

Estimating the Impact of Medical Innovation: A Case Study of HIV Antiretroviral Treatments

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Abstract

As health care consumes a growing share of GDP, the demand for better evidence regarding the effects of health care treatments and how these vary across individuals is increasing. Estimating this with observational data is difficult given the endogeneity of treatment decisions. But because the random assignment clinical trials (RACTs) used in the FDA approval process only estimate average health effects and do not consider spending, there is no good alternative. In this study we use administrative data from California's Medicaid program to estimate the impact of HIV antiretroviral treatments (ARVs). We use data on health care utilization to proxy for health status and exploit the rapid takeup of ARVs following their FDA approval. Our estimate of a 68 percent average mortality rate reduction is in line with the results from RACTs. We also find that the ARVs lowered annual health care spending by reducing expenditures on other categories of medical care. Combining these two effects we estimate the cost per life year saved at \$19,000. Our results suggest that data that is readily available from programs like Medicaid, combined with a properly specified econometric model, can produce reliable estimates of the impact of health care treatments in real-world settings.

I. Introduction

During the 2004 calendar year, health care expenditures accounted for 16 percent of GDP in the U.S., with this share substantially greater than in any other industrialized country and more than twice as large as the corresponding value in 1970. The Centers for Medicare and Medicaid Services predict that this rapid growth will continue, with health spending expected to account for 20 percent of GDP by 2015. Much of the past and projected growth in health care spending has been fueled by the Medicaid and Medicare programs, which provided health insurance to nearly 90 million individuals in 2005 at an annual cost of more than \$650 billion. According to estimates from the Congressional Budget Office, the share of federal spending accounted for by these two programs will increase from 22 to 35 percent during the coming decade (CBO, 2006).

Previous research has suggested that the key contributor to rising health care costs is the introduction and diffusion of new and more expensive treatments (Newhouse, 1992; Cutler, 2004). While many of these treatments have undoubtedly led to significant improvements in health, it is plausible that a substantial fraction of treatment decisions are not optimal. Most consumers of medical care in the U.S. have health insurance, which partially or fully insulates them from price differences when choosing between alternative treatments. Similarly, health care providers may have financial or other incentives to advocate for certain treatments over others. Even absent these considerations, both consumers and providers often have imperfect information about the effects of alternative treatments.

As health care spending continues to grow, it is likely that the demand for better evidence regarding the health and expenditure effects of new treatments in real-world settings will increase (Garber, 2004). At present, health care providers rely to a large extent on the results from random assignment clinical trials (RACTs), which are the dominant method for estimating causal relationships in medicine. For example, the U.S. Food and Drug Administration (FDA) uses the result from RACTs when deciding whether to approve new treatments. While these trials make

important contributions to knowledge, they have a number of important limitations. For example, they rarely consider the effect of a treatment on expenditures but instead focus only on health effects. Additionally, results from RACTs may not apply to real-world settings where adherence to a treatment regimen may be different from in the controlled environment of an RACT. Finally, RACTs are well-suited to estimating average effects but not how those effects vary across patients. It is plausible that a treatment is very effective on average but has little effect on the margin, a phenomenon referred to as “flat of the curve medicine” (Fuchs, 2004).¹

Researchers must therefore use alternative methods and data sources to estimate the impact of health care treatments in real world settings. One possible strategy is to use administrative data on health care utilization generated by government programs such as Medicaid and Medicare. These claims data sets have the advantage of large sample sizes, which can be important for obtaining precise estimates of treatment impacts for a relatively rare outcome such as mortality or for a highly skewed variable such as health care spending. They also have the advantage of capturing treatment patterns in the real world. But claims data sets also have limitations. The two most important are that treatments are not randomly assigned and that there is limited clinical information that can be used to measure health status. Failing to account appropriately for both of these issues could lead to misleading estimates of treatment impacts.

In this paper, we use individual-level data on the utilization of medical care from the state of California’s Medicaid program to estimate the effect of new treatments on both health care spending and health outcomes. We select HIV antiretroviral treatments (ARVs) as our case study for two main reasons. First, these treatments are differentially used by beneficiaries of the Medicaid program, with almost half of U.S. residents with HIV/AIDS insured by Medicaid (Bhattacharya et al, 2003). Second, several RACTs have demonstrated the average health benefits of ARVs, and thus we have a

¹ See Chan and Hamilton (2006) for a comprehensive discussion of the limitations of medical researchers’ analysis and interpretation of clinical trial data. An additional limitation of clinical trials not mentioned in that study is that there can be placebo effects, which can lead to biased estimates as shown in a recent study by Malani (2006).

baseline against which we can compare our estimates. This is especially important because, as we explain below, the suggested protocols for ARVs mean that there is 'negative selection' into use, with sicker patients much more likely to be prescribed the treatments. If we can replicate the RACT results for average health effects, we potentially expand the types of questions that can be addressed with data on health care utilization from a real-world setting. For example, what effect did ARVs have on health care expenditures? How did the health and expenditures effects of ARVs vary across individuals? RACTs have many virtues but they do not consider the effects of treatments on spending nor do they estimate the extent to which effects vary across individuals.

The key obstacle to obtaining credible answers to these questions is that treatment is endogenous. Individuals who take an ARV may differ in important ways from their observably similar counterparts who do not. For example, the guidelines in effect during our study period recommended that HIV-positive individuals abstain from taking ARVs until their health deteriorated to a certain level. Failing to account for this could lead us to understate the benefits of ARVs.

We account for this endogeneity issue and related ones in two ways. First, we exploit the fact that there are sharp changes in the treatment of HIV/AIDS immediately following the FDA's approval of certain ARVs. By controlling for the pre-existing trends in our outcome variables of interest, we can obtain credible estimates for the average short-term effect of these treatments as they are rapidly diffusing. Second, we utilize the detailed information on health care utilization to construct proxies for health status. This allows us to estimate the variation across individuals in effectiveness of treatment by essentially comparing individuals who take the treatments once they are available with their observably similar counterparts from the period just prior to FDA approval.

An analysis of trends in the average values of our key outcome variables of interest demonstrates that, prior to the approval of Epivir and three protease inhibitors (hereafter Epivir/PI) in late 1995, quarterly mortality rates and average spending among California Medicaid recipients with HIV/AIDS were fairly stable at 7 percent and \$5400, respectively. But within 1.5 years of the

approval of Efavir/PI, the fraction of our sample taking one or more of these ARVs had increased to almost 60 percent while the quarterly mortality rate had fallen to 2 percent. This decline coincides closely with trends at the national level, suggesting that the low-income beneficiaries of the Medicaid program were approximately as successful as other U.S. residents with HIV/AIDS in complying with the recommended treatment regimen. During the same period, average quarterly Medicaid expenditures declined by almost \$400, with a substantial increase in prescription drug spending more than offset by spending on hospitalizations and other health care services.

