Patterns of Survival with AIDS in the United States

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We examined patterns of survival with AIDS (acquired immune deficiency syndrome) using the Centers for Disease Control (CDC) "AIDS Public Information Data Set." Analyses used a census of 23,271 cases diagnosed between January 1, 1984 and December 31, 1986. Three Cox proportional hazards models were fit to the data. The first used clinical and demographic parameters only in an effort to replicate Rothenberg's analysis of survival for patients diagnosed in New York City prior to 1986. The second model included variables that capture the effect of time of diagnosis in order to determine whether temporal trends exist. The third model included variables indicating the geographic region from which the cases were reported. The results of these models support earlier findings of demographic and clinical survival correlates. Controlling for covariates, patients diagnosed during 1986 lived significantly longer than those diagnosed earlier; the difference was most profound when Pneumocystis carinii *(PCP) was present. Last, we observed large regional differences; their implications for health services planning are discussed.*

While length of inpatient stays and number of visits have fallen for some patient groups (Seage 1987), AIDS patients remain heavy users

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This project was supported in part by a grant from the Robert Wood Johnson Foundation.

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of medical and social services. Current estimates suggest that the average AIDS-related hospitalization lasts 13.3 days, and that patients experience between 1.6 and 3.5 hospitalizations per year (Lafferty, Hopkins, Honey, et al. 1988; Andrulis et al. 1987). Data on outpatient care suggest that utilization and costs for these services are high as well (Seage, Landers, Barry, et al. 1986; Seage, Landers, Mayer, et al. 1988). Many of these patients lack adequate insurance coverage (Mor, Piette, and Fleishman 1989). This is particularly true for those for whom IV drug use is the primary mode of infection. Thus, the resource drain will continue to fall disproportionately on the already overburdened public sector.

Effective planning for the volume of medical and social service needs of this population necessitates accurate estimates of survival for patient subgroups (Bongaarts 1988). One of the most comprehensive analyses of survival remains the study by Rothenberg, Woefel, Stoneburner, et al. (1987) of 5,833 AIDS patients diagnosed in New York City before 1986. Nonwhites, patients older at time of diagnosis, and those with opportunistic diseases other than Kaposi's sarcoma (KS) all had worse prognoses. More recent studies have found similar relationships between disease presentation, risk group, race, age, and survival (Baccetti, Osmond, Chaisson, et al. 1988; Marasca and McEvoy 1986; Lemp, Payne, Neal, et al. 1990; Justice, Feinstein, and Wells 1989).

Efforts to compare estimates across studies have been hindered by a number of factors. Studies have been done over a wide range of time points, and most report survival of patients diagnosed prior to 1986. Changes in treatment since the early 1980s may limit the usefulness of these results. Further, studies have been done on patients from differing regions of the country with differing patient populations and systems of care. Last, many studies of survival have been characterized by small sample sizes that have limited researchers' ability to determine significant differences among groups.

Since the beginning of the epidemic, treatment modalities have evolved quickly as information on the efficacy of new practices becomes available. The use of the antiviral AZT (zidovudine) is only one of many practices that have affected the survival distribution for persons with AIDS (Vella, Ippolito, Agresti, et al. 1989; Fanning, Johnson, Osachoff, et al. 1989; Lemp, Payne, Neal, et al. 1990). Early detection, prophylaxis, and treatment of *Pneumocystis carinii* pneumonia (PCP) have also improved the survival rate for patients with this disease (Leoung, Montgomery, Abrams, et al. 1989; Centers for Disease Control 1989). Rothenberg's study revealed that survival improved for successive cohorts of patients diagnosed between 1981 and 1985, and

that this pattern varied by whether or not PCP was present at diagnosis. Lemp's study showed a similar temporal pattern; however, it did not report whether temporal improvements varied or not by disease type. Rapid changes in treatment modalities may make prior estimates of survival out of date.

Observations of potential regional variations in survival have been reported (Baccetti, Osmond, Chaisson, et al. 1988). Bennett and his colleagues (1989) provided some empirical justification for these differences by reporting that California hospitals that had more familiarity with AIDS admissions with PCP had lower in-hospital mortality rates than did less experienced hospitals. Controlling for prior hospitalizations and emergency admissions, the authors found that patients admitted to hospitals that had treated few AIDS patients had a mortality rate 3.6 times higher than that of experienced hospitals. Further, Wennberg and Gittlesohn (1982) documented substantial variations in the process of care (e.g., surgery rates) across geographic areas. Differences in the pattern of AIDS care could have implications for mortality. However, no study to date has examined overall survival of comparable patients across geographic areas of the United States.

The purpose of the current study is threefold. We first seek to replicate Rothenberg's analysis, in an attempt to validate his findings of clinical and demographic correlates of survival, using a national sample. Second, we estimate the improvements in survival for various patient groups over time. Last, using data collected nationwide, we provide an indication of regional variation in survival with AIDS. The implications of temporal and regional survival differences are discussed in light of the organization of health services for persons with AIDS.

METHODS

We obtained the Centers for Disease Control (CDC) Public Information data set, which contains patient level information on all cases of AIDS reported by health departments as of September 30, 1989. Data include dates of diagnosis and death; the presence or absence of 25 commonly occurring opportunistic diseases; and demographic characteristics of the patient, such as age, race, gender, and risk group. In order to protect the confidentiality of all patients, no data are provided in the CDC data set to indicate the city in which the case was diagnosed. Instead, residence of patients from cities with more than a million inhabitants is aggregated into five regions of the United States; for patients from smaller Metropolitan Statistical Areas (MSAs),

region is coded as unknown. (See Table 1 for a listing of the cities within each region.)

