

SPECIAL ARTICLE

PHYSICIANS' EXPERIENCE WITH THE ACQUIRED IMMUNODEFICIENCY SYNDROME AS A FACTOR IN PATIENTS' SURVIVAL

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Abstract Background. Previous studies have found that patients with the acquired immunodeficiency syndrome (AIDS) who are admitted to hospitals that admit many such patients have lower mortality rates than patients in hospitals with less experience with AIDS. We examined the relation between physicians' experience with AIDS and the survival of their patients with AIDS.

Methods. We studied 403 adult male patients enrolled in a staff-model health maintenance organization in whom first AIDS-defining illnesses were diagnosed from 1984 through mid-1994; we determined that these illnesses met the 1987 case definition of the Centers for Disease Control. We defined three levels of experience for the patients' 125 primary care physicians according to their experience with AIDS during residency training and the cumulative number of patients with AIDS they had cared for in their practices.

Results. The median survival of the patients of physi-

cians with the least experience in the management of AIDS was 14 months, as compared with 26 months for the patients of physicians with the most experience ($P < 0.001$). Controlling for the severity of illness and the year of diagnosis, we found that the patients cared for by physicians with the most experience had a 31 percent lower risk of death than the patients cared for by physicians with the least experience ($P < 0.02$). Among 244 patients with an AIDS-defining illness diagnosed from 1989 through 1994, after adjustment for the CD4+ cell count and the severity of illness, the risk of death was 43 percent lower for patients of the most experienced physicians than for patients of the least experienced ($P < 0.02$).

Conclusions. The experience of primary care physicians in the management of AIDS is significantly associated with survival among their patients. (N Engl J Med 1996;334:701-6.)

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MANY practicing physicians have received no formal training in the care of patients infected with the human immunodeficiency virus (HIV). Moreover, because standards of care for the acquired immunodeficiency syndrome (AIDS) change rapidly, primary care physicians must continually assimilate and apply new information as HIV-infected people become their patients. It is important to know whether differences in the level of physicians' experience with AIDS are associated with differences in patients' outcomes.

Because previous studies of hospitals have found a relation between the admission of higher numbers of patients with AIDS-related conditions and lower inpatient mortality,¹⁻⁴ we sought to determine whether more experience with the management of AIDS on the part of primary care physicians is associated with increased survival among their patients with AIDS.

METHODS

Study Setting

We conducted a retrospective cohort study at Group Health Cooperative of Puget Sound, a staff-model health maintenance organization (HMO) with headquarters in Seattle. Group Health provides comprehensive medical care for a fixed, prepaid fee to approximately

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385,000 enrollees in western Washington, 84 percent of whom have their premiums at least partly paid by their employers. Family physicians provide most primary care at Group Health and are responsible for both outpatient and inpatient care of defined groups of patients. The care of patients infected with HIV is distributed among all primary care physicians in Group Health's generalist-based model of care. Referral to specialists is at the discretion of the primary care physicians, and there are no financial incentives to limit referrals. Insurance coverage for patients with AIDS is maintained through several financial arrangements that extend beyond the end of their employment; as a result, less than 3 percent of these patients leave Group Health for reasons other than death.

Study Patients

We identified 429 adults in whom initial AIDS-defining illnesses were diagnosed between January 1, 1984, and June 30, 1994; these diagnoses met the 1987 surveillance case definition of the Centers for Disease Control⁵ and were recorded in the Group Health HIV/AIDS Surveillance Database. A review of medical records enabled us to apply these criteria to all cases consistently. We were not able to use the expanded case definition of AIDS, which includes a CD4+ cell count of less than 200 per cubic millimeter (or less than 14 percent of lymphocytes⁶), because CD4+ cell counts were not included in the computerized records before 1989. All patients had serologically confirmed HIV infection. Of the Group Health patients with AIDS, 95 percent were men whose risk factor for HIV transmission was that they had had sexual contact with men. We excluded from the study 13 women and 6 men who had other risk factors. We also excluded four men because their primary care physicians changed within a year before the diagnosis of AIDS or at any time thereafter; three more men were excluded because their primary care physicians had subspecialty certification in infectious diseases or pulmonary medicine. The remaining 403 men made up the study cohort.