While these changes in average health and health care spending are striking, they shed little light on the extent to which the effects of the new treatments varied across individuals. We therefore next turn to individual-level data, where we demonstrate that controlling for pre-treatment health status substantially increases our estimate for the average effect of the treatments on mortality probabilities. Moreover, we uncover substantial heterogeneity in this effect, with the sickest patients deriving the largest health benefits.

Our findings for the effect of the treatments on expenditures also reveal substantial heterogeneity, with large reductions in spending for the sickest patients but statistically significant increases for healthier patients. The mechanism for this is that the use of the new treatments increased pharmaceutical spending but reduced the need for hospitalizations and other types of medical care. Healthier patients had little other medical care to offset and thus the increase in ARV utilization increased total spending on them.

In the final section of our paper, we investigate the effect of the new treatments on long-term Medicaid spending, life expectancy, and the corresponding cost per life-year saved.² The new treatments reduced quarterly Medicaid spending by an average of 16 percent but increased life expectancy by a factor of three. Combining these two effects leads us to estimate the cost per life

² These treatments may have influenced other outcome variables as well. For example, Lakdawalla et al. (2006) find that ARVs increase risky behavior such as unprotected sex and intravenous drug use. While important, we consider these outcomes and some others (e.g. pharmaceutical firm profits) to be outside the scope of the current study.

year saved of the four treatments introduced in late 1995 and early 1996 at close to \$19,000, well within the range of what is considered to be cost effective.

Claims data sets from programs such as Medicaid and Medicare are inexpensive, have large sample sizes, and capture treatment patterns in a real-world setting. While it is not possible with such data to eliminate all possible sources of endogeneity bias, our results suggest that one can use this data - combined with an econometric model that allows for heterogeneous takeup and effectiveness - to reliably estimate the effects of new health care treatments.³ The results from these studies can be a useful complement to the results from RACTs as patients, physicians, insurers, and policymakers strive to allocate resources optimally in the health care sector.

II. Background on HIV/AIDS and Antiretroviral Treatments

AIDS is a chronic disease that damages, and ultimately destroys, an individual's immune system. AIDS is caused by HIV, an infection that kills the body's "CD4 cells", a type of white blood cell that helps the body fight off infections. When this epidemic first appeared, providers could only treat opportunistic illnesses resulting from the weakened immune system rather than attack the virus itself. This changed with the entry of Retrovir (AZT) to the market in 1987. This drug was the first one approved by the FDA in the therapeutic class known as NRTIs (nucleoside reverse transcriptase inhibitors). Despite the entry of three additional NRTIs from 1991 to 1994, use of these drugs among AIDS patients actually declined from 1992 through 1995. This trend reversed following the approval of Efavir and three drugs from a new class known as protease inhibitors (PIs) in late 1995 and early 1996. The first NNRTI (non-nucleoside reverse transcriptase inhibitor) was approved in June of 1996. Twelve additional drugs were approved in the seven years from 1997 to 2003 (Table 1).

The release of Efavir/PI spawned the use of highly active antiretroviral therapy (HAART),

³ A related literature has estimated the benefit to consumers of new products. For example, Petrin (2002) develops a technique for estimating the benefits of the minivan. A key feature of the health care sector is that consumers do not typically share in the cost of their medical care, and thus price is a less useful guide to consumer valuation.

which is the simultaneous use of two or more ARVs to treat HIV. The optimal time to initiate HAART depends both on the strength of the patient's immune system and on the concentration of HIV in the patient's blood. Current guidelines recommend HAART for all patients with less than 200 CD4 cells per cubic millimeter of blood and suggest that all patients with CD4 cell counts between 200 and 350 be offered treatment (NIH, 2004; Yeni et al., 2002). Thus those HIV-positive individuals who take the drugs will tend to be sicker than their counterparts who do not.⁴ In a short period after the approval of Epivir/PI, HAART became the standard treatment for those infected with HIV. The sharp increase in the use of the drugs coincided with a substantial decline in the mortality rate among AIDS patients. According to data from the U.S. Centers for Disease Control, the mortality rate for individuals with AIDS fell by 70 percent between 1995 and 1998.

A large number of studies, some using randomized research designs (Hammer et al., 1997; Delta Coordinating Committee, 2001; Floridia et al., 2002) and others using observational data with detailed clinical information (Palella et al., 1998; Detels et al., 1998; CASCADE Collaboration, 2003) investigated the life saving benefits of the new ARVs.⁵ All of these studies found that the new treatments generated statistically significant reductions in mortality. For example, in an RACT examining the effectiveness of one protease inhibitor in combination with Retrovir and Epivir, Hammer et al. (1997) found that 48-week mortality rates were 55 percent lower among those taking a protease inhibitor. Palella et al. (1998) used observational data for 1255 patients in eight U.S. cities to examine the impact of ARVs on mortality. Controlling for a variety of socioeconomic factors and CD4 count levels prior to treatment, the authors found that mortality fell by more than 70 percent among those using protease inhibitors with two or more NRTIs.⁶

⁴ Individuals with HIV are defined as having AIDS once their CD4 count falls below 200 or once they are diagnosed with an AIDS-defining illness. The main benefit of starting HAART early is that it can prevent both the degradation of the immune system and the elevation of viral loads. The main costs are that patients often experience severe side effects and they can also develop drug resistance, thereby reducing future treatment options.

⁵ Lichtenberg (2003) uses aggregate, national-level data for the U.S. to estimate the effect of ARV approvals.

⁶ There are no RACTs of which we are aware that compare the use of both Epivir and PI with the use of neither.

Demonstrating that we could replicate the results from RACTs or studies with more detailed clinical information would potentially expand the types of questions that can be addressed with claims data. We therefore view estimates from these previous studies as a useful benchmark. If the treatments are similarly effective for those on Medicaid and if these individuals adhere well to the treatment regimens then we should detect a similar average mortality effect.

