

The association between primary source of ambulatory care and access to and outcomes of treatment among AIDS patients

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Abstract

Objectives. To examine the relationship between having a primary source of ambulatory care (PSAC), access to AIDS treatment and prophylaxis for opportunistic infection, and hospital and mortality outcomes among heterosexual men and women with AIDS.

Methods. Using a linked AIDS Registry–Medicaid database, 366 adults were identified (1989–1991) with at least 1 year of continuous Medicaid enrollment before AIDS diagnosis, who survived 2 weeks after diagnosis, and with no antiretroviral use or *Pneumocystis carinii* pneumonia (PCP) prophylaxis during the pre-diagnosis year. Outcomes included times to zidovudine treatment, PCP prophylaxis, hospitalization and death following diagnosis. Multivariate proportional hazards models were used to estimate the effects of patients' PSAC status in the 12-month post-diagnosis period on outcomes, controlling for demographic and case-mix variables.

Results. Study criteria preferentially included females, non-whites and enrollees eligible on the basis of aid to families with dependent children. A total of 49% of the patients had no PSAC. Patients with a PSAC were more likely to have received zidovudine [relative risk (RR) = 1.75, 95% confidence interval (CI) = 1.2, 2.2] or PCP prophylaxis (RR = 2.22, 95% CI = 1.5, 3.3). Regression models simultaneously examining association of the propensity to use zidovudine and PCP prophylaxis agents with death indicated that zidovudine-treated and PCP-prophylaxed patients were 64% and 51% less likely to die, respectively ($RR_{\text{death,zidovudine}} = 0.36$, 95% CI = 0.2, 0.4; $RR_{\text{death,PCP prophylaxis}} = 0.49$, 95% CI = 0.3, 0.8).

Conclusions. Patients' underuse of zidovudine and PCP prophylaxis was systematically associated with not having a PSAC. Lack of PSAC, in turn, predicted shorter survival but not increased hospitalization. Female gender, injecting drug use, non-white race and earlier diagnosis year also predicted poorer outcomes.

Keywords primary source of care, AIDS, access to treatment, outcomes

Over the last decade progress in the clinical management of AIDS patients has resulted in increased longevity and decreased morbidity attributed, in part, to the use of combinations of anti-viral therapies and prophylactic antibiotics to prevent opportunistic infections [1–6]. Access to these effective agents has varied substantially as reflected in differential use across a wide variety of patient socio-demographic, provider and organizational factors [7–12].

A growing body of research suggests that attributes of primary care, including coordination of care, physicians' knowledge of the patient as well as interpersonal communication, may be associated with improved health outcomes and cost-effective care [13]. The importance of a primary source of ambulatory care (PSAC) in facilitating access to and outcomes of effective AIDS therapies has not been well studied in large populations with validated Center

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for Disease Control (CDC)-defined AIDS. A prior study has suggested that patients having any kind of regular source of care had better access to preventive and primary care utilization [14]. Another report from an AIDS clinic at an academic research center found that new patients were more likely to have received antiretroviral drugs previously, but not *Pneumocystis carinii* pneumonia (PCP) prophylaxis, prior to enrollment if they could identify a regular medical care provider [15]. In a study of AIDS patients identified through diagnostic information from New York Medicaid claims data, treatment rates for zidovudine among patients in primary care clinics lagged behind those of infectious disease specialists in the 3 years after introduction of antiretroviral therapy [16]. However, whether these variations were due to differences in access to treatment on patient outcomes remains unknown. In a study of 1130 HIV-infected, pregnant women in the New York State Medicaid program, less than half had a usual source of prenatal care [17].

