at Any Time in ASD, Baseline or Follow-up

This figure shows the proportions of persons with follow-up data recorded during the two-year period that had had a history of depression or psychosis at any time, during the two-year period or before.



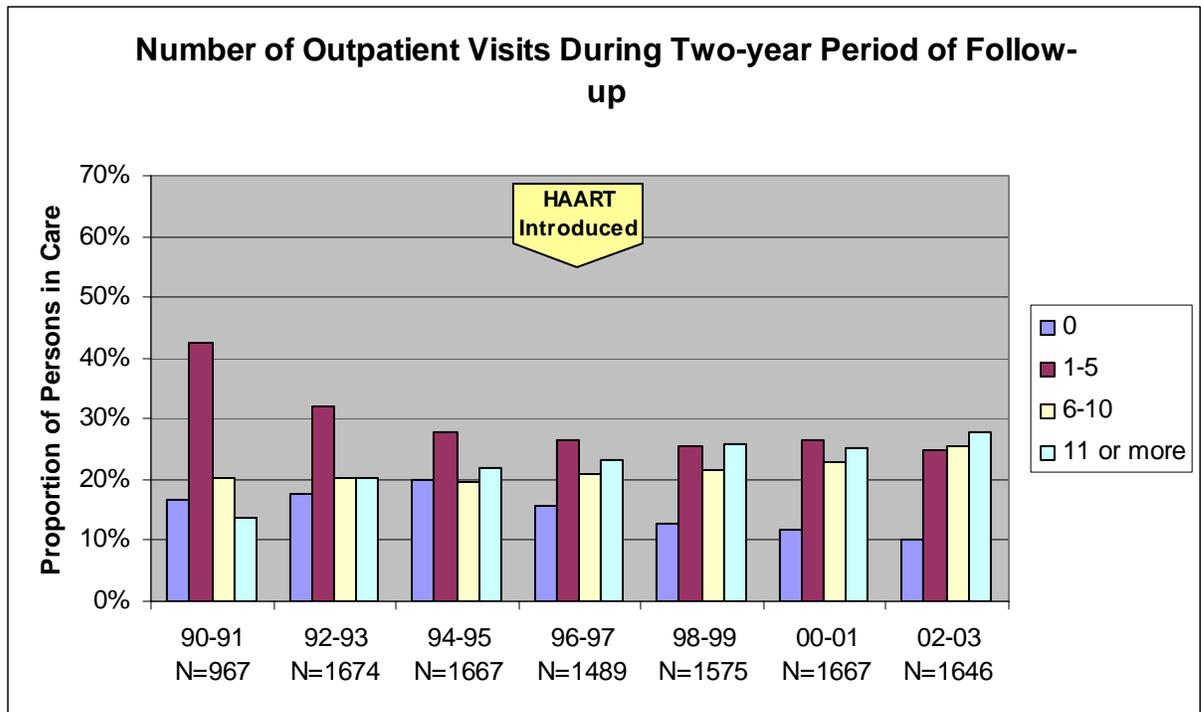
The proportions of persons in follow-up who had a history of depression or psychosis increased over the project period.

Figure 16
Utilization of Health Care Services During Follow-up, by Two-year Periods
 A, Hospitalizations; B, Outpatient clinic visits; C, Emergency room visits.