III. Constructing the Analysis Files

A. The California Medicaid Claims and Eligibility Data

We utilize claims and eligibility data for a random 24 percent sample of Medicaid recipients from the state of California to estimate the effect of ARVs.⁷ In our data there are 4.03 million people eligible for Medicaid in at least one month from 1993 to 2003. The eligibility files contain demographic information including gender, month and year of birth, and race. Additionally, there are two variables in each month that allow us to determine whether each individual is dually eligible for health insurance through Medicare or enrolled in a Medicaid managed care plan.⁸

The claims data includes all fee-for-service payments made from January of 1993 until June of 2004, though because there is often a lag in processing the claims, we consider utilization through the end of 2003. There are three types of claims in our data. Inpatient claims are generated for admissions to hospitals and long-term care facilities and include information about the patient's primary and secondary diagnosis, the dates of service, and the amount paid by Medicaid. Outpatient claims have similar data about payments to physicians, emergency rooms, and other health care providers. Finally, prescription drug claims provide data on payments made to pharmacies for drugs covered by Medicaid. Each pharmacy claim includes an eleven-digit National Drug Code that allows

⁷ This data was obtained from the California Department of Health Services' Medical Care Statistics Section. See Duggan (2005) for a detailed description of this data.

⁸ Many Medicaid recipients are also eligible for Medicare, either because they are over the age of 65 or because they receive benefits from the Social Security Disability Insurance program.

us to determine the drug and the dosage amount. All three types of claims include the patient's Medicaid identifier (an encrypted social security number), which we match to the eligibility files.

Finally, our data has been merged to death records from the California Center for Health Statistics for the 1993 through 2001 period. These records identify date and cause of death for all California residents, though 8 percent of our sample cannot be linked because they do not have a valid (encrypted) social security number.

B. Defining the HIV/AIDS Sample

A number of previous researchers have used Medicaid claims data to construct samples of HIV/AIDS patients (Eichner and Kahn, 2001; Morin et al., 2002). Following this research, we use ICD-9 diagnosis codes on the Medicaid inpatient and outpatient claims to determine whether individuals are diagnosed with this illness. To reduce the possibility of false positives, we restrict attention to patients with two or more non-prescription HIV/AIDS claims.⁹ This algorithm yields a sample of 12,932 individuals who have one or more HIV/AIDS claims, are eligible for Medicaid at some point during our study period, have a valid social security number, and have consistent age and gender information across years in the eligibility files.¹⁰

Although our Medicaid claims data contain a rich set of information, it does have some important limitations. First, our data is for just one state and thus our results may not generalize to Medicaid recipients elsewhere in the country. Second, we lose patients who temporarily or permanently exit because they become ineligible for Medicaid.¹¹ Third, we do not know when patients were first diagnosed with HIV or AIDS but instead only the date of their first Medicaid

⁹ False negatives are also a possible concern, though as we describe below the number in our sample is similar to what we would expect given that approximately half of California residents with HIV/AIDS are on Medicaid.

¹⁰ Research by Rosenblum et al., (1993) using Medicaid claims data has found that this algorithm captures the vast majority of recipients diagnosed with HIV/AIDS.

¹¹ Fewer than 2 percent of the sample exits the sample per quarter and this exit rate declines during our study period. For example it falls from 1.96% in the last quarter of 1995 to 1.42% in the first quarter of 1998.

HIV/AIDS claim during our study period. Fourth, claims data do not contain diagnostic information about patients such as CD4 cell counts or HIV viral loads. This information is important because it indicates who is recommended to receive ARVs. Fifth, we do not have Medicare expenditure data for people also eligible for that program and we will therefore understate health care expenditures by the government for this group.¹² Finally, we have incomplete utilization data for patients enrolled in a Medicaid managed care plan and thus exclude them from our analyses.

C. *Sample Characteristics*

On the left-hand axis in Figure 1, we plot the number of Medicaid recipients in our sample who were alive at the beginning of half-year periods starting in January of 1994. The patients in each half-year cell had their first HIV/AIDS claim by the end of that period although they may have been enrolled in Medicaid for some time before that date. Roughly one-fourth of the sample appears in the first half-year of the time period and the sample grows steadily after that date. On the right-hand axis of the figure, we graph the total number of people living with AIDS in California¹³ at the end of each six month period as reported by the U.S. Centers for Disease Control in their publication *HIV/AIDS Surveillance Report*. These two series track one another quite closely. Our numbers suggest that roughly 52 percent of people living with AIDS in California are on Medicaid,¹⁴ a number close to the national average (Bhattacharya et al., 2003). Similarly the number of individuals in our sample grows at an almost identical rate to the statewide total (58 percent for both from 1994

¹² Medicare did not cover prescription drugs for dual eligibles during our study period.

¹³ We should note that our sample includes not only patients with AIDS but also some who are just HIV-positive. Unfortunately, in most years California only reported to the CDC the number of people living with AIDS, not the number with HIV. Thus in one respect it is plausible that the patients in our sample would be healthier than the typical AIDS patient in California. However, most of the individuals in our sample qualify for Medicaid through the means-tested Supplemental Security Income (SSI) program. Thus they must be in relatively poor health to meet SSI's medical eligibility criteria. As we document below, the death rates for our sample are substantially higher than for non-Medicaid AIDS patients in California. Therefore, comparing trends in the number of HIV/AIDS patients on Medicaid to overall trends of AIDS patients seems a reasonable compromise given the available data.

¹⁴ Consider the first half of 1994 when there are 3,237 individuals in our sample. To estimate the number on Medicaid with HIV/AIDS one must multiply this by (1/.24). Additionally we must multiply by 1.058 to account for the exclusion of those with an invalid SSN. This yields 14,270, which is 52.0% of the statewide total of 27,454.

to 2001). Given the possible limitations with using claims data outlined above, our algorithm for identifying Medicaid recipients with HIV/AIDS appears to work quite well.¹⁵

In Figure 2, we graph half-year mortality rates for the Medicaid recipients in our sample during the 1994-2001 period and compare this with the corresponding mortality rate among all California AIDS patients. Death rates in our sample are approximately 2 percentage points higher on average, indicating that Medicaid recipients are in worse health. Additionally, the timing and magnitude of the declines in mortality for the two groups are similar.

In Table 2, we report descriptive information for our sample in four years: 1994, 1997, 2000 and 2003. In constructing this sample we drop the 1,063 individuals who live in one of the eight counties that moved its Medicaid recipients into a county-organized health system during our study period because our claims data would often be incomplete for them. We also drop the 1,802 individuals with one or more months in a Medicaid managed care plan during our eleven-year study period.¹⁶ This leaves us with a final sample of 10,067 HIV/AIDS patients. As the table shows, the annual mortality rate in the sample fell from 23.0 percent in 1994 to 5.2 percent in 2000, contributing to a large increase in the average age of the sample. The fraction of the population under 40 fell from 50 percent in 1994 to 28 percent nine years later. During our study period the fraction of the sample that is black and female increased by 47 and 19 percent, respectively.