In this population-based study, we examined access to and outcomes of treatment among individuals with CDC-defined AIDS enrolled in Medicaid during the years 1989 through 1991, using a linked Medicaid–AIDS Surveillance database. We took advantage of the high number of treatment-naïve AIDS patients diagnosed in the years shortly following the introduction of the first major AIDS therapies, including zidovudine monotherapy and PCP prophylaxis. Zidovudine monotherapy represented the major treatment strategy for HIV infection during the late 1980s and early 1990s when placebo controlled studies of zidovudine showed a clear survival benefit for people with AIDS [18]. Zidovudine monotherapy became a standard-of-care prior to the mid-1990s, and failure to use zidovudine was even considered as reason for ‘malpractice’ [19]. Subsequent research reported that long-term zidovudine use resulted in resistance to antiviral treatment, with an increased risk of progression of HIV infection and mortality [20]. However, zidovudine monotherapy is still indicated for use in pregnant women to prevent perinatal transmission of HIV [21]. Antiviral combination therapy has displaced antiviral monotherapies as the recommended treatment strategy for HIV-infected individuals [6]. Nevertheless, the association between a primary source of care and initiation of innovative AIDS therapies perceived at the time of introduction as effective, life-saving treatments allows us to examine the important relationship between quality of care for HIV patients and a primary source of care.

Specifically, the overall aims of the study were: (i) to examine the association between patients’ PSAC and access to treatment; (ii) to estimate the effects of delays in antiretroviral treatment and PCP prophylaxis on rehospitalization and death rates. In addition, we measured changes over-time in adherence to treatment guidelines for zidovudine and PCP prophylaxis among people with AIDS. We focused on a large low-income population with a CDC-defined AIDS diagnosis whose onset of AIDS occurred while they were already enrolled in Medicaid. This incident cohort included disproportionate numbers of women and male injecting drug

users, populations that presently represent the largest risk pools for new HIV infection.

Methods

Data sources

We used two data sources to measure compliance with quality-of-care indicators: (i) New Jersey Medicaid enrollment and claims information; and (ii) New Jersey Department of Health (DOH) AIDS surveillance containing data on 13 704 unique New Jersey residents with AIDS ever reported to the state until June 30, 1991. Medicaid enrollment files included all unique patient identifiers for the period from January 1 1986 to June 30 1991), age, race, sex, and category of enrollment (e.g. Aid to the Permanently and Totally Disabled). Medicaid drug claims files contained complete and reliable patient-level data on the identity and dispensing date of each medication, number of units, and dose per unit for all medications dispensed in the community [22,23]. Complete longitudinal data for all hospitalization and outpatient services were available for all study subjects. New Jersey surveillance personnel linked the DOH and Medicaid data according to standard methods based on matching names, birth dates, sex and social security numbers.

Cohort definition

All adults (>12 years) from January, 1989 to March, 1991 were enrolled who: (i) had continuous Medicaid enrollment before the onset of AIDS; (ii) survived at least 2 weeks in the community following CDC-defined AIDS diagnosis; and (iii) received no antiretrovirals or PCP prophylaxis in the year prior to the AIDS-defining illness. These screening criteria preferentially excluded spend-down patients (e.g. homosexual males) and individuals dying shortly after diagnosis.

Patient demographic and case-mix characteristics

Demographic information was available in both the New Jersey Medicaid enrollment files and the New Jersey DOH AIDS Surveillance databases and included age, sex, race (white/non-white), and date of first CDC AIDS-defining illness. Age at the time of diagnosis was defined as an ordinal variables for five levels (12–19; 20–29; 30–39; 40–49; 50+ years). The CDC risk factor hierarchy was used to construct a binary indicator (yes/no) for injecting drug use (IDU) [24, 25]. Turner’s validated severity of HIV illness algorithm was used to construct a severity of illness variable ranging from one to four with the lowest level indicating the least severe category of AIDS-defining illness at the time of diagnosis [26].

Identification of primary care sources

We defined PSAC according to previously published methods as providers accounting for at least 50% of an individual’s visits in the 6 months following CDC-defined AIDS [27–29]. Individuals dying within 6 months of AIDS-defining illness