ANALYTIC SAMPLE

Cases reported as diagnosed between January 1, 1984 and December 31, 1986 were used for the analyses. The sample was limited to patients diagnosed before 1987 to avoid lead-time bias introduced by the broadening of the case definition, which was implemented that year (Centers for Disease Control 1987). This should also minimize the effect of differential reporting lag for deaths, since it allows over 30 months between diagnosis and the date the data set was made available. Because of missing data for race or risk group, 662 patients (2.7 percent) were excluded.

Children under 12 years of age were excluded from the sample for several reasons. Research has shown that the prognostic course of pediatric human immunodeficiency virus (HIV) infection is radically different from that of adults (Pizzo, Eddy, and Faloon 1988). Second, in order to protect the confidentiality of pediatric patients, no data on region of residence is provided in the data set for children under 12. Finally, Rothenberg limited his study to adults, so we chose to do the same to ensure comparability.

ANALYTIC METHOD

Survival time is defined as the length of time between date of diagnosis and death. In the CDC data set, death date is reported in quarter-year units. The mid-month of the recorded quarter was used to estimate survival times. We constructed clinical and demographic variables to match those used in the Rothenberg study as closely as possible. All independent variables match Rothenberg's exactly except age, where, due to the structure of the CDC data base, the four categories used deviate slightly from those used in the earlier study.

Life tables were constructed to determine the cumulative probability of survival over time within each subgroup of patients. The numbers of months at which 75 percent, 50 percent, and 25 percent of the patient group remained alive are presented in Table 1. For patients who were reported dead, the percentage reported dead within three months of diagnosis was also calculated.

In order to assess the joint effect of the various determinants of survival, three Cox proportional hazards models were fitted to the data (Cox and Oakes 1984). The first used only clinical and demographic variables in an effort to replicate Rothenberg's analysis (Table 2/

Table 1: Univariate Survival Statistics

	N	*Total (%)*	*Dead (%)*	*Dead In Qtr* (%)*	*75% CPS†*	*50% CPS†*	*25% CPS†*
Age							
<30	4732	20.3	78.9	27.1	4.18	12.71	29.71
30-39	11295	48.5	81.1	27.2	3.95	12.20	26.29
40-49	4978	21.4	83.3	29.6	3.08	10.77	22.37
50+	2266	9.7	87.5	41.9	1.28	7.34	15.76
Race							
White	14256	61.3	81.4	24.9	4.44	12.55	26.39
Black	5496	23.6	82.8	36.3	1.87	9.90	21.91
Hispanic	3519	15.1	81.5	35.8	1.93	9.66	21.98
Gender							
Male	21853	93.9	81.5	28.6	3.50	11.67	25.12
Female	1418	6.1	84.6	39.0	1.50	8.81	18.12
Risk Group‡							
Homosexual	16251	69.8	81.5	26.1	4.10	12.23	25.85
IVDU	3790	16.3	82.9	38.1	1.58	9.15	19.94
Homosexual/IVDU	1856	8.0	81.9	28.9	3.36	11.45	24.94
Other	1374	5.9	81.4	42.2	1.42	8.80	23.12
Diagnoses§							
KS only	2917	12.5	69.3	16.6	7.15	17.49	60+
KS/PCP	1795	7.7	87.9	10.7	7.19	13.67	22.45
KS/Plus	682	2.9	86.1	19.3	4.73	11.73	22.79
PCP alone	9286	39.9	82.5	34.3	1.84	11.13	22.46
PCP/Other	3610	15.5	88.7	21.2	4.71	12.25	21.41
One other	4004	17.2	77.8	43.5	1.69	7.46	26.05
>One other	977	4.2	87.5	33.3	2.33	7.79	16.41

Continued

Table 1: Continued

	N	*Total* (%)	*Dead* (%)	*Dead In Qtr** (%)	*75% CPS†*	*50% CPS†*	*25% CPS†*
Year of Diagnosis							
1984	4188	18.0	87.0	27.4	3.36	10.65	19.17
1985	7454	32.0	85.1	28.0	3.34	11.15	20.74
1986	11629	50.0	77.7	30.9	3.31	12.25	30.15
Region‖							
Northeast	8919	38.3	80.7	32.1	2.76	10.98	23.57
Central	1753	7.5	85.5	27.8	3.37	11.97	22.74
West	6602	28.4	80.7	24.5	4.58	12.91	27.96
South	4090	17.6	82.4	31.3	2.77	10.88	23.65
Mid-Atlantic	1907	8.2	85.6	29.3	2.98	10.88	21.13
TOTAL	23271	100.0**	81.7	29.3	3.54	11.51	24.60

*"Dead in Qtr (%)" refers to the proportion of deceased cases reported dead during the same quarter year as their diagnosis with AIDS.

†CPS = cumulative probability of survival in months.

‡IVDU = intravenous drug user.

§KS = Kaposi's sarcoma; PCP = *Pneumocystis carinii* pneumonia.

‖Cities included in each region are: Northeast = Bergen-Passaic NJ; Buffalo NY; Boston MA; Hartford CT; Nassau-Suffolk NY; New York City NY; and Newark NJ. Central = Chicago IL; Cincinnati OH; Cleveland OH; Columbus OH; Denver CO; Detroit MI; Indianapolis IN; Kansas City MO; Milwaukee WI; Minneapolis-St. Paul MN; St. Louis MO. West = Anaheim CA; Los Angeles CA, Oakland CA, Phoenix AZ; Portland OR; Riverside-San Bernardino CA; Sacramento CA; Salt Lake City UT; San Diego CA; San Francisco CA; San Jose CA; Seattle WA. South = Atlanta GA; Charlotte NC; Dallas TX; Fort Lauderdale FL; Fort Worth TX; Houston TX; Miami FL; New Orleans LA; San Antonio TX; San Juan PR; Tampa FL. Mid-Atlantic = Baltimore MD; Norfolk VA; Philadelphia PA; Pittsburgh PA; Washington DC.