In the bottom half of the table, we report information about health care utilization in our sample. Almost 48 percent of our sample had an inpatient stay in 1994 and this number fell to 28 percent during the next nine years. Annual inpatient spending fell by an even larger percentage from

¹⁵ One possible concern with focusing just on Medicaid recipients is that the incentive to enroll in the program will change after new treatments become available (Goldman et al., 2001), raising the possibility of composition bias. The fact that our series tracks closely with the total number in the state suggests this is not too problematic.

¹⁶ The lack of data for patients in managed care could be problematic if it leads to changes in the composition of our sample over time, though the fact that the number of individuals in our sample tracks the number statewide with AIDS quite closely (Figure 1) suggests that this issue is not too problematic.

\$7125 to \$3510.¹⁷ In contrast, annual outpatient spending increased slightly while spending on prescription drugs tripled, driven primarily by the increased use of ARVs and their high cost. Although average annual spending on prescription drugs increased by \$8,000 over the period, total spending increased by just \$4,800. The fraction of HIV/AIDS patients who are also eligible for Medicare increased from 28 to 45 percent, with this change likely contributing to the fall in Medicaid spending on inpatient care given that Medicare covers most inpatient costs for dual eligibles.

IV. The Impact of HIV Antiretroviral Treatments: A Graphical Presentation

The FDA's approval of Epivir in November of 1995 and of three protease inhibitors during the next four months coincided with a sharp decline in the mortality rate among the Medicaid recipients in our sample. As Figure 2 demonstrates, from the latter half of 1995 to the same period in 1997, the six-month mortality rate among California Medicaid recipients diagnosed with HIV/AIDS fell by 70 percent, from 11.3 to 3.4 percent. During the next four years the mortality rate in our sample declined gradually and was equal to 2.8 percent in the second half of 2001.

Figure 3 depicts the fraction of individuals in the sample filling at least one prescription for an ARV in the quarter. From the third quarter of 1995 to the second quarter of 1997, this fraction more than doubled, increasing from 29 to 59 percent. As Figure 4 shows, this growth was driven by an increase in the use of Epivir/PI, with 56 percent of our sample taking one or more of these treatments in the second quarter of 1997. There were no significant changes in utilization for other ARVs. Taken together, the series depicted in Figures 2, 3, and 4 strongly suggest that Epivir/PI was the primary cause of the sharp decline in mortality rates observed during our study period.

This is more easily represented in Figure 5, where on the left vertical axis, we report the fraction of patients that are using either Epivir or protease inhibitors, and on the right vertical axis,

¹⁷ Expenditure data cited here and elsewhere in the paper are adjusted to December, 2001 dollars using the Bureau of Labor Statistics' Consumer Price Index for Urban consumers (CPI-U).

we report the patient quarterly mortality rate. There are three things to highlight in this graph. First, notice that prior to the first quarter of 1996, quarterly mortality rates had been trending down slightly. Second, as Epivir/PI use increased from zero to 56 percent between the fourth quarter of 1995 and the second quarter of 1997, quarterly mortality rates fell by 72 percent, from 6.7 percent to 2.0 percent. As Epivir/PI use stabilized in mid-1997, so did mortality rates. Between mid 1997 and the end of our study period, mortality rates varied between 1.4 and 2.0 percent with no obvious trend.

The potential importance of Epivir/PI as an explanation for the decline in mortality is most easily illustrated with a simple time series model in which we regressed the first-difference in quarterly mortality rates on the first difference in quarterly Epivir/PI use among HIV/AIDS patients in our sample during the 1994-2001 period. The coefficient on the change in Epivir/PI use is -0.079 (with a standard error of 0.015), which implies an average reduction of 7.9 percentage points in the quarterly mortality rate.¹⁸ This is actually greater than the mortality rate in our sample just prior to the approval of these treatments, which is not so surprising given that the individuals who took the new ARVs are likely to have been in worse health and thus have higher baseline mortality rates.

Given the major improvements in health resulting from the use of Epivir/PI, it is plausible that the treatments partially or fully paid for themselves by reducing the demand for hospitalizations and other health care services. Figure 6 plots average Medicaid spending in our sample along with average spending on both prescription drugs and all other health care services. As is clear from the figure, average spending on prescription drugs increased substantially following the introduction of Epivir/PI, increasing from \$1391 in the third quarter of 1995 to \$2505 just two years later. But spending on all other services fell by an even greater amount, so that average overall spending

¹⁸ It is worth noting that many taking Epivir and/or a protease inhibitor were also taking one or more other ARVs. Thus our estimates may to some extent be capturing the effect of a combination of new and existing treatments.

declined by approximately 8 percent from \$5401 to \$5030. As we demonstrate below, this change in average Medicaid expenditures masks important changes in its overall distribution.¹⁹

V. The Impact of the New Treatments on Mortality: Individual-Level Evidence

In this section we estimate the impact of Epivir/PI use on mortality using individual-level claims data. There are two key factors we must consider when constructing an econometric model. First, individuals who are in worse health are both more likely to die and to use these treatments. Failing to account for this would lead us to underestimate the health benefits of the treatments. Second, the effect of the treatment is likely to vary across individuals, with more severe patients deriving greater benefits. These two considerations motivate a model of the following type for the effect of taking a treatment Z in the current period on health status H in the next period:

$$(1) H_{j,t+1} = \mu * H_{jt} + \gamma(H_{jt}) * Z_{jt} + \theta * X_{jt} + \varepsilon_{j,t+1}$$

In this equation, H_{jt} represents individual j 's health status in period t and Z_{jt} is an indicator that equals one if person j takes the treatment in period t and zero otherwise. The average effect of the treatment is assumed to vary only with the individual's health status according to the function $\gamma(H_{jt})$. Other background characteristics such as gender, age, and race, all of which are potentially important determinants of changes in health status, are controlled for in the vector X_{jt} .

A. Estimating Health Status

To construct a proxy for health status H_{jt} , we exploit the diagnosis and treatment information contained in our Medicaid claims data. We recognize that our data is not perfect for this, as it does not include detailed clinical information such as CD4 counts or viral loads. Our data does however contain a record of every health care treatment paid for by the Medicaid program for the individuals

¹⁹ We also investigated whether the treatments affected the exit rate from the program for reasons other than mortality (e.g. return to work) and found little evidence to support this as shown in Appendix Figure 1.

in our sample. In this section, we investigate whether the claims data can capture variation across individuals in their mortality probabilities in the period just prior to the release of Epivir/PI. To the extent that this is successful, we can then use these predicted probabilities to investigate differences in the utilization and in the impact of Epivir/PI as suggested by equation (1).