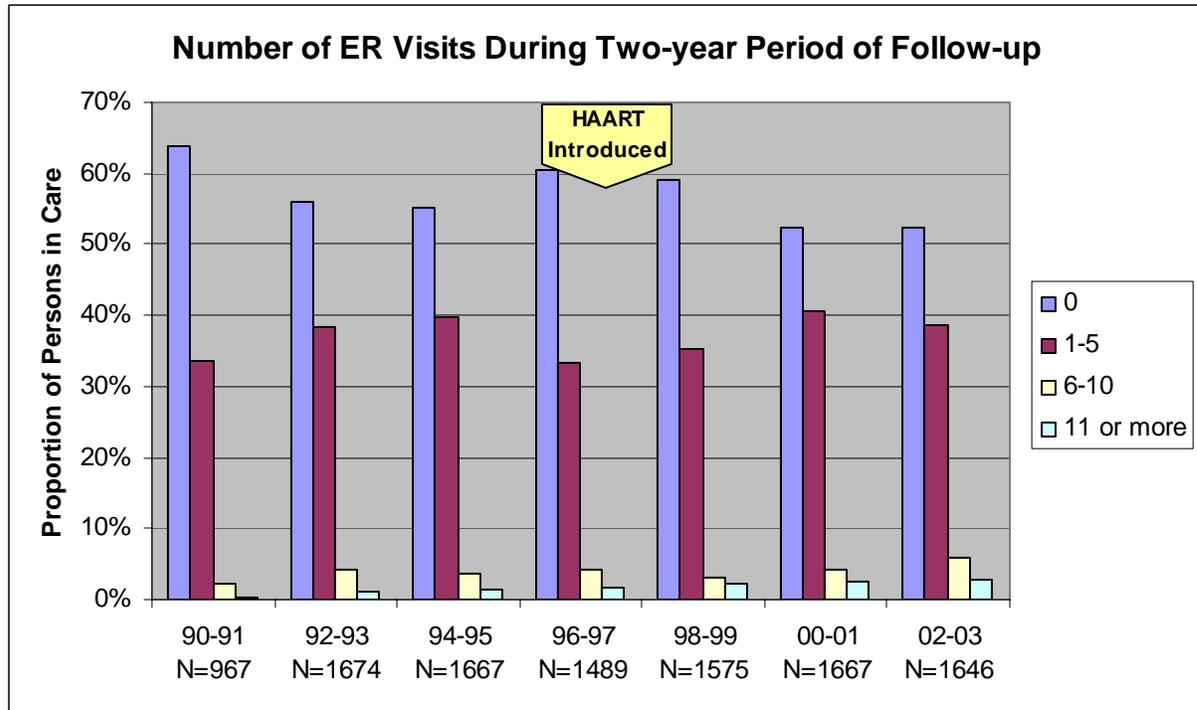
The frequency of hospitalization decreased over the project period. The proportions of persons with data recorded in their follow-up records that did not have any inpatient stay in a two-year period increased after the introduction of HAART ($p < 0.001$), as well as over the entire project period ($p < 0.001$). Conversely, the proportion with three or more inpatient stays decreased.

B



Utilization of the outpatient clinic increased over the project period. The proportion of persons in care that did not visit the outpatient clinic during the two-year period decreased after the introduction of HAART ($p < 0.001$), as well as over the entire project period ($p < 0.001$). The proportion that visited the outpatient clinic one to five times in a two-year period of follow-up also decreased, while the proportions with six to ten or eleven or more outpatient visits increased.

C



Utilization of the emergency room also increased over the project period. The proportion of persons in care that did not visit the emergency room in a two-year period decreased after the introduction of HAART ($p=0.001$), as well as over the entire project period ($p<0.001$). The proportion that visited the emergency room one to five times ranged from 30 to 40%, and the proportions of persons in care that visited the emergency room six to ten times or eleven times or more in a two-year period increased over the project period.

Figure 17
Sources of Reimbursement for the Costs of Care During Follow-up, by Two-year Periods

Collection of this information was phased in during the 1998-1999 period. Consequently, the N for 98-99 in this analysis is smaller than the N's for this period in earlier figures.