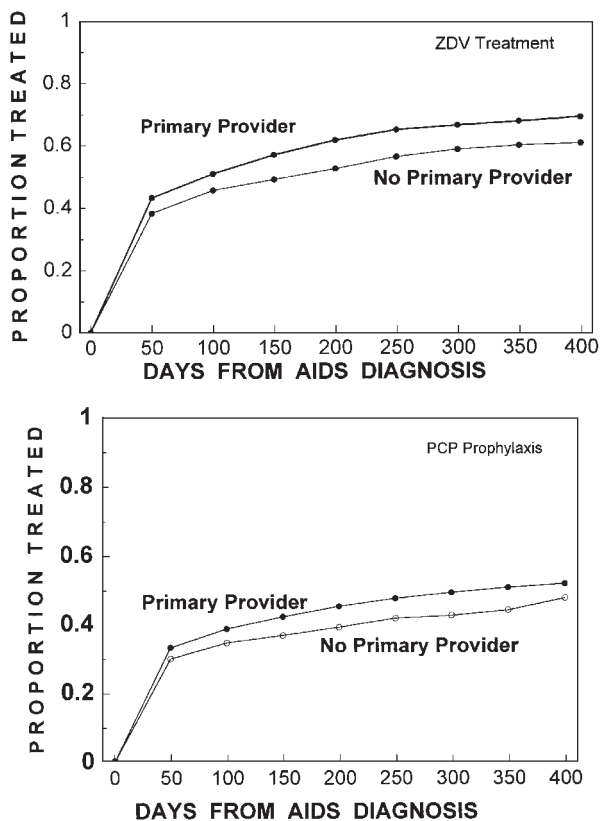


Figure 1 Influence of patient primary source of care status on zidovudine treatment (top) and on PCP prophylaxis (bottom).

were included in the PSAC identification process if they had more than one visit during the post-diagnosis survival period and met the 50% rule.

Quality of care indicators for treatment of HIV infection and for PCP prophylaxis

Indicators of quality of care for PCP prophylaxis and for primary anti-viral treatment of HIV infection were developed as consensus statements by a panel of clinician members of the research team and five other infectious disease experts. As treatment recommendations changed over the study period, indicators were developed that were sensitive to these changes. Because zidovudine was the only anti-retroviral agent available from March 1987 until October 1991 for people with AIDS, analysis was restricted to the Medicaid pharmacy claims data to this agent. Because some patients received treatment of opportunistic infections as inpatients, analysis of treatment of opportunistic infections was restricted to maintenance or prophylactic therapy. For PCP all prescription claims for trimethoprim-sulfamethoxazole (TMP-SMX), pentamidine and dapsone were extracted for the study patients after January, 1989 when treatment guidelines for prevention of PCP began to be disseminated in the scientific and lay press. Identification of TMP-SMX, pentamidine and dapsone as

PCP prophylactic medications was refined further by including only those prescribing patterns applicable to HIV infection (e.g. use of TMP-SMX for urinary tract infections was excluded – this is typically prescribed for periods of less than 21 days and at a higher average daily dose). For TMP-SMX those claims with an average daily dose of 1600 mg trimethoprim in combination with 320 mg sulfamethoxazole and with a 30 day supply of product were targeted. All aerosolized pentamidine was assumed to be indicated for PCP prophylaxis.

All study patients were considered eligible for a trial of zidovudine and were targeted if they received at least one prescription for this agent following CDC-defined AIDS diagnosis. As a second indicator of quality of care, we flagged any AIDS patient with prescriptions for TMP-SMX, dapsone or aerosolized pentamidine at levels and for the times indicated immediately above as having received an adequate trial of PCP prophylaxis.

To monitor secular trends in use of study drugs, drug use data for the years 1987–1991 were obtained for all Medicaid patients with AIDS whether or not they met the inclusion criteria; use was reported as the proportion of AIDS patients enrolled in Medicaid who received zidovudine or PCP prophylaxis in any given month.

Statistical analysis

Proportional hazards regression models were used to examine the relative effect of patient characteristics on time to zidovudine use or PCP prophylaxis among study patients. For all analyses, variables for age interval, sex, year of diagnosis, IDU and PSC indicators were included. Relative risk (RR) estimates contrasting the conditional probability of receiving zidovudine or PCP prophylaxis in one group versus another (e.g. males versus females) were estimated from the regression coefficients by exponentiation of these statistics, and the 95% confidence intervals (CI) were determined. Patients were censored from analysis at death or disenrollment from Medicaid.

In addition to modeling or adjusting for factors affecting study treatment and outcomes, additional analysis was conducted to adjust more completely for potentially confounding variables. In this approach, propensity scores for zidovudine treatment and PCP prophylaxis was calculated for each study patient to adjust the estimated effect of zidovudine use and PCP prophylaxis on mortality and hospitalization outcomes, which were measured in proportional hazards regression models. To do this the propensity scores were entered as covariates in the proportional hazards models for these outcomes which also included severity of illness measures [30]. RR and CI were estimated as described above.