**Under the heading "Total (%)," deviations from 100.0% in some categories are due to rounding.

Model 1). In order to determine whether changes in care since Rothenberg's study have improved patients' prognosis, a second model (Table 3) was fitted using this same set of parameters plus an indicator variable showing whether the patient was diagnosed before or during 1986. Interaction terms between this time indicator and the various diagnostic groups were included to determine if prognosis varied according to the patients' constellation of illnesses. A third model (Table 4) was fitted, which included dummy variables for region as well as interactions between region and race. In both Models 1 and 2 (Tables 2 and 3) as well as in Rothenberg's study, the interaction between race and risk group did not significantly add to the models' explanatory power. For the sake of parsimony, this interaction was dropped from the third model.

The validity of the proportional hazards assumption was tested by comparing the log-minus log survival function for each level of the independent variables to the function for the referent group (Kalbfleish and Prentice 1980). Crossing-hazard functions in these plots would indicate that the estimates of the model might not have been valid. In no case were crossing hazards observed.

RESULTS

The median survival for all patients was 11.51 months; however, substantial differences were observed across patient subgroups (Table 1). Males experienced an almost three-months greater median survival than females; whites experienced an almost three-months greater survival than either blacks or Hispanics. Median survival (i.e., the number of months at which 50 percent of the subgroup had died) decreased monotonically with advanced age at diagnosis. Patients diagnosed in 1986 survived over three months longer than patients diagnosed in 1984. Substantial differences were also observed across risk groups and across regions. The number of months at which 25 percent and 75 percent of the subgroups had died supports the patterns observed in median survival.

Since many of these dimensions are highly correlated, their true effect on the survival function can only be assessed through a multivariate model. Table 2 presents estimated coefficients and adjusted odds ratios for the proportional hazards model in which only clinical and demographic variables are included (Model 1). The ratios can be interpreted as the relative effect on the risk of death for patients in a particu-

Table 2: Model 1. Cox Proportional Hazards Model Using Demographic and Clinical Variables Only

Variable	*Coefficient*	*(s.e.)*	*Odds Ratio*	*95% Confidence (Lower*	*Upper)*
*Age**					
<30	-0.0689	(.02)	0.93	(0.90	0.97)
40-49	0.1161	(.02)	1.12	(1.08	1.17)
50+	0.3496	(.03)	1.42	(1.35	1.49)
Race†					
Black	0.1513	(.02)	1.16	(1.11	1.22)
Hispanic	0.1150	(.03)	1.12	(1.07	1.18)
Gender‡					
Women	0.1228	(.04)	1.13	(1.05	1.21)
Risk§					
IVDU**	-0.0350	(.05)	0.97	(0.87	1.07)
Homosexual/IVDU	0.0472	(.03)	1.05	(0.99	1.11)
Other	0.1950	(.05)	1.22	(1.10	1.34)
Diagnosis‖					
PCP††	0.3323	(.02)	1.39	(1.33	1.46)
KS/PCP††	0.3272	(.03)	1.39	(1.30	1.48)
KS/Plus	0.3444	(.05)	1.41	(1.29	1.55)
PCP/Plus	0.3817	(.03)	1.46	(1.39	1.55)
One other	0.3705	(.03)	1.45	(1.37	1.53)
>One other	0.5245	(.04)	1.69	(1.55	1.84)
Interactions					
Black/IVDU	-0.0503	(.06)	0.95	(0.85	1.06)
Black/Other	-0.4697	(.07)	0.63	(0.55	0.72)
Hispanic/IVDU	-0.0582	(.06)	0.94	(0.84	1.06)
Hispanic/Other	-0.0240	(.10)	0.98	(0.80	1.18)
PCP/IVDU	0.2072	(.04)	1.23	(1.14	1.33)

*Reference group: 30-39.

†Reference group: White.

‡Reference group: Men.

§Reference group: Homosexual/Bixexual.

‖Reference group: Kaposi's sarcoma only.

**IVDU = intravenous drug user.

††PCP = *Pneumocystis carinii* pneumonia; KS = Kaposi's sarcoma.

lar category when compared to the referent group. (To estimate odds ratios for patients who vary from the referent group on a number of covariates simultaneously, one computes the antilog of the sum of their coefficient estimates.)

Several factors were found to be significant predictors of increased mortality. Women experienced a 13 percent increased risk of death

compared to men and both blacks and Hispanics experienced a greater risk of death compared to whites (16 percent and 12 percent, respectively). Survival decreased with patient age. Patients over 50 years of age experienced a 42 percent increased risk of death compared to the referent group and a 52 percent increased risk compared to patients between 20 and 29.

Patients with KS experienced better survival compared to patients in any of the other disease categories. Patients with PCP and no other diseases experienced a 39 percent increased risk of death compared to patients with KS alone. Patients with the worst prognosis were those with two or more opportunistic diseases other than KS or PCP. These patients experienced a 69 percent increased risk of death. The significant interaction between intravenous drug users (IVDUs) and PCP indicates that survival for IV drug users with PCP was substantially worse than survival for the referent group. When added to the main effects of PCP and drug use, the odds of death were 66 percent higher.

The only risk group that differed significantly from homosexual males was the "other risk category." Patients in this group are evenly distributed between cases of heterosexual transmission (32.2 percent), blood product transmission (37.2 percent), and patients from "Pattern II" countries (30.1 percent). Pattern II countries are those in which the ratio of female to male cases of AIDS is nearly 1:1 and heterosexual transmission is the most common vehicle of disease spread.