Study Physicians

The study physicians were the 125 physicians who provided primary care for patients in the cohort. These primary care physicians had been trained in internal medicine, family medicine, or general practice. We

defined the physicians' level of experience with AIDS with a modification of criteria developed by Ramsey and colleagues that measure experience in the care of patients with AIDS in medical school, residency, and practice.^{7,8} Estimates of physicians' experience in medical school and residency were derived from the rates of incidence of AIDS for the metropolitan areas where the physicians trained and the calendar years in which their training was completed.^{7,8} We defined practice experience as the cumulative number of patients with AIDS whose care a physician had managed at the time a patient in the physician's practice was given a first diagnosis of an AIDS-defining illness; the new patient was included in this total. As each patient entered the cohort, he was identified as his physician's first, second to fifth, or sixth or subsequent patient with AIDS. The categories of medical school and residency experience were equivalent for the study physicians. Therefore, we combined the residency and practice experience of the individual physicians to define three levels of a physician's experience with AIDS: least experience, moderate experience, and most experience (Fig. 1). Some physicians moved from lower to higher experience categories during the 10-year study period, as AIDS-defining illnesses developed in more of their patients. Therefore, some physicians were not assigned to the same experience category for all of their patients with AIDS.

Sources of Data

We obtained information on the patients in the study, including age at diagnosis, race or ethnic group, AIDS-defining illness and date of diagnosis, risk factors for HIV transmission, and date on which care from Group Health ended (because of death or transfer from the HMO), from the Group Health HIV/AIDS Surveillance Database. Dates of death were confirmed by cross-matching with the Washington State vital records. We obtained laboratory and pharmacy data and the name of each patient's primary care physician from Group Health's Utilization Management/Cost Management Information System. Personnel records provided information on the study physicians' specialty training and the locations and dates of their medical school and residency training.

Statistical Analysis

To control for improved survival due to advances in the treatment of AIDS, we grouped the dates on which patients were given diagnoses of AIDS-defining illnesses into three calendar-year periods. The first period, 1984 to 1986, preceded the availability of zidovudine and chemoprophylaxis against *Pneumocystis carinii* pneumonia, which be-

		Practice		
		1 Patient	2 to 5 Patients	>5 Patients
Residency	Low	Least	Moderate	Most
	High	Moderate	Most	

Figure 1. Categories of Physicians' Experience with AIDS.

Experience with AIDS during residency and practice was combined into three overall categories: least, moderate, and most. Physicians who completed their residency training before 1984 or trained in a metropolitan area with an incidence of AIDS of less than 15 per 100,000 were classified as having a low level of residency experience. Those who completed training in 1984 or later in a metropolitan area with an incidence of AIDS of 15 or more per 100,000 were classified as having a high level of residency experience. A physician's practice-experience category was separately determined at the time an AIDS-defining illness was diagnosed in each patient, according to whether the patient was the physician's first, second to fifth, or sixth or subsequent patient with AIDS. No physician in our study had both a high level of residency experience and a high level of practice experience.

Table 1. Characteristics of the 403 Study Patients.

CHARACTERISTIC	NO. OF PATIENTS (%)*
Age at diagnosis	
18–29 yr	41 (10)
30–39 yr	175 (43)
40–49 yr	134 (33)
≥50 yr	53 (13)
Race or ethnic group	
White	379 (94)
Black	17 (4)
Hispanic	6 (1)
Asian	1 (<1)
Initial AIDS-defining diagnosis	
<i>P. carinii</i> pneumonia	149 (37)
Other opportunistic infections	134 (33)
Kaposi's sarcoma	43 (11)
Neurologic disease	43 (11)
Cytomegalovirus or herpes simplex virus	26 (6)
Lymphoma	8 (2)

*Because of rounding, percentages may not total 100.