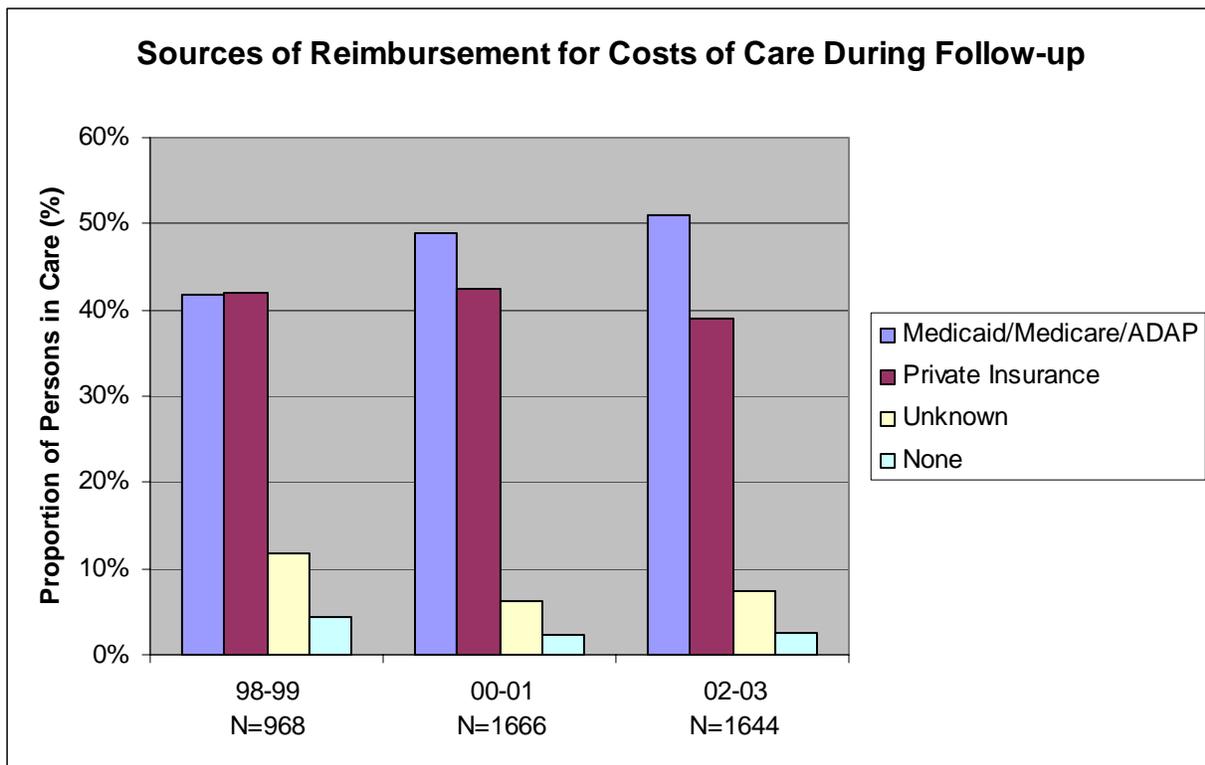
The sources of reimbursement were classified into the following mutually exclusive categories:

Medicaid/Medicare/AIDS Drug Assistance Program (ADAP)—At some time during the two-year period at least part of the person's costs were reimbursed by one of these governmental funding sources.

Private Insurance—At some time during the two-year period the person's costs were reimbursed by private insurance, and at no time were they reimbursed by Medicaid, Medicare or ADAP.

Unknown Insurance—No information about the person's cost reimbursement was recorded in the follow-up record.

None—The person's costs were not reimbursed, as noted in the medical record.



The costs of care were reimbursed by private insurance and by the federally funded programs (Medicaid, Medicare and ADAP) for approximately equal proportions of persons. It appeared that the proportion of persons in care whose costs were reimbursed by Medicaid, Medicare, or ADAP increased over the six years during which this data was collected, while the proportion who had private insurance decreased ($p < 0.001$). However, this trend in the data on the proportion with private insurance may not represent reality. If the proportions with unknown insurance in 2000-2001 and 2002-2003 were added to the private insurance category, the difference between private insurance and federally funded programs would be much smaller.