Results

Study population

Of 1860 persons with AIDS present in the linked New Jersey AIDS Registry–Medicaid database in the study period, 366

Table 1 Descriptive characteristics of AIDS incident cases (1989–1991)

| | Medicaid AIDS <i>n</i> = 1860 | Study cohort <i>n</i> = 366 |
|--|-------------------------------------|-----------------------------------|
| Mean age (years) | 36 | 35 |
| Female (%) | 33 | 63 |
| Non-white (%) | 75 | 89 |
| Transmission mode (%) | | |
| Homo-/bisexual | 18 | 6 |
| Injecting drug use | 62 | 67 |
| Homosexual and injecting drug use | 3 | 2 |
| Heterosexual | 10 | 17 |
| Other | 7 | 8 |
| AIDS diagnosis year | | |
| 1989 | 51% | 48% |
| 1990 | 43% | 44% |
| 1991 | 6% | 8% |
| Eligibility category | | |
| Disability | 78% | 46% |
| Aid to families with dependent children | 22% | 54% |

adults with AIDS were identified who met inclusion criteria. As expected, the study cohort preferentially included females, injecting drug users and those enrolled in Medicaid on the basis of AFDC eligibility while tending to exclude males, non-injecting drug users, and individuals enrolled in Medicaid because of disability (Table 1). Although only about one-third of the overall Medicaid AIDS population consisted of women, the screening criteria employed in the definition of the cohort nearly doubled this percentage. In addition, the proportion of non-white individuals is higher in the final study cohort when compared with all Medicaid AIDS cases (90% versus 75%).

Identification of PSAC

Nearly half of all patients had no identifiable PSAC (49%). Of 187 patients with a known PSAC, the vast majority ($n = 168$) used outpatient clinics as their primary caregivers, and the remainder received health services from individual medical or osteopathic physicians. At the univariate level, patient sex, race, and IDU status were not associated with having a PSAC. Of the women ($n = 231$), 60% had a PSAC, slightly higher than the males (45%). Forty-nine percent of white, non-Hispanic individuals, 50% of blacks and 63% of Hispanics had an identifiable PSAC. In univariate analysis examining the association between PSAC and time to zidovudine treatment or PCP prophylaxis, it was found that study patients who regularly received care from the same provider had consistently higher levels of use of these effective agents at any time (Figure 1). The observation of the positive association

between a PSAC and earlier use of study treatments was examined further in multivariate models described below, which included other study characteristics (age, sex, race, diagnosis year and IDU status).

Association of AIDS treatment with patient characteristics

The influence of age, IDU, sex, race, diagnosis year and PSAC on initiation of use of zidovudine or PCP prophylaxis was examined. Table 2 shows the RR for each study characteristic controlling for all other variables. In general, increased age, IDU, female sex and non-white race independently predicted a reduced likelihood of treatment with zidovudine or PCP prophylactic antibiotics although these differences were not always significant. Consistent with the more rapid use of the study drugs observed during later years in the unadjusted analyses of the overall Medicaid AIDS population (Figure 2), year of diagnosis was associated with more rapid antiviral or PCP prophylaxis treatment even when all other variables were entered into the model. For example, an individual diagnosed in 1990 was almost 50% more likely to be treated with zidovudine than patients diagnosed in the previous year, even after controlling for all other study characteristics (adjusted RR = 1.41, 95% CI = 1.1, 1.8). There was also a non-significant trend towards earlier PCP prophylaxis by each subsequent year (adjusted RR = 1.20, 95% CI = 0.9, 1.2).

A proportional hazards multivariate analysis extended and confirmed the univariate observation that PSAC was associated with earlier use of zidovudine or PCP prophylaxis. Controlling for all other study characteristics, it was observed that patients with a primary source of ambulatory care were more likely to receive zidovudine (RR = 1.75, 95% CI = 1.2, 2.2) or PCP prophylaxis (RR = 2.22, 95% CI = 1.5, 3.3).