came available by the second period, 1987 to 1988.^{9,10} By the third period, 1989 to 1994, both drug regimens were in general use^{11,12} and zidovudine was recommended for patients with CD4+ cell counts below 500 per cubic millimeter.¹³ Previous cohort studies of HIV-infected homosexual and bisexual men have found increases in survival from the earliest to the latest of these periods.^{14,15}

Severity of illness at entry into the study was determined according to a three-stage classification of AIDS-defining diagnoses developed by Turner and colleagues.¹⁶ Conditions such as Kaposi's sarcoma are included in the category of least severe illness, moderately severe illness is defined as *P. carinii* pneumonia, and the category of most severe illness includes diagnoses such as disseminated infection with *Mycobacterium avium* complex. CD4+ cell counts at the time of the diagnosis of AIDS were available for 244 of the 278 patients in whom first AIDS-defining illnesses were diagnosed from 1989 to 1994 (88 percent) and were classified into four levels: 0 to 49, 50 to 99, 100 to 199, and 200 or more per cubic millimeter.

We estimated median survival and survival curves from the time of the diagnosis of AIDS according to the patient's age, the calendar period of the diagnosis, the severity of illness, the CD4+ cell count at diagnosis, and physician-experience category, using Kaplan-Meier survival analysis.¹⁷ Statistical significance was evaluated with the log-rank test. Unadjusted and adjusted relative risks of death according to physician-experience category, the calendar period of the diagnosis, the severity of illness, and the CD4+ cell count at diagnosis were estimated with Cox proportional-hazards analysis.^{18,19} Statistical significance for the relative risks was evaluated with the likelihood-ratio test. The test for trend in proportions²⁰ was used to examine the relation between a physician's use of prophylaxis against *P. carinii* pneumonia, measurement of CD4+ cells, and use of antiretroviral therapy and that physician's level of experience with AIDS. The association between the use of prophylaxis against *P. carinii* pneumonia and the occurrence of *P. carinii* pneumonia as a patient's AIDS-defining illness was evaluated with the chi-square test. We used generalized estimating equations to evaluate the robustness of the results with respect to the assumption of statistical independence among patients.²¹ We also examined physician-experience category as a time-dependent covariate to take into account the experience gained during the care of an individual patient with AIDS. Two-tailed P values of 0.05 or less were considered to indicate significance in all statistical tests.

RESULTS

The mean age of the patients at the time of the diagnosis of AIDS was 39 years (range, 23 to 67). Ninety-four percent of the patients were white, and for 70 percent

the AIDS-defining diagnoses were *P. carinii* pneumonia and other opportunistic infections (Table 1). Of the study physicians, 85 percent were trained in family medicine or general practice, and 15 percent in internal medicine. By the end of the study period, 49 physicians (39 percent) remained in the category of least experience, having managed the care of only one patient with AIDS during the 10 years. By the end of the study, 52 physicians (42 percent) had acquired moderate experience, and 24 (19 percent) had entered the category with the most experience.

We found significant differences in survival among the patients with AIDS under the care of physicians with different levels of experience, as shown in Figure 2. Median survival for the patients of physicians with the least experience was 14 months, as compared with 21 months for the patients of physicians with moderate experience and 26 months for the patients of physicians with the most experience ($P < 0.001$ by the log-rank test). As in previous studies, there was a significant increase in survival during the later years of the study period^{14,15} and a significant decrease in survival among the patients with more severe illness¹⁶ and lower CD4+ cell counts²² (Table 2). Neither age at diagnosis nor use of antiretroviral therapy was associated with survival in our cohort (data not shown). An appropriate survival model showing the effects of prophylaxis against *P. carinii* pneumonia could not be constructed because we were not able to study survival from the beginning of immunologic AIDS¹⁴ — that is, from the point when a patient's CD4+ cell count dropped below 200 per cubic millimeter or 14 percent.⁶ There were too few nonwhite patients in the cohort to enable us to estimate an effect of race on survival.