Table 3 shows the coefficient estimates and odds ratios for Model 2, which includes the pre/post-1986 indicator variable as well as interactions between time and diagnostic group. All significant predictors from Model 1 remain significant when these new parameters are included. Patients diagnosed before 1986 experienced an increased mortality rate relative to patients diagnosed during that year. This is especially true for patients diagnosed with PCP. The significant interaction term (PCP alone by time) suggests that patients with this disease diagnosed prior to 1986 experienced an additional 24 percent increased hazard rate over the estimated 40 percent increased risk captured by the main effects. For those diagnosed with PCP and at least one other disease, the interaction contributes an additional 16 percent increase to the hazard rate.

In order to determine whether a consistent trend in improved survival was observed over the three years, the model was rerun replacing the pre/post-1986 indicator with two dummy variables for diagnosis in 1984 and 1985 (data not shown). Patients diagnosed in 1984 experienced a 15 percent increased mortality compared to those in 1986 (CI = 1.06, 1.26). Prognosis improved in 1985 when patients'

Table 3: Model 2. Cox Proportional Hazards Model Including Pre/Post-1986 Variables and Interactions

Variable	*Coefficient*	*(s.e.)*	*Odds Ratio*	*95% Confidence (Lower*	*Upper)*
*Age**					
<30	-0.0733	(.02)	0.93	(0.89	0.97)
40-49	0.1165	(.02)	1.12	(1.08	1.17)
50+	0.3497	(.03)	1.42	(1.35	1.49)
Race†					
Black	0.1463	(.02)	1.16	(1.11	1.21)
Hispanic	0.1056	(.03)	1.11	(1.06	1.17)
Gender‡					
Women	0.1294	(.04)	1.14	(1.06	1.22)
Risk§					
IVDU††	-0.0438	(.05)	0.96	(0.86	1.06)
Homosexual/IVDU	0.0420	(.03)	1.04	(0.99	1.10)
Other	0.2037	(.05)	1.23	(1.11	1.35)
Diagnosis‖					
PCP††	0.2456	(.04)	1.28	(1.19	1.37)
KS/PCP††	0.3610	(.05)	1.43	(1.30	1.58)
KS/Plus	0.3674	(.07)	1.44	(1.25	1.66)
PCP/Plus	0.3154	(.04)	1.37	(1.26	1.49)
One other	0.3838	(.04)	1.47	(1.35	1.59)
>One other	0.4823	(.06)	1.62	(1.43	1.83)
*Cohort***					
<1986	0.0928	(.04)	1.10	(1.01	1.19)
Interactions					
Black/IVDU	-0.0473	(.06)	0.95	(0.85	1.06)
Black/Other	-0.4931	(.07)	0.61	(0.53	0.70)
Hispanic/IVDU	-0.0429	(.06)	0.96	(0.85	1.08)
Hispanic/Other	-0.0133	(.10)	0.99	(0.81	1.20)
PCP/IVDU	0.1947	(.04)	1.21	(1.12	1.32)
<1986/PCP	0.2119	(.05)	1.24	(1.13	1.36)
<1986/PCP/Plus	0.1466	(.06)	1.16	(1.04	1.29)
<1986/KS/PCP	-0.0548	(.07)	0.95	(0.83	1.08)
<1986/KS/Plus	-0.0348	(.10)	0.97	(0.80	1.17)
<1986/One other	0.0074	(.06)	1.01	(0.90	1.12)
<1986/>One other	0.1055	(.09)	1.11	(0.94	1.31)

*Reference group: 30-39.

†Reference group: White.

‡Reference group: Men.

§Reference group: Homosexual/Bisexual.

‖Reference group: Kaposi's sarcoma only.

**Reference group: Patient's diagnosed in 1986.

††IVDU = intravenous drug user.

‡‡PCP = *Pneumocystis carinii* pneumonia; KS = Kaposi's sarcoma.

Table 4: Model 3. Cox Proportional Hazards Model Including Regional Indicator Variables

Variable	*Coefficient*	*(s.e.)*	*Odds Ratio*	*95% Confidence (Lower*	*Upper)*
*Age**					
<30	-0.0793	(.02)	0.92	(0.89	0.96)
40-49	0.1193	(.02)	1.13	(1.09	1.17)
50+	0.3778	(.03)	1.46	(1.39	1.53)
Race†					
Black	0.1726	(.03)	1.19	(1.12	1.26)
Hispanic	0.1732	(.03)	1.19	(1.12	1.27)
Gender‡					
Women	0.1471	(.04)	1.16	(1.08	1.24)
Risk§					
IVDU‡‡	-0.0629	(.03)	0.94	(0.88	1.00)
Homosexual/IVDU	0.0501	(.03)	1.05	(1.00	1.11)
Other	-0.0468	(.04)	0.95	(0.89	1.03)
Diagnosis‖					
PCP§§	0.2441	(.04)	1.28	(1.19	1.37)
KS/PCP§§	0.3433	(.05)	1.41	(1.28	1.56)
KS/Plus	0.3585	(.07)	1.43	(1.24	1.65)
PCP/Plus	0.3045	(.04)	1.36	(1.25	1.47)
One other	0.3763	(.04)	1.46	(1.34	1.58)
>One other	0.4671	(.06)	1.60	(1.41	1.81)
*Cohort***					
<1986	0.0981	(.04)	1.10	(1.02	1.20)
Region††					
Central	0.1539	(.04)	1.17	(1.09	1.25)
West	0.0192	(.02)	1.02	(0.97	1.07)
South	0.1699	(.03)	1.19	(1.12	1.25)
Mid-Atlantic	0.1944	(.04)	1.21	(1.13	1.31)

Continued

mortality risk was only 7 percent greater than those diagnosed the following year (OR = 1.07; CI = 0.99, 1.17).