We are especially interested in the severity of each individual's HIV/AIDS illness, as this is by far the most common cause of death for the individuals in our sample prior to the introduction of Epivir/PI and will influence whether individuals are encouraged to take Epivir/PI soon after it becomes available. We therefore focus attention on inpatient and outpatient claims with a primary or secondary diagnosis of HIV/AIDS when estimating linear probability models of the following form:

$$(2) D_{j,t+1} = \beta_0 + \beta_1 * HIV_IP_{jt} + \beta_2 * HIV_OP_{jt} + \beta_3 * HIV_PAID_{jt} + \zeta_{t+1} + \varepsilon_{j,t+1}$$

In this model, the variable $D_{j,t+1}$ is equal to 1 if individual j dies in quarter $t+1$ and zero otherwise.

The variables HIV_IP_{jt} and HIV_OP_{jt} represent the number of inpatient and outpatient claims, respectively, with a primary or secondary diagnosis of HIV/AIDS for person j in quarter t .

Individuals with more severe cases of HIV/AIDS would presumably have more contact with the health care system and thus more Medicaid claims. Of course, not all claims are equal, with some reflecting payment for intensive services (e.g. emergency room visits or hospital stays) and others simply payment for annual checkups. In an effort to account for this, we also include a variable HIV_PAID_{jt} , which is equal to total Medicaid spending (in thousands of dollars) for inpatient and outpatient claims with a primary or secondary diagnosis of HIV/AIDS.²⁰

We estimate this model using data for all four quarters of 1994, approximately one year prior to the introduction of Epivir/PI. The number of individuals in this estimation sample is 2781 and

²⁰ Our results in this section and in the subsequent sections were very similar if we used a richer set of utilization controls to predict quarterly mortality rates.

the number of observations is 7854.²¹ The estimates for β_1 , β_2 , and β_3 using 1994 data are .0332 (se = .0126), .0027 (se = .0003), and .0034 (se = .0015), respectively, with the estimate for β_0 of .0426 (se = .0031). All three estimates are positive and statistically significant, suggesting that our utilization measures capture important dimensions of health status. We then use the coefficient estimates from equation (2) to calculate a predicted quarterly mortality probability – our proxy for health status - for each individual in the sample in every one of the next eight quarters. This two year period (from the first quarter of 1995 to the final quarter of 1996) includes the period leading up to and immediately following the introduction of Epivir/PI and is the focus of our subsequent analyses.

Before proceeding to these analyses, we test the predictive power of our proxy in two ways. We first investigate whether it is significantly positively related with quarterly mortality outcomes just prior to the release of Epivir/PI by estimating specifications of the following type using data from the first three quarters of 1995:

$$(3) D_{j,t+1} = \lambda \hat{D}_{j,t+1} + \phi X_{jt} + \pi_{t+1} + \xi_{j,t+1}$$

In this equation, $\hat{D}_{j,t+1}$ is individual j 's predicted mortality probability in quarter $t+1$ and $D_{j,t+1}$ is the actual mortality outcome for j in that same quarter, which equals one if the person dies in quarter $t+1$ and zero otherwise. The vector X_{jt} includes a set of control variables for the person's age, gender, race, and Medicare eligibility. π_{t+1} represents a set of eight indicator variables for each quarter that we consider to control for common changes over time in mortality probabilities. The equations are estimated as linear probability models.

The results presented in the first column of Table 3 demonstrate that our proxy for HIV/AIDS severity is a powerful predictor of mortality during the 1995 calendar year. Specifically the coefficient estimate for λ is 1.042 (t-statistic of 11.2) and is not significantly different from 1.

²¹ For a particular person-quarter observation to be included in this estimation sample, the person must be eligible for Medicaid during all three months in the quarter and still be alive at the end of the quarter.

Interestingly there are also statistically significant differences in mortality probabilities by age and gender, even after controlling for our measure of health status. For example, women are significantly less likely to die and the mortality probability generally increases with age.

We next investigate whether – as expected – $\hat{D}_{j,t+1}$ is significantly positively related with the likelihood that an individual in our sample takes Epivir/PI during the 1996 calendar year. To examine this question, we estimate a model similar to equation (3) but use as the outcome of interest an indicator that equals 1 if person j was taking either Epivir/PI in quarter $t+1$. The coefficient estimate on the predicted mortality probability $\hat{D}_{j,t+1}$ of 0.979 (t-statistic of 7.6) displayed in the second column of Table 3 reveals that sicker patients were the ones most likely to select into the new treatment following its release. The results presented in this column also demonstrate that there are significant differences by gender, age, and race in the takeup of the new treatments.

The results described in this section demonstrate that the Medicaid claims data can be used to estimate the health status of individuals with HIV/AIDS. We next use this proxy to estimate the effect of the new pharmaceutical treatments released in late 1995 and early 1996 on mortality outcomes and the extent to which this effect varied across individuals.

B. Individual-Level Estimates

In this section we estimate the effect of Epivir/PI on mortality outcomes for the individuals in our sample. We focus on the two year period from the first quarter of 1995 to the final quarter of 1996. This gives us four quarters of information prior to the introduction of Epivir/PI and four quarters when the new treatments were rapidly diffusing. There are four reasons for focusing on this two-year period even though we have several more years of data. First, it allows us to contrast outcomes for individuals with HIV/AIDS prior to the introduction of the new treatments with their observably similar counterparts one year later. Second, it is readily apparent from the trends in

mortality that this period is the most important one, with mortality rates falling by almost 60 percent in the year following the release of Efavir/PI. Third, there were no other HIV treatments released in 1995 and 1996, except for one that had very low utilization (1.0 and 3.3 percent in the third and fourth quarters, respectively, of 1996). This reduces the possibility that changes in other treatment patterns might bias our results. The fourth and most important reason is that, once the new treatments were released, the distribution of health status in our Medicaid sample begins to change rapidly. As a result of this, the relationship between treatment patterns and health status may also have changed, which would lead our proxy to be a less reliable measure of health over time.