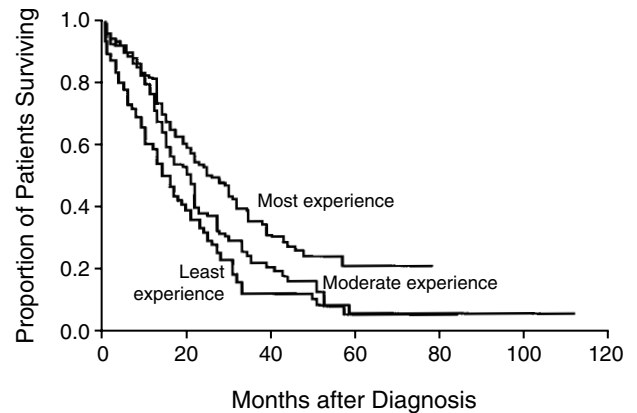


Figure 2. Kaplan-Meier Analysis of Survival after the Diagnosis of AIDS, According to Physician-Experience Category. $P < 0.001$ by the log-rank test.

As shown in Table 2, the adjusted relative risk of death was 0.69 for patients of the physicians with the most experience as compared with patients of the physicians with the least experience, after we controlled for the severity of illness and the calendar period in which the diagnosis was made ($P < 0.02$). Figure 3 shows that for each multiyear period, patients cared for by physicians with more experience with AIDS had a lower risk of death. Controlling for the time of diagnosis in one-year increments yielded virtually the same estimates of the effect of physicians' experience on the relative risk of death (data not shown). Allowing for the increases in the level of physicians' experience that took place during the period of care of an individual study patient also did not affect the results (data not shown). The results

Table 2. Median Survival and Relative Risk (RR) of Death According to Selected Variables.*

VARIABLE	NO. OF PATIENTS (%)	MEDIAN SURVIVAL (MO)	UNADJUSTED RR (95% CI)†	ADJUSTED RR (95% CI)‡	P VALUE	ADJUSTED RR FOR PATIENTS WITH CD4 COUNTS (95% CI)§	P VALUE
Physicians' experience							
Least¶	99 (25)	14	1.00	1.00	<0.02	1.00	<0.02
Moderate	139 (34)	21	0.73 (0.63–0.85)	0.83 (0.71–0.97)		0.75 (0.60–0.94)	
Most	165 (41)	26	0.53 (0.46–0.62)	0.69 (0.59–0.80)		0.57 (0.45–0.71)	
Period of diagnosis of AIDS							
1984–1986¶	47 (12)	13	1.00	1.00	<0.001	NA	<0.001
1987–1988	78 (19)	17	0.64 (0.44–0.92)	0.72 (0.49–1.05)			
1989–1994	278 (69)	25	0.40 (0.29–0.56)	0.50 (0.35–0.71)			
Severity of illness at diagnosis							
Low¶	166 (41)	30	1.00	1.00	<0.001	1.00	<0.001
Medium	149 (37)	19	1.71 (1.30–2.26)	1.49 (1.12–1.98)		1.10 (0.73–1.65)	
High	88 (22)	13	2.40 (1.75–3.30)	2.12 (1.53–2.93)		1.96 (1.28–3.02)	
CD4+ cell count							
0–49/mm ³ ¶	87 (36)	14	1.00	NA	<0.001	1.00	<0.001
50–99/mm ³	47 (19)	26	0.46 (0.29–0.72)			0.47 (0.30–0.73)	
100–199/mm ³	57 (23)	32	0.33 (0.21–0.53)			0.37 (0.23–0.60)	
≥200/mm ³	53 (22)	51	0.19 (0.11–0.33)			0.21 (0.12–0.37)	

*CI denotes confidence interval.

†P values for all covariates in univariate analyses were <0.001.

‡Relative risks were adjusted for all the other variables in the table.

§CD4+ cell counts were available for 244 of the 278 patients in whom a diagnosis was made between 1989 and 1994.

¶Reference category.

||NA (not applicable) denotes that the relative risk could not be calculated because of the unavailability of CD4+ cell counts for patients in whom a diagnosis was made before 1989.

of analyses with generalized estimating equations were similar to the results of the analysis of survival.