Model 3 shows that when the region indicators are entered into the model, significant geographic variation is apparent (Table 4). The Central, Southern, and Mid-Atlantic regions experience significantly worse survival than the Northeast. No differences were observed between the Northeast and the West. Controlling for other covariates, patients diagnosed in the Central region experienced a 17 percent increased risk of death compared to patients in the Northeast; the region with the poorest hazard rate is the Mid-Atlantic region with an increased risk of 21 percent.

Table 4: Continued

Variable	Coefficient	(s.e.)	Odds Ratio	95% Confidence (Lower	Upper)
Interactions					
PCP/IVDU	0.1876	(.04)	1.21	(1.11	1.31)
Black/Central	-0.2030	(.07)	0.82	(0.71	0.93)
Black/West	-0.1195	(.06)	0.89	(0.79	1.00)
Black/South	-0.2003	(.05)	0.82	(0.74	0.91)
Black/Mid-Atlantic	-0.1375	(.06)	0.87	(0.78	0.98)
Hispanic/Central	-0.0430	(.11)	0.96	(0.76	1.20)
Hispanic/West	-0.0381	(.06)	0.96	(0.86	1.07)
Hispanic/South	-0.2046	(.06)	0.81	(0.73	0.91)
Hispanic/Mid-Atlantic	-0.2204	(.14)	0.80	(0.61	1.05)
<1986/PCP	0.2093	(.05)	1.23	(1.12	1.35)
<1986/PCP/Plus	0.1403	(.05)	1.15	(1.03	1.28)
1986/KS/PCP	-0.0490	(.07)	0.95	(0.79	1.15)
1986/KS/Plus	-0.0378	(.10)	0.96	(0.86	1.07)
<1986/One other	-0.0007	(.06)	1.00	(0.90	1.12)
1986/>One other	0.1001	(.09)	1.11	(0.94	1.31)

*Reference group: 30–39.

†Reference group: White.

‡Reference group: Men.

§Reference group: Homosexual/Bisexual.

‖Reference group: Kaposi's sarcoma only.

¶Reference group: Patient's diagnosed in 1986.

††Reference group: Northeast.

‡‡IVDU = intravenous drug user.

§§PCP = *Pneumocystis carinii* pneumonia; KS = Kaposi's sarcoma.

Several significant interactions between region and race were observed. Since all race-by-region coefficients show a pattern of improved survival for nonwhites compared to whites in some regions, these counterintuitive results probably represent differences in loss of death records. It is noteworthy, however, that in no instance does the negative interaction coefficient compensate for the increased risk of death estimated by the main effects of region and race. For example, while the interaction between black race and Central region is strong and negative, blacks from this region still experience an estimated 13 percent increased risk of death compared to the referent group.

DISCUSSION

A variety of determinants of survival were observed in these analyses. Persons diagnosed at an older age, nonwhites, and females all have increased mortality rates relative to white homosexual males between the ages of 30 and 39. All disease groups showed significantly worse survival than that of patients with KS alone. It is important to interpret these disease effects with considerable caution. Differences in the severity of disease across sociodemographic groups may bias these results. Further, many diseases occurring later in the course of a patient's illness may go unreported to the CDC.

As in other studies, the estimated effect of IV drug use on survival is negligible both in magnitude and statistical significance. This is counterintuitive, since patients in this risk category are often impoverished, have little contact with the medical care system, and are in generally poorer health when infected with HIV. However, the substantial interaction between PCP and IV drug use indicates that the deleterious effects for this population are explained by increased prevalence of diseases controlled for in the models. When this interaction is excluded from Model 1, the estimated increase in mortality risk among IVDUs relative to homosexual men is 8.4 percent.

The interaction between PCP and drug use may be due to a number of factors, including poorer access to medical care. One recent study showed that IVDUs are substantially less likely to be offered AZT (Stein, Piette, Mor, et al. in press). Another study showed that most cases of PCP are diagnosed in patients with severely compromised immune systems (Phair, Munoz, Detels, et al. 1990). IV drug users with greater immunosuppression may be particularly vulnerable to other opportunistic infections if they are unable to avail themselves of primary care. Similar interactions between disease complex and socioeconomic factors such as race, gender, or insurance status should be investigated in future research.

Model 2 suggests that survival rates have improved over time, and that improvements have been especially great for patients with PCP. Most of the patients in this sample died prior to the wide use of treatments that forestall PCP recurrence. Hence, these temporal improvements probably represent advances in curative treatment and earlier detection of disease. PCP prophylaxis is now commonly prescribed, and the Public Health Service has recommended that all patients who have had PCP use some form of preventive regimen (Centers for Dis-

ease Control 1989). More recent cohorts will likely experience even more dramatic improvements in their mortality rates.

These trends have important implications for the planning and financing of services in the future. Prediction of the proportion of the prevalent population that will require medical treatment and assistance with daily living needs must consider that the population eligible for public assistance will grow faster than would be projected by the incidence curve alone. Prevalence projections will need to be constantly adjusted in light of current information on the impact of prophylactic and treatment methods on the survival rates of various patient groups.

All of these findings are similar to those reported in previous research. Rothenberg estimated that females experienced a 17 percent increased risk of death relative to males compared to our estimates of between 12 percent and 15 percent. The Rothenberg study estimated that blacks had a 17 percent increased risk of death compared to our estimates of between 16 and 19 percent. Similar estimates were also reported for the various risk and age categories as well as strikingly similar estimates of median survival times. This replication not only adds to the weight of evidence for the importance of these factors; it also gives credence to the assumption that the CDC data base is sufficiently reliable to merit statistical analyses.