To estimate the effect of Efavir/PI on mortality, we estimate specifications that allow the effect of the treatment to vary across individuals as a function of the predicted mortality probability $\hat{D}_{j,t+1}$. Specifically, we assume that the treatment effect is a linear function of an individual's predicted mortality probability when estimating linear probability models of the following type:

$$(4) D_{j,t+1} = \theta_1 * E_{jt} + \theta_2 * \hat{D}_{j,t+1} + \theta_3 * E_{jt} * \hat{D}_{j,t+1} + \rho X_{jt} + \omega_{t+1} + \xi_{j,t+1}$$

In this equation, E_{jt} is equal to 1 if individual j fills one or more Efavir or protease inhibitor prescriptions in quarter t and zero otherwise. The main effect of the treatment is captured by the parameter θ_1 and the interaction of this effect with health status by θ_3 . The vector of indicator variables ω_{t+1} is included to control for common changes over time in mortality.

Our prediction that the treatments reduce mortality rates by a larger amount for sicker patients seems reasonable given the trends summarized in Figure 7. In this figure, we plot quarterly mortality rates for the sickest 20 percent of patients (quintile 5), the next sickest 20 percent (quintile 4), and all other patients. As the figure demonstrates, beginning in the first quarter of 1996, quarterly mortality rates in our sample fell substantially, with the largest drop apparent for the sickest patients. By the first quarter of 1997, quarterly mortality rates had fallen by 70 percent in the fifth quintile

(from 19.8 to 5.2 percent) and by 66 percent in quintile four (from 5.6 to 1.9 percent). Consistent with this, the fraction taking Epivir/PI in the fourth quarter of 1996 was approximately similar in the two groups at 68 and 71 percent, respectively. In contrast, just 40 percent of those in quintiles 1 through 3 filled a prescription for Epivir or protease inhibitors during this same quarter.

Before proceeding to the results, it is worth considering two potentially important sources of bias that could be present when estimating this model. First, our measure of health status is not perfect. To the extent that two individuals with identical values of $\hat{D}_{j,t+1}$ have different values of E_{jt} , it is plausible that the person taking the treatment is on average in worse health. This would most likely lead us to understate the health benefits of the treatment. Second, even if our proxy for health status were perfect, if the effect of the treatments varies across individuals and individuals with the highest perceived benefits self-select into treatment, we might overstate the average benefits of the treatment. We think this second source of bias is unlikely to be important, especially right after the treatments were released when patients and their health care providers had little experience with the new treatments. In an effort to reduce both potential sources of bias, our identification strategy essentially uses HIV/AIDS patients from before the treatments were available as a comparison group for observably similar individuals who had the option to take Epivir/PI after it reached the market.

The empirical results summarized in Table 4 examine the impact of Epivir/PI use on mortality. The equation we estimate is similar to (4) above and the estimation sample is constructed from the sample of patients described in section 3, though because we are considering a two-year period rather than the full eleven-year period the number of individuals considered here is lower. For person j to be included in our estimation sample in quarter t , he/she must be eligible for Medicaid in all three months of the current quarter and in all three months of the previous quarter, and must still be alive at the end of the current quarter. There are 15,882 quarterly observations for 3,413

individuals, with the number of observations for each person ranging from one to eight. All specifications are estimated as linear probability models and include eight quarter indicators.

In the first column of Table 4, we report results that include only the time effects and the dummy indicating whether the patient takes Epivir/PI in the current quarter. Because sicker patients were likely to take these treatments, the magnitude of this estimate is likely to be biased down. The statistically significant point estimate of $-.0085$ suggests that the treatments reduce mortality rates by less than one percentage point. This is much smaller in magnitude than the time series estimate presented above or than the estimates from random assignment clinical trials mentioned in section two. The inclusion of demographic variables and the fraction of months in which the person was enrolled in Medicare lead to a modest increase in this coefficient estimate to $-.0113$.

Neither of these first two specifications includes our proxy for health status. In the third specification we add the predicted mortality measure defined above to the set of explanatory variables. The inclusion of this variable leads to an almost threefold increase in the magnitude of the estimate for the impact of Epivir/PI to $-.0280$. The coefficient estimate of 0.9731 for the predicted mortality probability $\hat{D}_{j,t+1}$ is not significantly different from one. Because our measure of health status is undoubtedly measured with error, we include the value of j 's predicted mortality probability from the preceding quarter in the fourth specification. Interestingly the inclusion of this variable has virtually no impact on the other coefficient estimates, with the estimate for the effect of Epivir/PI increasing slightly in magnitude to $-.0285$. In the fifth specification we add controls for the utilization of medical care for other conditions, which should to some extent capture additional dimensions of health status that are not captured by $\hat{D}_{j,t+1}$. The coefficients on these additional variables have the expected (positive) sign and their inclusion increases our estimate for the effect of Epivir/PI to $-.0360$, which is more than four times greater than the estimate from column one.

In the sixth and final specification, we allow the effect of the treatments to vary with severity by interacting the treatment indicator E_{jt} with $\hat{D}_{j,t+1}$. If patients in worse health experience larger reductions in their mortality probabilities, one would expect a negative estimate for the coefficient on this interaction term. And this is indeed what we find, with an estimate of -0.6387 for σ_3 that is significant at the one percent level. Including this interaction term reduces the magnitude of our estimate for σ_1 to a statistically insignificant .0115, implying that relatively healthy patients experienced no significant mortality decline as a result of taking the treatment.

One possible concern with our estimates not mentioned above concerns the change in health care utilization induced by Efavir/PI. To the extent the treatments reduce the number of hospital admissions or physician visits, this will reduce patients' predicted mortality probabilities but this indirect effect would not be captured by the estimates for θ_1 and θ_3 . To account for this possibility, we estimated a companion set of specifications in which we "freeze" each patient's predicted mortality probability at its value in the fourth quarter of 1995. Our results using this alternative specification yielded similar though slightly larger results for the effect of the treatments.

Despite the fact that our health status measure is imperfect and treatment is not randomly assigned, our estimates suggest that Efavir/PI reduced mortality rates by approximately 68 percent (θ_3 / θ_2). This is similar to the results reported above for the RACTs²² and for studies that had detailed clinical information on patients. It therefore appears that our estimates do a good job of replicating the results for average impacts from studies with superior data or with the benefits of randomization.²³ This is true despite the fact that sicker individuals clearly self-select into the

²² It is not strictly comparable to the RACT results because most of these studies considered the effect of just protease inhibitors when combined with AZT and Efavir. This underscores the point raised above that we are capturing the effect of a combination of treatments rather than of one specific pharmaceutical treatment.

²³ Of course the average impact could have differed for the Medicaid population if, for example, they did not comply with the recommended treatment regimen as well as individuals in the RACTs.

treatment. And in contrast to estimates from RACTs, our estimates allow us to estimate the extent to which the effects of the treatments varied across individuals in a real-world setting.