Among the 244 patients for whom CD4+ cell counts were available (patients in whom AIDS was diagnosed from 1989 to 1994), the adjusted relative risk of death was 0.57 for patients of the most experienced physicians as compared with patients of the least experienced, after adjustment for CD4+ cell count and the severity of illness ($P < 0.02$). Among the first three patients with AIDS cared for by each physician (a total of 219 patients), the adjusted relative risks of death for the second and third patients as compared with the first patient were 0.73 and 0.54, respectively, after adjustment for the calendar period of diagnosis, the severity of illness, and experience during residency training ($P < 0.02$ by the likelihood-ratio test; data not shown). The effect of experience on patients' relative risk was similar for both patients of the physicians who ultimately reached the highest level of experience and patients of the physicians who ended the study period at the level of least or moderate experience (data not shown).

Table 3 shows characteristics of the care of the 212 patients in whom AIDS was diagnosed from 1989 to 1994 who had CD4+ cell counts of less than 200 per cubic millimeter before diagnosis. With increasing experience on the part of physicians, there was a significant increase in the proportion of patients receiving prophylaxis against *P. carinii* pneumonia before being given a diagnosis of AIDS. Of the patients who did not receive prophylaxis against *P. carinii* pneumonia, 54 percent had *P. carinii* pneumonia as their AIDS-defining illness, as compared with 16 percent of the patients who did receive appropriate prophylaxis ($P < 0.001$). The patients of physicians with greater experience were more likely to have had at least two CD4+ cell counts performed in the year before the diagnosis of AIDS than were patients of physicians with less experience ($P < 0.001$), and there was a

trend toward an increased use of antiretroviral therapy by the more experienced physicians ($P = 0.06$).

DISCUSSION

The experience of primary care physicians in the management of AIDS is significantly associated with their patients' survival. After adjusting for the severity of disease and changes in the treatment of AIDS over time, we found a 31 percent lower risk of death for patients cared for by physicians with the most experience as compared with patients of physicians with the least experience. Among patients in whom AIDS was diagnosed from 1989 to 1994, the adjusted risk of death was 43 percent lower for the patients of the most experienced physicians than for the patients of the least experienced, after we controlled for the CD4+ cell count and the severity of illness.

Our results support the hypothesis of Luft and colleagues that, in the treatment of disease, practice makes perfect.²³ It has been proposed that experience resulting from higher patient volume may lead to better management strategies and improved outcomes for patients.^{24,25} A possible explanation for our findings is that physicians acquire general knowledge about AIDS either during their residency training or while taking care of the first patient with AIDS in their practice. They are then exposed to a greater number of AIDS-related conditions through caring for their next few patients, but they may require a case load of more than five patients to gain enough experience to achieve the best outcomes. The primary care physicians in our study were responsible for both outpatient and inpatient care. This study complements previous research on the experience of hospitals with AIDS by showing that the experience of individual physicians is important as well and suggests that physicians' experience may be an important component of the hospital experience.

We addressed the possibility that selective referral²³ may have biased our results in several ways. Some physicians who are perceived to be more comfortable taking care of HIV-infected patients may have a disproportionate number of patients with AIDS in their practices. Furthermore, patients who selected these physicians to direct their care may have been more knowledgeable about their disease or more compliant with treatment. To limit this possible form of bias, we excluded patients whose primary care physician changed within the year before the diagnosis of AIDS or thereafter. We also verified that similarities among the patients within individual physicians' practices did not account for the effect of physicians' experience on survival. Finally, it is unlikely that patients would be selectively referred to physicians who had directed the care of only one or two previous patients with AIDS and who had not demonstrated relatively good outcomes. We examined the first three patients of all study physicians and found a steady improvement in survival for each successive patient. This was true for the first three patients of both the physicians who ultimately acquired the most patients with