Controlling for clinical, demographic, and cohort effects, differences were observed in the survival of patients across geographic regions of the country. Since this finding is unprecedented, we give special attention at this point to the potential biases and artifacts of the surveillance data system that may lead to the differences we observed.

For most communicable diseases, the estimated proportion of cases that go unreported is well over 40 percent (Marier 1977). Biases will be introduced into the estimates from the current study if the survival distribution for cases that go unreported is systematically different from those that are reported. One study has estimated that up to 17 percent of all AIDS cases are not reported to the CDC (Hardy, Starcher, Druker, et al. 1987). Another study of underreporting of AIDS cases in South Carolina found that, in 1986 and 1987, 40.5 percent of all cases identified were not reported to the surveillance system. Further, reporting varied by racial, gender, and treatment groups (Conway, Colley-Niermeyer, Pursley, et al. 1989). Not known is the extent to which underreporting varies by region in a manner that biases survival estimates.

Lead-time bias is a phenomenon whereby observed variation in survival time across groups results from systematic differences in early diagnosis rather than from actual prolonged survival for patients at a

given point in the disease process. Early diagnosis may result from several factors including targeted educational campaigns in the community, greater awareness of the risk of AIDS among clinicians, and greater ability to seek care among certain groups of patients.

Lead-time bias undoubtedly confounds all studies of survival with AIDS that focus on clinical and sociodemographic parameters. Patients with poorer access to the health care system (e.g., drug users, nonwhites, and women with children) may have their disease identified later than patients with more ongoing contact with clinical care. Until AIDS epidemiologists identify a means of staging AIDS cases according to the milieu of clinical manifestations, lead-time bias will remain a contributing factor to variation in survival across patient groups.

If the time lag of death reports in the Northeast and West were longer than that in other regions, patients might be considered still alive in these regions, biasing the median survival times upward. However, sufficient time has elapsed to make it likely that even the more negligent health departments have reported most deaths.

Nonreporting of deaths poses the greatest threat to the validity of these results. Linking deaths with diagnostic information requires, first, that the death be identified by the state's surveillance unit and, second, that the death be matched with the incident report. All states currently receive funds from the CDC for actively soliciting information on possible AIDS-related deaths. This is done through contacting hospital staff, as well as through searching data sources such as vital statistics records, tumor registries, and Medicaid claims files. Once identified, deaths are matched with incidence data on the basis of patient name, birth date, and other information. Many health departments have reciprocity agreements with neighboring states whereby death certificates of AIDS cases diagnosed elsewhere are routinely sent to the patient's state of origin.

Despite the aggressive surveillance of AIDS cases and deaths across the country, significant numbers of cases undoubtedly go unreported for a variety of reasons. Until recently, CDC funding for active surveillance was targeted only to high-incidence areas such as New York, New Jersey, and parts of California. Resources devoted to matching death certificates with identified cases and canvassing hospital records may depend on factors such as the size of the incident population. Staff devoted to performing these activities may not necessarily grow in accordance with the size of the work load. Alternatively, regions with fewer cases may be unable to justify the cost of hiring designated staff to perform these functions.

Death reporting can vary across patient subgroups. Patients who

are diagnosed in one hospital and die in another may not have death data successfully matched with incident files. This problem may be especially common among patients who are transient, lack proper identification, or use aliases in order to claim Medicaid coverage. Other patients may die at home or be otherwise lost to follow-up. If loss to follow-up varies by region, a pattern similar to the one we observed could result. Finally, many physicians are reluctant to list AIDS as a cause of death since this may lead to stigmatization of the patient's family and/or friends, or even of the medical practice itself. Particularly for patients with a private source of care, alternative causes may be listed so that the case goes undetected by the surveillance system.

Nonreporting of deaths does exist and is likely to differ in incidence by risk group. One study has estimated that 10–25 percent of HIV-related deaths occurring in 1986 among men age 25–44 were not reported to the CDC (Buehler, Berkelman, and Devine 1989). Indeed, this is the most likely explanation for the observed negative interactions between black race and geographic region.

Despite all of these factors, we contend that nonreporting of deaths is an insufficient explanation for the observed regional differences. Since Model 3 (Table 4) estimates the differences across regions controlling for race, risk group, and gender, differences in the proportion of these groups across regions should not bias the results even if their AIDS-related deaths are more likely to be underreported. Overall, there is evidence that death reporting in the CDC surveillance system is at least as complete as from other sources of information. A recent study compared the deaths reported to the surveillance system with those included in the data base of death certificates routinely collected by *Vital Statistics* (Chevarley, Kochanek, and Beuler 1989). The authors found that the ratio of AIDS surveillance to vital statistics deaths was 1.23 in 1983 and 0.95 in 1986, and then increased to 1.02 in 1987. No differences were found in the sex distribution across the two systems.

Further, the Centers for Disease Control (1990) reports that both reporting lag and percentage of cases unreported are lower in areas of high prevalence. Even if all cases not reported dead were assumed to be lost to follow-up, Table 1 indicates that death reporting is still between 80 and 90 percent complete across nearly all patient subgroups. Given the enormous number of clinicians, hospital administrators, and public health officials involved in compiling this data set, this finding in itself is astounding.

Tracking a patient for the purposes of death reporting becomes increasingly difficult the longer the patient lives, since his/her likeli-

hood of moving or changing providers increases with time. Other administrative burdens of tracking a case, such as monitoring growing medical records or recontacting hospital personnel, also increase over time. If patients are being differentially lost to follow-up across regions, we would expect more of the deaths that are reported to have occurred soon after diagnosis, possibly during the same hospitalization. While Table 1 shows that the Northeast has the largest proportion of deaths that occur shortly after diagnosis, the West shows the lowest proportion, thereby making it difficult to explain the regional pattern in terms of loss to follow-up alone.