Association of delayed treatment with death and hospitalization rates

After controlling for age, IDU, diagnosis year, race, sex and time to treatment (or censoring) and severity of the AIDS-defining illness, proportional hazard models which included indicators of both study treatments suggested that patients receiving either zidovudine treatment or PCP prophylaxis had improved survival. It appeared that both zidovudine and PCP prophylaxis independently predicted this improved mortality. Regression analysis indicated that the adjusted RR of death associated with zidovudine treatment was 36% that of untreated patients (95% CI = 0.2, 0.4). Independently, the adjusted RR of death among patients receiving prophylaxis for PCP was 49% (95% CI = 0.3, 0.8). We were unable to detect any effect of either study treatment on hospitalization rates.

In analyses stratified by sex, it was found that men and women with a PSAC had improved survival (Figure 3) compared with individuals without a PSAC. No differences in hospitalization rates were observed in these analyses.

Table 2 The Influence of study variables on risks of zidovudine treatment and PCP prophylaxis

| Variable | Adjusted RR of zidovudine treatment (95% CI) | Adjusted RR of PCP prophylaxis (95% CI) |
|--------------------------------------|--|---|
| Patients age interval | 0.89 (0.7, 1.1) | 0.72 (0.6, 0.9)* |
| Patient injecting drug use indicator | 0.66 (0.5, 0.9)* | 0.86 (0.6, 1.3) |
| Female | 0.71 (0.5, 0.9)** | 0.50 (0.3, 0.7)* |
| Non-white | 0.76 (0.6, 0.9)* | 0.57 (0.4, 0.7)* |
| AIDS diagnosis year | 1.41 (1.1, 1.8)* | 1.20 (0.9, 1.2) |
| Primary source of care indicator | 1.75 (1.2, 2.2)* | 2.22 (1.5, 3.3)* |

* $P < 0.05$; ** $0.05 < P \leq 0.10$.

Secular trends in antiretroviral treatment and PCP prophylaxis for individual with AIDS

Figure 2 indicates the influence of year of diagnosis upon the likelihood of treatment with antiretrovirals or PCP prophylaxis medication from 1987 through mid-1991. Throughout the study the likelihood of treatment increases over time and there is a trend towards more rapid use of both antiviral agents and PCP medications. However, despite their indication for all patients, use of both treatments was low. In the year following diagnosis of CDC-defined AIDS only about 42% of patients diagnosed in 1990 ever received a trial of any antiretroviral agent. For the same year, 33% of the study patients were treated with any PCP prophylaxis medications, a treatment pattern which did not change over the 30-month period of observation.

Discussion

This study represents a population-based investigation of quality of care among individuals with CDC-validated AIDS. By linking New Jersey's AIDS Registry data with nearly 14 000 unique New Jersey Medicaid enrollment records from 1989 through mid-1991, we were able to overcome the limitations of prior reports based on probabilistic identification of AIDS cases solely using unvalidated diagnostic information in administrative claims data or small numbers of patients from referral AIDS clinics. We were able to define a treatment-naïve AIDS cohort at the time of introduction of innovative AIDS therapies to study the association of a PSAC on the adoption of zidovudine and prophylaxis for PCP, agents which were then perceived as the standard of care for individuals with AIDS.

This study demonstrates that patients without a PSAC were less likely to have received either antiretroviral treatment or PCP prophylaxis; in turn, this reduced use of study treatments predicted increased mortality rates but not hospitalization outcomes. Increased age, IDU, female sex and