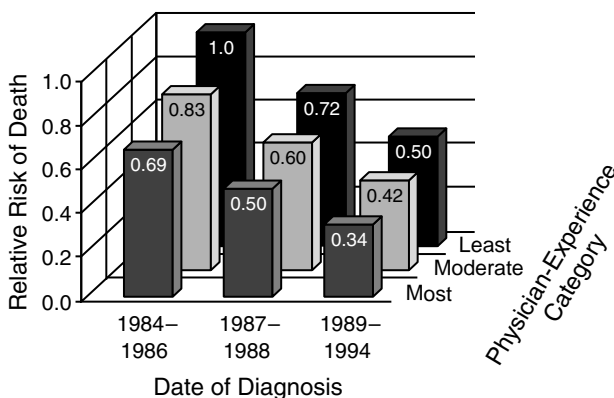


Figure 3. Relative Risk of Death for Patients in Each Physician-Experience Category, According to the Date of Diagnosis of AIDS.

The reference category was the patients in whom AIDS was diagnosed in 1984 through 1986 whose physicians had the least experience with AIDS. The relative risks were adjusted for severity of illness.

Table 3. Management Strategies for 212 Patients with CD4+ Cell Counts of Less Than 200 per Cubic Millimeter before the Diagnosis of AIDS, According to Physicians' Experience.*

MANAGEMENT STRATEGY	LEAST EXPERIENCE	MODERATE EXPERIENCE	MOST EXPERIENCE	P VALUE†
	percent of patients			
Prophylaxis against <i>P. carinii</i> pneumonia before diagnosis of AIDS	30	52	78	<0.001
At least two CD4+ cell counts in the year before diagnosis of AIDS‡	34	52	76	<0.001
Antiretroviral therapy in the year before diagnosis of AIDS or later	42	49	59	0.06

*Least experience denotes patients of physicians with the least experience (43 patients [20 percent]); moderate experience denotes patients of physicians with moderate experience (75 patients [35 percent]); and most experience denotes patients of physicians with the most experience (94 patients [44 percent]). Only patients in whom AIDS was diagnosed in 1989 through 1994 are included.

†P values are for trend in proportions.

‡For the 173 patients in whom AIDS was diagnosed in 1990 or later.

AIDS and the physicians who remained in the two lower categories of experience. Therefore, our findings suggest that the physicians in this study went through a similar learning period and began to improve their management skills and strategies early in their experience.

Markson and colleagues found that primary care generalists adopted new therapies for AIDS more slowly than AIDS specialists.²⁶ The use of several methods of care was associated with the higher levels of physicians' experience in our study. The appropriate use of prophylaxis against *P. carinii* pneumonia was strongly linked to increasing experience. Such prophylaxis may delay or prevent the development of *P. carinii* pneumonia in patients infected with HIV^{14,27,28} and lengthen their survival.^{15,29,30} The patients of physicians with more experience also had more frequent CD4+ cell counts in the year before the diagnosis of AIDS, a finding that suggests there was closer follow-up of HIV-infected patients and an increased ability to begin prophylaxis against *P. carinii* pneumonia at an appropriate time. The use of antiretroviral therapy was also associated with the higher levels of physicians' experience, although the data on the effectiveness of such therapy are equivocal.³¹⁻³³ Further study is needed to determine whether other management strategies may have contributed to the effect of physicians' experience on survival.

There is ongoing debate about the role of generalists and specialists in the care of patients at all stages of HIV disease.^{34,35} Some authors suggest that primary care for patients infected with HIV should be integrated into general medical practice.^{36,37} This is currently the case in some settings,³⁸ although in others primary care is provided by specialists in the treatment of HIV disease.³⁹ There are only limited data to support the use of any particular organizational arrangement. The physicians in our study were generalists who provided primary care in a setting in which specialists are routinely involved in the care of patients with AIDS and in which there are

no financial incentives limiting referrals or hospitalizations. Therefore, our conclusions may be generalizable only to family physicians practicing in a managed-care setting that includes ready access to consultation with specialists. For a primary care physician, gaining experience may involve acquiring information from specialists and interacting effectively with consultants.

The patients of the most experienced physicians in our study had a median survival time similar to the longest reported in other clinical studies,^{15,40} demonstrating that in this type of environment, generalists who provide primary care for patients with AIDS can perform well.