Figure 18
Antiretroviral Resistance Testing During Follow-up, by Two-year Periods

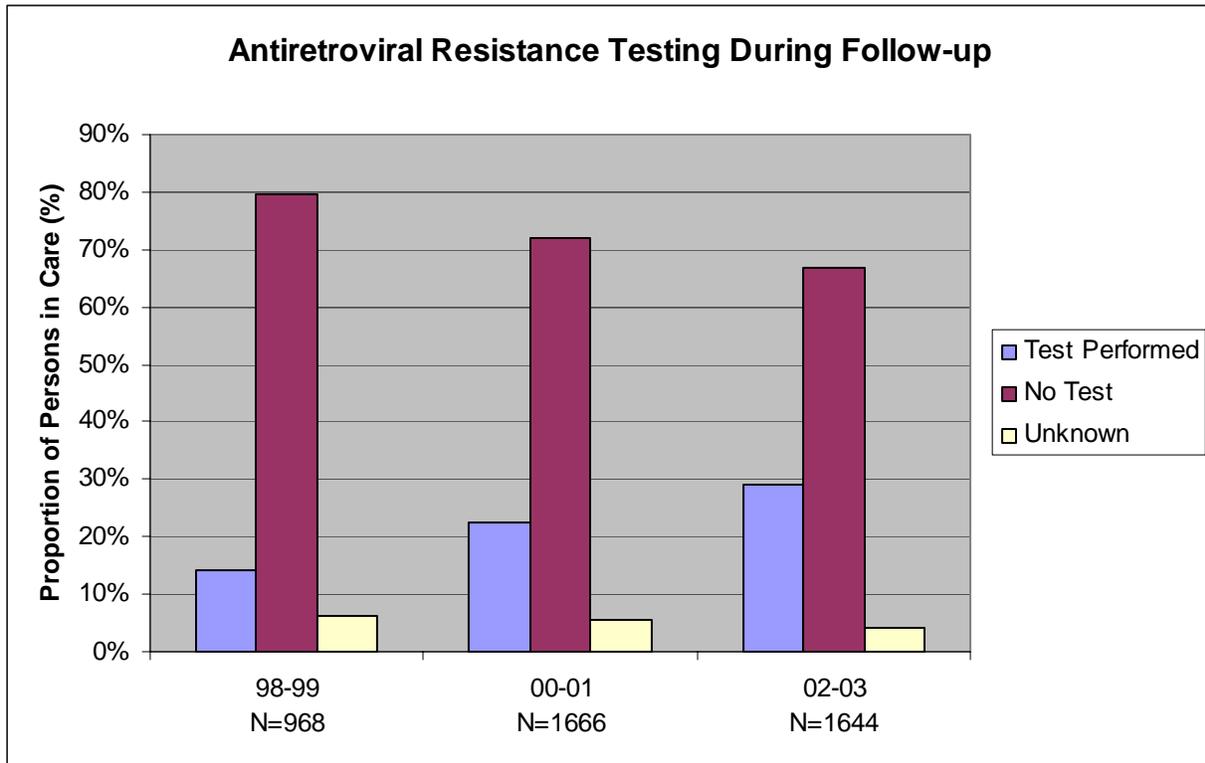
Collection of this information was phased in during the 1998-1999 period. Consequently, the N for 98-99 in this analysis is smaller than the N's for this period in earlier figures.

Antiretroviral resistance testing status was classified as follows:

Test Performed—At least one test was performed during the two-year period.

No Test—No tests were performed during the two-year period.

Unknown—No information about the person's antiretroviral resistance testing was recorded in the follow-up record.



The proportion of persons in follow-up care for whom at least one antiretroviral resistance test was performed in a two-year period increased over the six years this test was used ($p < 0.001$). This change reflected the growing use of the test to guide the choice of an initial antiretroviral regimen or a change in the regimen when treatment was failing.

More than 99% of the antiretroviral resistance tests performed were of the genotypic type, while phenotypic testing was rarely used.