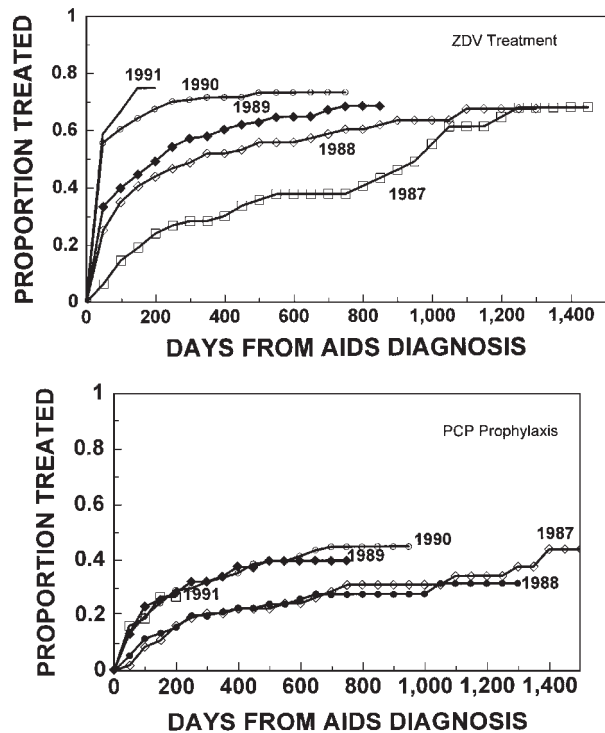


Figure 2 Influence of year of diagnosis on zidovudine treatment (top) and on PCP prophylaxis (bottom).

non-white race also predicted lower levels of use of zidovudine or antibiotics used for prophylaxis of PCP although all of these characteristics were less strongly associated with zidovudine use or PCP prophylaxis than a patient's PSAC status. For patients with a usual source of care, the likelihood of receipt of either study treatment was about two times higher than that of comparable patients without a PSAC, and survival in the 1-year period following diagnosis was markedly improved for treated patients. In the mortality analyses, we controlled for severity of HIV illness using a validated severity of AIDS index based upon observed patterns of initial AIDS diagnosis and 3-month complication post-diagnosis [26]. Subsequent severity indicators including the Boston AIDS Survival Score have used laboratory values or a combination of sociodemographic, physiological, diagnostic and functional status to predict long-term mortality [31]. The severity index for adults with AIDS employed in the results reported here has been shown to offer greater prognostic discrimination for survival than CD4 cell counts [32] and is optimal for predicting survival following AIDS-defining events and survival of 1 year [33].

Presently a debate continues about the optimal use of zidovudine, and evidence suggests that use of zidovudine may even contribute to increased disease progression and mortality, especially among those on long-term therapy or those initiated on treatment early in the course of their HIV infection [34]. Our observation of improved mortality benefit may be explained by the fact that zidovudine treatment in the study subjects occurred among drug-naïve patients in the latter stages of illness. In a multivariate analysis of survival

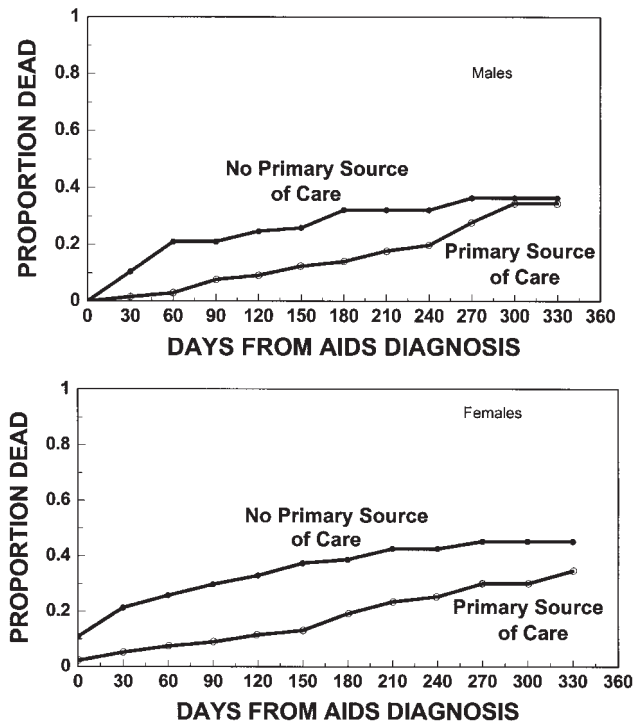


Figure 3 Adjusted survival curves for death among males (top) and females (bottom) with AIDS by PSAC status.

trends for patients with AIDS, Lemp *et al.* also reported increased survival among those treated with zidovudine [18]. As HIV resistance to zidovudine increases with duration of treatment, increased patterns of survival might be expected to occur among patients with AIDS-defining HIV illness recently begun on treatment. In our study, the median survival time for zidovudine treated AIDS patients was approximately 1 year, comparable to previously reported estimates in similar zidovudine-treated populations experiencing improved death outcomes. Nevertheless, research reporting improved patient outcomes associated with combination anti-HIV therapy, including the new class of protease inhibitors, has demonstrated the relative effectiveness of this therapeutic strategy compared with antiviral monotherapies [6].