Our results suggest that there is a need to organize health care delivery and training for physicians in ways that will optimize outcomes for patients with AIDS who are cared for by physicians at all levels of experience. A combination of generalist and specialist care may be effective in managing the complex medical conditions associated with AIDS.

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REFERENCES

- Bennett CL, Garfinkle JB, Greenfield S, et al. The relation between hospital experience and in-hospital mortality for patients with AIDS-related PCP. *JAMA* 1989;261:2975-9.
- Bennett CL, Adams J, Gertler P, et al. Relation between hospital experience and in-hospital mortality for patients with AIDS-related *Pneumocystis carinii* pneumonia: experience from 3,126 cases in New York City in 1987. *J Acquir Immune Defic Syndr* 1992;5:856-64.
- Turner BJ, Ball JK. Variations in inpatient mortality for AIDS in a national sample of hospitals. *J Acquir Immune Defic Syndr* 1992;5:978-87.
- Stone VE, Seage GR III, Hertz T, Epstein AM. The relation between hospital experience and mortality for patients with AIDS. *JAMA* 1992;268:2655-61.
- Revision of the CDC surveillance case definition for acquired immunodeficiency syndrome. *MMWR Morb Mortal Wkly Rep* 1987;36:Suppl 1S:3S9S.
- 1993 Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *MMWR Morb Mortal Wkly Rep* 1992;41(RR-17):1-19.
- Ramsey PG, Wenrich MD, Carline JD, Curtis JR, Paaau DS. Primary care of patients with or at-risk for HIV infection: final report to the Agency for Health Care Policy and Research. Rockville, Md.: Department of Health and Human Services, 1994.
- Curtis JR, Paaau DS, Wenrich MD, Carline JD, Ramsey PG. Physicians' ability to provide initial primary care to an HIV-infected patient. *Arch Intern Med* 1995;155:1613-8.
- Graham NMH, Zeger SL, Kuo V, et al. Zidovudine use in AIDS-free HIV-1-seropositive homosexual men in the Multicenter AIDS Cohort Study (MACS), 1987-1989. *J Acquir Immune Defic Syndr* 1991;4:267-76.
- Lang W, Osmond D, Samuel M, Moss A, Schragger L, Winkelstein W Jr. Population-based estimates of zidovudine and aerosol pentamidine use in San Francisco: 1987-1989. *J Acquir Immune Defic Syndr* 1991;4:713-6.
- Graham NM, Jacobson LP, Kuo V, Chmiel JS, Morgenstern H, Zucconi SL. Access to therapy in the Multicenter AIDS Cohort Study, 1989-1992. *J Clin Epidemiol* 1994;47:1003-12.
- Holmberg SD, Conley LJ, Buchbinder SP, et al. Use of therapeutic and prophylactic drugs for AIDS by homosexual and bisexual men in three U.S. cities. *AIDS* 1993;7:699-704.
- Volberding PA, Lagakos SW, Koch MA, et al. Zidovudine in asymptomatic human immunodeficiency virus infection: a controlled trial in persons with fewer than 500 CD4-positive cells per cubic millimeter. *N Engl J Med* 1990;322:941-9.
- Munoz A, Schragger LK, Bacellar H, et al. Trends in the incidence of outcomes defining acquired immunodeficiency syndrome (AIDS) in the Multicenter AIDS Cohort Study: 1985-1991. *Am J Epidemiol* 1993;137:423-38.