Further, if proportionally more cases are being lost to follow-up in the Northeast and West, this should be even more apparent for patients with more tenuous ties to the health care system. When only IVDUs are considered, the proportion of deceased patients reported dead within three months differs substantially across all regions, but not in the pattern expected if cases were more likely to be lost to follow-up in the Northeast and West. Only the Central region had a lower proportion of deaths reported within the first three months after diagnosis than the Northeast (34.7 percent versus 36.8 percent). Comparable proportions were 42.1 percent in the West, 39.9 percent in the Mid-Atlantic region, and 48.6 percent in the South.

The sheer size and diversity of these regions makes it unlikely that reporting patterns within each are uniformly dissimilar. While several epicenters dominate each region in terms of prevalent cases, the regions cover a large number of cities with a multitude of hospitals reporting in each. Thus, it seems unlikely that physicians across such large areas would systematically be reporting differently.

The inclusion of region in the analysis should not be interpreted as an evaluation of the efficacy of specific care systems. Region represents the place of residence where patients were first diagnosed and not necessarily where treatment occurred. Large immigration and emigration among persons with AIDS may exist. Patients with a poorer prognosis may migrate out of the large urban centers of the Northeast and West to be closer to their families of origin. Alternatively, patients with a better prognosis may be migrating toward the AIDS care systems in New York City and San Francisco in order to gain access to experimental treatments that are less available in other parts of the country. No data currently exist that assess the effect of translocation on region-specific mortality rates. Further, these analyses are based solely on patients diagnosed in MSAs with more than one million inhabitants. Of all cases diagnosed prior to 1987, 23.1 percent came from MSAs

with smaller populations; survival patterns for these patients may differ.

Nonetheless, it is noteworthy that significant variation seems to exist in the predictors of survival across regions of the country. The Northeast and Western regions account for a disproportionately large percentage of AIDS patients. Care systems in regions with lower prevalence may have neither the resources allocated to AIDS care nor the level of clinical expertise in medical management that the Northeast and West can claim. This interpretation is consistent with those of Bennett and his colleagues (1989), who found that in-hospital mortality was higher for AIDS patients with PCP admitted to hospitals with little AIDS experience than to those with more experience.

The interpretation of these regional differences is unclear; analysis using city level data would provide insight into the specific mechanisms involved. Unfortunately, these data are not currently available to the public due to stringent laws concerning the release of potentially damaging information. The regional pattern observed in the CDC data set may represent differences in reporting or disease detection, or a previously unrecognized epidemiology parameter of the epidemic. Given the implications of these differences for future research and health services program planning, further analysis is needed in order to determine the source(s) of the observed variation.

The demand for health services that AIDS patients will make during the second decade of the epidemic will test the care system to its limit. The successes of increased survival over recent years have been purchased through longer periods of morbidity and intensive utilization of preventive care. Over time, it may be most appropriate for patients to be served by the relatively small number of clinics and hospitals in each community that have general experience in managing the clinical complications of AIDS. Bennett and his colleagues conclude that a conscious policy may be required either to channel AIDS cases into medical care systems that have experience with the disease, or to provide intense education to providers in low-prevalence areas in order to prepare them for the expected onslaught. In large measure, the wisdom of adopting a "specialist" tertiary care center model versus integrating AIDS into the general practice of primary care medicine may hinge on survival projections as well as incidence. Further research attempting to localize areas within regions with shorter-than-expected mortality is needed so that strategies appropriate to larger and smaller areas can be devised.

ACKNOWLEDGMENTS

We would like to thank Sally Zierler, Ph.D. of the Brown University Department of Community Health for her insightful comments on an earlier draft of this manuscript. We would also like to thank the anonymous reviewers for their thorough reading and valuable criticism.

REFERENCES

Andrulis, D., V. S. Beers, J. D. Bentley, and L. S. Gage. "The Provision and Financing of Medical Care for AIDS Patients in the United States Public and Private Teaching Hospitals." *Journal of the American Medical Association* 258, no. 8 (September 1987):1343-46.

Baccetti, P., D. Osmond, R. E. Chaisson, S. Dritz, G. W. Rutherford, L. Swig, and A. R. Moss. "Survival Patterns of the First 500 Patients with AIDS in San Francisco." *Journal of Infectious Diseases* 157, no. 5 (May 1988):1044-47.

Bennett, C. L., J. B. Garfinkle, D. Draper, W. Rogers, W. C. Mathews, and D. E. Kanouse. "The Relation between Hospital Experience and In-Hospital Mortality for Patients with AIDS-Related PCP." *Journal of the American Medical Association* 261, no. 20 (26 May 1989):2975-79.

Bongaarts, J. "A Model of the Spread of HIV Infection and the Demographic Impact of AIDS." Paper presented at the Conference on Statistical and Mathematical Modeling of the AIDS Epidemic. Johns Hopkins University, November 1988.

Buehler, J., R. Berkelman, and O. Devine. "Estimate of HIV-Related Deaths in Young Adult Men, United States." In *Abstracts of the Fifth International Conference on AIDS*. Montreal, Canada, June 4-9, 1989.

Centers for Disease Control. *AIDS Public Information Data Set Documentation*. Atlanta, GA: CDC, September 30, 1989.

———. "Guidelines for Prophylaxis against Pneumocystis Carinii Pneumonia for Persons Infected with Human Immunodeficiency Virus." *Morbidity and Mortality Weekly Review* 38, no. S-5 (June 1989):1-90.

———. *HIV/AIDS Surveillance Report*. Atlanta, GA: CDC, January 1990.

Centers for Disease Control. "Revision of the CDC Surveillance Case Definition for Acquired Immunodeficiency Syndrome." *Morbidity and Mortality Weekly Review* 36, supplement 1S (1987):1S-15S.