One important limitation with the RACTs described above is that they do not consider the effect of new treatments on health care expenditures. This is an important factor to consider when evaluating the value of any new medical innovation and is the focus of the next section.

VI. The Impact of the New Treatments on Health Care Expenditures

A. Changes in the Distribution of Medicaid Expenditures

Theoretically, the effect of Epivir/PI on average short-term health care spending is ambiguous. As shown in Figure 6, the release of Epivir/PI coincided with a significant increase in spending on prescription drugs, which was presumably driven both by the increase in use of ARVs and by the substantially higher prices of the new treatments relative to their predecessors. But as this same figure shows, spending on other categories of medical care declined during this same period. Which of these two effects dominated is not clear.

In considering this issue, it is important to differentiate between individuals eligible only for Medicaid and their counterparts eligible for both Medicaid and Medicare. For this latter group, the Medicare program is the primary payer for inpatient and outpatient care, though Medicaid does share the cost for most services. Thus to the extent that Epivir/PI lowered spending on other health care services, one would expect – all else equal – to see a smaller decline (or a larger increase) in spending for those also “dual eligibles” who are also insured by the Medicare program.

Figure 8 sheds some light on this issue. In this figure, we plot average spending for dual eligibles and for their counterparts eligible only for Medicaid. As the figure shows, in the period leading up to the fourth quarter of 1995, there were substantial differences in spending for the two groups. Specifically, in the third quarter of 1995 average Medicaid spending was more than twice as high for those only covered by Medicaid (\$6242 versus \$3037) and both of these trends were fairly

stable. But beginning in the fourth quarter of 1995, spending for dual eligibles began to increase while the opposite occurred for those only covered by Medicaid. By the final quarter of 1996, average spending for dual eligibles had increased by 36 percent (to \$4122) versus a 16 percent decline for Medicaid-only recipients (to \$5256). This latter change suggests that the new treatments more than “paid for themselves” in the short term by reducing spending on other categories of medical care. The benefits of this expenditure offset for dual eligibles are not as apparent in our Medicaid data because most inpatient and outpatient care for this group is financed by Medicare.

These trends in average spending may mask important changes in the overall distribution of spending. In Table 5 we list five different percentiles (30th, 50th, 70th, 90th, and 95th) in the distribution of Medicaid expenditures. If Epivir/PI did reduce the use of other health care services, one might expect to detect larger declines in spending at the high end of the expenditure distribution. In contrast, total spending might actually increase at the low end given that there would be relatively few health care services to offset for this group. Consistent with this, the data summarized in Table 5 reveals that spending at the 30th and 50th percentiles increased by 71 and 42 percent, respectively, from the third quarter of 1995 to the fourth quarter of 1996. But during that same period, Medicaid spending at both the 90th and the 95th percentiles declined by 24 percent. The change at the 70th percentile lied between these two extremes, with a 12 percent increase during the period. Thus, although there was very little change in average spending during the period when Epivir/PI was rapidly diffusing, there was a substantial change in the distribution of this spending.

B. Individual Level Estimates

In this section, we present results from specifications analogous to (4) above, though in this case we focus on Medicaid spending. Following previous research (Manning et al, 1987), we use the log rather than the level of health care spending as our outcome variable given that – as shown in

Table 5 – spending is highly skewed to the right.²⁴ We focus primarily on individuals only eligible for Medicaid given that our data does not include spending by the Medicare program for dual eligibles when estimating specifications of the following type:

$$(5) \log(S_{j,t+1}) = \sigma_1 * E_{jt} + \sigma_2 * \hat{D}_{j,t+1} + \sigma_3 * E_{jt} * \hat{D}_{j,t+1} + \rho X_{jt} + \omega_{t+1} + \xi_{j,t+1}$$

The parameters of particular interest in this equation are σ_1 and σ_3 , which represent the main effect of Eпивir/PI and the interaction of this effect with our proxy for health status $\hat{D}_{j,t+1}$.

Given that relatively sicker patients were more likely to take Eпивir/PI following its release, one would expect that average Medicaid spending for individuals who took these treatments was higher on average than for their counterparts who did not. The results presented in the first column of Table 6 support this prediction, with a statistically significant estimate of 0.834 for σ_1 when no other covariates are included. This estimate declines when additional covariates are included in the next four specifications, though it remains significantly positive. This is not surprising given that Medicaid expenditures did increase at most points in the distribution as shown in Table 5.

In the sixth specification we include the interaction of our treatment indicator with our proxy for health status. As expected, the estimate for σ_3 is negative and is statistically significant, suggesting that sicker patients experienced a smaller increase in spending. According to the model, individuals with a predicted mortality probability in excess of 27 percent experienced a decline in spending. The estimates are qualitatively similar in the final specification in which we include both dual eligibles and individuals eligible only for Medicaid.

The results in this section demonstrate that the introduction and rapid diffusion of Eпивir/PI in late 1995 and throughout 1996 increased Medicaid spending for relatively healthy patients and for individuals also eligible for the Medicare program. Despite this, the substantial reductions in

²⁴ Given that more than 90 percent of the person-quarter observations in 1995 and 1996 have strictly positive spending and there is little change in this fraction over time, we do not also consider the effect on the probability of strictly positive spending as the Manning et al (1987) study does.

spending for the sickest individuals more than offset this, so that average quarterly Medicaid spending in our sample declined by more than 7 percent in the year following the release of these treatments.

VII. The Impact on Long-Term Medicaid Spending and the Cost per Life-Year Saved

In this section we simulate the impact of Epivir/PI on long-term health care spending in the Medicaid program. There are two factors that diverge when calculating these costs. First, our results suggest that average spending declined when these treatments were introduced. In contrast, the large reduction in mortality generated by Epivir/PI use increased life expectancy, and hence the amount of time that individuals were eligible for Medicaid.²⁵ In this section, we build an illustrative model that allows us to capture these two opposing factors in a simple calculation.

Consider an HIV positive patient that has progressed in their illness to the point that physicians would recommend Epivir/PI use, which we label as quarter 0. Suppose in the absence of ARVs, a patient will have medical expenditures of M_0 in period 0, and for simplicity, assume this amount grows at a real rate of ρ per quarter. Patients are assumed to die at a rate of δ in each quarter and this rate is assumed to be constant over time. If r is the quarterly interest rate, the discounted expected lifetime costs LT_0 for this patient in the absence of antiretroviral treatments are:

$$(6) \quad LT_0 = \sum_{t=0}^{\infty} M_0 [(1 + \rho)/(1 + r)]^t (1 - \delta)^t$$

For simplicity, assume that ρ is equal to r ²⁶ and therefore, that discounted lifetime costs equal M_0/δ .