15. Osmond D, Charlebois E, Lang W, Shiboski S, Moss A. Changes in AIDS survival time in two San Francisco cohorts of homosexual men, 1983 to 1993. *JAMA* 1994;271:1083-7.
16. Turner BJ, Markson LE, McKee LJ, Houchens R, Fanning T. The AIDS-defining diagnosis and subsequent complications: a survival-based severity index. *J Acquir Immune Defic Syndr* 1991;4:1059-71. [Erratum, *J Acquir Immune Defic Syndr* 1992;5:214.]
17. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc* 1958;53:457-81.
18. Cox DR. Regression models and life-tables. *J R Stat Soc [B]* 1972;34:187-220.
19. Kalbfleisch JD, Prentice RL. *The statistical analysis of failure time data*. New York: John Wiley, 1980.
20. Brown BW Jr, Hollander M. *Statistics: a biomedical introduction*. New York: John Wiley, 1977.
21. Zeger SL, Liang K-Y. Longitudinal data analysis for discrete and continuous outcomes. *Biometrics* 1986;42:121-30.
22. Yarchoan R, Venzon DJ, Pluda JM, et al. CD4 count and the risk for death in patients infected with HIV receiving antiretroviral therapy. *Ann Intern Med* 1991;115:184-9.
23. Luft HS, Hunt SS, Maerki SC. The volume-outcome relationship: practice-makes-perfect or selective-referral patterns? *Health Serv Res* 1987;22:157-82.
24. Maerki SC, Luft HS, Hunt SS. Selecting categories of patients for regionalization: implications of the relationship between volume and outcome. *Med Care* 1986;24:148-58.
25. Luft HS, Bunker JP, Enthoven AC. Should operations be regionalized? The empirical relation between surgical volume and mortality. *N Engl J Med* 1979;301:1364-9.
26. Markson LE, Cosler LE, Turner BJ. Implications of generalists' slow adoption of zidovudine in clinical practice. *Arch Intern Med* 1994;154:1497-504.
27. Hoover DR, Saah AJ, Bacellar H, et al. Clinical manifestations of AIDS in the era of pneumocystis prophylaxis. *N Engl J Med* 1993;329:1922-6.
28. Graham NM, Zeger SL, Park LP, et al. Effect of zidovudine and *Pneumocystis carinii* pneumonia prophylaxis on progression of HIV-1 infection to AIDS: the Multicenter AIDS Cohort Study. *Lancet* 1991;338:265-9.
29. Graham NMH, Zeger SL, Park LP, et al. The effects on survival of early treatment of human immunodeficiency virus infection. *N Engl J Med* 1992;326:1037-42.
30. Chaisson RE, Keruly J, Richman DD, Moore RD. Pneumocystis prophylaxis and survival in patients with advanced human immunodeficiency virus infection treated with zidovudine: the Zidovudine Epidemiology Group. *Arch Intern Med* 1992;152:2009-13.
31. Volberding PA, Lagakos SW, Grimes JM, et al. The duration of zidovudine benefit in persons with asymptomatic HIV infection: prolonged evaluation of protocol 019 of the AIDS Clinical Trials Group. *JAMA* 1994;272:437-42.
32. Lundgren JD, Phillips AN, Pedersen C, et al. Comparison of long-term prognosis of patients with AIDS treated and not treated with zidovudine: AIDS in Europe Study Group. *JAMA* 1994;271:1088-92.
33. Concorde Coordinating Committee. Concorde: MRC/ANRS randomised double-blind controlled trial in immediate and deferred zidovudine in symptom-free HIV infection. *Lancet* 1994;343:871-81.
34. Cotton DJ. Improving survival in acquired immunodeficiency syndrome: is experience everything? *JAMA* 1989;261:3016-7.
35. Shapiro MF, Greenfield S. Experience and outcomes in AIDS. *JAMA* 1992;268:2698-9.
36. Northfelt DW, Hayward RA, Shapiro MF. The acquired immunodeficiency syndrome is a primary care disease. *Ann Intern Med* 1988;109:773-5.
37. Smith MD. Primary care and HIV disease. *J Gen Intern Med* 1991;6:Suppl 1:S56-S62.
38. Makadon HJ, Delbanco SF, Delbanco TL. Caring for people with AIDS and HIV infection in hospital-based primary care practice. *J Gen Intern Med* 1990;5:446-50.
39. Volberding P. The clinical spectrum of the acquired immunodeficiency syndrome: implications for comprehensive patient care. *Ann Intern Med* 1985;103:729-33.
40. Vella S, Chiesi A, Volpi A, et al. Differential survival of patients with AIDS according to the 1987 and 1993 CDC case definitions. *JAMA* 1994;271:1197-9.