We were unable to characterize the type and range of providers caring for study subjects. The majority of patients received care from outpatient clinics, and it remains unclear what percentage of patients received treatment from generalists or specialists and how this variation might affect access to treatment or study outcomes. Nor is it known what effect multiple providers within an outpatient clinic might have on the coordination and clinical management of individuals with symptomatic HIV illness.

A quality improvement clinical trial of HIV-infected patients in outpatient general medicine practices at an urban teaching hospital reported that computer-generated alerts reminding physicians to initiate antiviral therapy or PCP prophylaxis, monitor blood counts, or change medication doses resulted in improved and more rapid adherence to already-agreed upon clinical standards of care [35]. Although

the reasons underlying gaps in adherence to these HIV-treatment guidelines were not reported, a similar study of follow-up for hypertensive patients failing to receive therapy after diagnosis reported that errors were typically due to administrative oversight [36]. As the majority of the patients in this study received their care from hospital-based outpatient clinics, it is likely that individual patients have several providers, ranging from physician assistants and primary care providers to infectious disease specialists. This pattern of care may be associated with suboptimal clinical management of patients with symptomatic HIV-infection, which is complicated by the rapidly changing field of HIV infection. Alternatively, observed differences in access to treatment might be due to patients' sociocultural, economic and historical factors such as differences in patient preferences or domestic responsibilities. In addition, provider characteristics such as the physician's sex and provider-patient interactions may influence the quality of care we observed among women patients.

This study also demonstrated only a gradual adoption of the study therapies despite the fact that zidovudine and PCP prophylaxis were the only recommended treatments available for AIDS. Although improvement in anti-viral therapy of HIV as well as the prevention and treatment of opportunistic infections of HIV infected patients has occurred during the last decade, our results indicate that use of anti-retroviral therapies and PCP prophylaxis appeared suboptimal during the time frame of this study. Four years after becoming available, only 60–70% of patients with AIDS received a trial of an antiretroviral agent within 3 months of diagnosis. Only 50–60% of patients received trials of prophylaxis against PCP within 1 year of diagnosis, suggesting marked under-use of the single most cost-effective therapy for individuals with AIDS [37]. There appeared to be an increase in the use of these prophylactic agents after dissemination of treatment guidelines in 1989. Other recent findings also suggest only a gradual improvement in the quality of prescribing for HIV infected individuals. The EuroSIDA Study Group prospectively followed 7230 HIV infected individuals in 17 European countries [38]. These investigators reported that the percentage of untreated patients declined from 37% in 1994 to 9% in 1997 and outdated antiviral treatment strategies declined from 42% to 3%. This study did not examine the influence of a PSAC on the observed lags in adoption of preferred treatment strategies.

In a recent publication, researchers found that an increasing number of individuals have no usual source of care and were less likely to receive needed care [39]. Although every population studied experienced an increased lack of usual source of care, the trend was more pronounced among the poor, less educated, and Hispanics. Results from a study of the New York State Medicaid program reported that only 43% of pregnant, HIV-infected women had a usual source of prenatal care. Although current antiviral treatment reduces perinatal transmission of HIV, the patterns of care we report raise the critical public health issue of whether lower levels of preventable cases of perinatal transmission of HIV might not be achievable.

Although more effective antiviral regimens for HIV infection are available today [6], there are no population-based data available to inform us about the penetration of these therapies into the HIV-infected population and how use of these treatment regimens is affected by the presence of a primary source of medical care. Furthermore, newer treatments such as combination anti-HIV strategies are more complicated than antiviral monotherapies, raising the concern that the disparities we report would be even more pronounced today. Unfortunately, the association between a lack of PSAC for individuals with AIDS and patterns of reduced access might extend to other populations, including asymptomatic and early cases of HIV-infection which are even more challenging to manage than patients with AIDS.

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