DEFINITIONS

Surveillance Case Definition for AIDS. For the purpose of reporting cases to the CDC, AIDS is defined as the condition of being HIV-infected and having a diagnosis of one of the AIDS-defining conditions or a CD4⁺ T-cell count <200 cells/mm³. The AIDS-defining conditions are listed in Figure 12 and in the published case definition.²

Modes of HIV Transmission. MSM, men who have sex with men; IDU, injection drug users; MSM/IDU, men who have sex with men and inject drugs; Heterosexual Contact, persons who have had heterosexual contact with a person who is known to be HIV-infected or has known risk factors for HIV infection; Blood Exposure, persons who had a blood transfusion, received blood components or an organ transplant. These categories are applied hierarchically in the order listed. The first risk factor that applies to a person is the one that is used.⁷

High-risk Heterosexual and Presumed Heterosexual. Persons who are classified as having Heterosexual Contact as their Mode of HIV Transmission in the above classification are described as High-risk Heterosexual. Persons who have had heterosexual contact and are not included in any of the above risk categories are described as Presumed Heterosexual.

HAART. Highly active antiretroviral therapy, which consists of two or more nucleoside/nucleotide reverse transcriptase inhibitors in combination with at least one additional drug from the non-nucleoside reverse transcriptase inhibitor category or the protease inhibitor category.

ART. Antiretroviral therapy, which consists of any one or more antiretroviral medications.

HARS. HIVAIDS Reporting System, which is the database system that was used by Michigan to collect reports of HIV and AIDS.

AIDS-defining Condition. One of the conditions, a diagnosis of which constitutes a diagnosis of AIDS according to the CDC Surveillance Case Definition for AIDS. These are listed in Figure 12 and in the published case definition.²

CDC. United States Centers for Disease Control and Prevention, Atlanta GA.

In care. For the purpose of this report, a person was counted as being in care if data was recorded in one or more of their follow-up records (starting six months or more after enrollment) in the specified time period. The data recorded represented utilization of any type of health care at an ASD site.

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APPENDIX

Selection of persons and records

			N
Baseline (forms 1 and 2)	Figure 1	All persons enrolled during 1991-2002	4288
	Figure 2	Persons enrolled during 1999-2002 whose race/ethnicity was recorded as Black or White	874
	Table 1	Persons enrolled during 1991-2002 whose vital status in the baseline record was 1 (alive) or 2 (dead)	4285
	Figure 3	Persons enrolled during 1991-2002 whose status in the baseline record was 1 or 2, and who had a CD4 ⁺ T-cell count or percent recorded in their baseline or their first follow-up record (form 1 or 2)	3692
	Figure 4	Persons enrolled during 1991-2002 whose status in the baseline record was 1 or 2, and who had a CD4 ⁺ T-cell count recorded in their baseline or their first follow-up record (form 1 or 2)	3631
	Figure 5	Persons enrolled during 1999-2002 whose race/ethnicity was recorded as Black or White and whose status in their baseline record was 1 or 2. The analysis for AIDS diagnosis included only those who also had a CD4 ⁺ T-cell count or percent recorded in their baseline or their first follow-up record.	Hospitalization/Vital Status-874 AIDS Diagnosis-794

			N for 92-93	N for 02-03
Follow-up records (forms 3 and higher)	Figure 6	All persons in follow-up, including those whose status as of their last record in the two-year period was 9 (unknown) or 4 (lost)	2017	1921
	Figure 7	Persons in follow-up, including those whose status as of their last record in the two-year period was 9 or 4, whose race/ethnicity was recorded as Black or White	1973	1825
	Figure 8	Persons who had any record in the two-year period with vital status 1,2,5 (alive after lost) or 6 (dead after lost)	1674	1646
	Figure 9	Persons who had any record in the two-year period with vital status 1,2,5 or 6 in which a CD4 ⁺ T-cell count was recorded	1194	1431
	Figure 10	Persons who had any record in the two-year period with vital status 1,2,5 or 6 in which a viral load measurement was recorded	0	1369
	Figure 11	Records with at least one outpatient visit recorded (not ER), in 1998-2003		See figure
	Figures 12-17	Persons who had any record in the two-year period with vital status 1,2,5 or 6	1674	1646
	Figure 18, 19	Persons who had any record in the two-year period with vital status 1,2,5 or 6 NOTE: N for 98-99 included only part of the persons in care because collection of data on cost reimbursement was phased in during this period.	0	1644