Chevarley, F., K. Kochanek, and J. Beuler. "Comparison of U.S. HIV Mortality Trends from *Vital Statistics* and AIDS Surveillance." In *Abstracts of the Fifth International Conference on AIDS*. Montreal, Canada, June 4-9, 1989.

Conway, G., B. Colley-Niermeyer, C. Pursley, C. Cruz, S. Burt, P. Rion, and C. W. Health. "Underreporting of AIDS Cases in South Carolina, 1986 and 1987." *Journal of the American Medical Association* 262, no. 20 (24 November 1989):2859-63.

Fanning, M., K. Johnson, J. Osachoff, J. Montaner, R. Coates, J. Rueday,

et al. "Clinical and Laboratory Effects of AZT in HIV Positive Men Compared to a Concurrent Control Group." In *Abstracts of the Fifth International Conference on AIDS.* Montreal, Canada, June 4–9, 1989.

Cox, D. R., and D. Oakes. *Analysis of Survival Data.* New York: Chapman and Hall, 1984.

Hardy, A. M., E. T. Starcher, and W. M. Morgan, J. Druker, A. Kristal, J. M. Day, C. Kelly, E. Ewing and J. W. Curran. "Review of Death Certificates to Assess Completeness of AIDS Case Reporting." *Public Health Reports* 102, no. 4 (July–August 1987):386–91.

Justice, A., A. Feinstein, and C. Wells. "Importance of Age in Prognostic Staging System for AIDS." *New England Journal of Medicine* 321, no. 20 (16 November 1989):1408–1409.

Kalbfleish, J. D., and R. L. Prentice. *The Statistical Analysis of Failure Time Data.* New York: Wiley & Sons, Inc., 1980.

Lafferty, W. E., S. G. Hopkins, J. Honey, J. D. Harwell, P. C. Shoemaker, and J. M. Kobayashi. "Hospital Charges for People with AIDS in Washington State: Utilization of a Statewide Hospital Discharge Data Base." *American Journal of Public Health* 78, no. 8 (August 1988):949–52.

Lemp, G., S. Payne, D. Neal, T. Temelso, and G. Rutherford. "Survival Trends for Patients with AIDS." *Journal of the American Medical Association* 263, no. 3 (January 1990:402–406.

Leoung, G. S., A. B. Montgomery, D. I. Abrams, L. Wardlaw, K. Corkery, D. Busch, S. Gordan, D. W. Feigal, and the SF County Community Consortium. "Aerosol Pentamidine for Pneumocystis Carinii Pneumonia Prophylaxis: A 3-Arm Randomized Trial." In *Abstracts of the Fifth International Conference on AIDS.* Montreal, Canada, June 4–9, 1989.

Marasca, G., and M. McEvoy. "Length of Survival of Patients with Acquired Immune Deficiency Syndrome in the United Kingdom." *British Medical Journal* 292, no. 6357 (28 June 1986):1727–29.

Marier, R. "The Reporting of Communicable Diseases." *American Journal of Epidemiology* 105, no. 6 (1977):587–89.

Mor, V., J. Piette, and J. Fleishman. "Challenges to Community Case Management for Persons with AIDS." *Health Affairs* 8, no. 4 (Winter 1989):139–53.

Phair, J., A. Munoz, R. Detels, R. Kaslow, C. Rinaldo, A. Soah, and the Multicenter AIDS Cohort Study Group. "The Risk of Pneumocystic Carinii Pneumonia among Men Infected with Human Immunodeficiency Virus Type 1." *New England Journal of Medicine* 322, no. 3 (18 January 1990):161–65.

Pizzo, P., J. Eddy, and J. Faloon. "Acquired Immune Deficiency Syndrome in Children: Current Problems and Therapeutic Considerations." *American Journal of Medicine* 85, no. 2A (August 1988):195–202.

Rothenberg, R., M. Woefel, and R. Stoneburner, J. Milberg, R. Parker, and B. Truman. "Survival with the Acquired Immunodeficiency Syndrome—Experience with 5,833 Cases in New York City." *New England Journal of Medicine* 317, no. 21 (19 November 1987):1297–1302.

Seage, G. R. "Cost of Medical Care for AIDS in Massachusetts: Trends over a Two-year Period." In *Abstracts of the Third International Conference on AIDS.* Conference proceedings. Washington DC: June 1–5, 1987.

Seage, G. R., S. Landers, A. Barry, J. Groopman, G. A. Lamb, and A. M.

Epstein. "Medical Care Costs of AIDS in Massachusetts." *Journal of the American Medical Association* 256, no. 22 (12 December 1986):3107-3109.

Seage, G. R., S. Landers, K. H. Mayer, M. A. Barry, G. A. Lamb, and A. M. Epstein. "Medical Costs of Ambulatory Patients with AIDS-Related Complex (ARC) and/or Generalized Lymphadenopathy Syndrome (GLS) Related to HIV Infection, 1984-1985." *American Journal of Public Health* 78, no. 8 (August 1988):969-70.

Stein, M., J. Piette, V. Mor, "Differences in Access to Azidothymidine (AZT) among Symptomatic HIV-Infected Persons." *Journal of General Internal Medicine* (in press).

Vella, S., F. M. Ippolito, M. G. Agresti, P. Pezotti, and D. Greco. "Survival Patterns of Zidovudine Treated AIDS Patients Compared to Untreated Controls." In *Abstracts of the Fifth International Conference on AIDS*. Montreal, Canada, June 4-9, 1989.

Wennberg, J., and A. Gittlesohn. "Variations in Medical Care among Small Areas." *Scientific American* 246, no. 4 (1982):120-35.