²⁵ As Meltzer (1997) outlines, there is some controversy about whether future medical costs should be considered in medical cost-effectiveness studies. Meltzer argues that for cost-effectiveness studies to be consistent with utility maximization, they must include all future lifetime costs, including non-medical expenses. At the other extreme, others argue that only future medical costs directly related to the illness should be included in these calculations. Given available data, we examine all future medical costs but do not include non-medical expenses.

²⁶ This assumption seems reasonable given that our estimate of the average growth rate in individual-specific quarterly Medicaid spending in both the pre and post periods was approximately 1 percent.

When Epivir/PI was introduced, assume baseline costs and the mortality rates changed to M_0^a and δ^a respectively, and therefore, lifetime costs would then be M_0^a/δ^a . The increase in life expectancy in quarters is simply $[1/\delta^a - 1/\delta]$ and the corresponding change in lifetime costs is $[M_0^a/\delta^a - M_0/\delta]$. Dividing this number by $4[1/\delta^a - 1/\delta]$ produces the cost per life year saved.

Prior to the introduction of the new treatments, the average quarterly mortality rate in our sample was 7 percent and average spending per person-quarter was equal to \$6242. Our results from above suggest that Epivir/PI reduced mortality rates by 68 percent and average Medicaid spending per quarter by 16 percent. Given our simplifying assumptions, this implies that Epivir/PI increased the average present value of Medicaid spending from \$89,000 to \$234,000 and life expectancy from 3.6 to 11.2 years, with a corresponding cost per life year saved of approximately \$19,000.²⁷ This is substantially lower than recent estimates of the average individual's valuation of a life-year, which Cutler and Richardson (1998) estimate lies between \$75 thousand and \$150 thousand.

We should note that we make a number of strong assumptions, including a constant mortality rate (rather than one that increases over time) and that the discount rate is equal to the growth in quarterly Medicaid expenditures. It is worth noting, however, that the marginal cost per life year saved calculation is not particularly sensitive to the assumed values of M_0 and M_0^a . If we assume there is no change in spending associated with ARVs then the cost per life year saved increases to roughly \$25,000. Likewise, the results are not very sensitive to the precise drop in mortality produced by ARVs. Thus even if we relax one of these or our other assumptions, the four ARVs studied here are well within the range of what is considered to be cost effective.

It is worth emphasizing that the estimates for this treatment do not generalize to other ARVs or to other new health care treatments. Indeed as shown in Figure 5, since the utilization of Epivir/PI

²⁷ This estimate is similar to estimates presented by Freedberg et al (2001). The authors use estimates from RACTs to simulate the cost-effectiveness of three-drug anti-retroviral regimens. They estimate that such a regimen costs \$13,000 to \$23,000 per quality adjusted life year in real 1998 dollars.

settled to its new equilibrium in early 1997, there has been little further decline in mortality rates among Medicaid patients with HIV/AIDS. This has been true despite a consistent increase in pharmaceutical spending in the last several years of our sample, which increased from \$2,385 in the second quarter of 1997 to almost \$3,900 per quarter in 2001. Of course it could be that mortality rates would have started to rise again had it not been for the new treatments. But the contrast between the drugs released one decade ago and those released since suggest that the cost-effectiveness of the more recent ARVs may be considerably lower.

VIII. Discussion

The steady increase in health care spending in recent years and that is projected for the coming decades suggests that greater scrutiny may be given to the benefits of new and more expensive health care treatments. Potential sources of data for these analyses are the claims data sets from insurers such as Medicare, Medicaid, or private insurance companies. These data sets have large sample sizes, have detailed information on individuals' treatments, and have very accurate data on expenditures. It is, however, difficult to reliably estimate the effects of interest with this data because of the absence of clinical information that would allow one to control for baseline health status and because treatment decisions are endogenous.

In this study we investigate whether claims data can shed light on the impact of new health care treatments by utilizing a sample of claims and eligibility data for more than 4 million individuals eligible for California's Medicaid program. This large sample size is especially important for our purposes given that AIDS is a relatively rare disease that currently afflicts just 0.14 percent of U.S. residents. We argue that given the ARV treatment guidelines in effect during our study period, an econometric model must allow for heterogeneity in both take-up rates and effectiveness based on patient health status. We show that by exploiting the longitudinal nature of the data it is possible to

construct proxies for health status. We focus primarily on four drugs released in late 1995 and early 1996, as these are the ones that appear to have generated the largest improvements in health.

Our findings for the average effects of the treatments are in line with those from previous studies that use randomized research designs or that have the benefit of more detailed clinical information. Specifically, our results suggest that the treatments led to a 68 percent reduction in mortality rates among the individuals who took them. In contrast to these earlier studies, we can investigate the extent to which the use of the treatments in real-world settings varies across individuals and how the effects of the treatments vary as well. Additionally, we can consider the effect on health care expenditures. For a variety of reasons, such as imperfect information, provider financial incentives, and the moral hazard effects of health insurance, current treatment patterns could substantially deviate from what is optimal. This possibility is not limited to HIV/AIDS treatments, the category of treatments considered here.

Of course, one could probe further on our estimates for the effect of Epivir/PI on both mortality and health care spending. For example, our model assumes that the effect of the treatment has a linear relationship with our measure of health status. Additionally, there remains some concern that endogenous treatment decisions are not being adequately controlled for. But the results from these specifications, combined with the trends in mortality and in the distribution of Medicaid spending, strongly suggest that one can use readily available data on health care utilization from a real-world setting to obtain credible estimates of the effect of new treatments on both spending and health outcomes and how these effects vary across individuals. The principal benefit of using the introduction of new treatments to do this is that one can examine how the distribution of key outcome variables evolves as the treatments diffuse, and use this as a check on the individual-level estimates.

The methods utilized in this paper could be applied to evaluate the impact of other health care treatments. Although RACTs are considered the gold standard in the medical community for estimating causal relationships, not all questions can be analyzed through experiments because of

cost considerations or other factors. For example, Raffi et al. (2001) notes that in the case of AIDS, ARVS have reduced the probability of death to such levels that samples sizes would have to be exceedingly large for mortality to be a clinical outcome in a drug trial. Likewise, because the variance of health care spending in a cross section of patients is typically very large, samples sizes would be prohibitively large to obtain precise estimates of expenditure impacts.

Researchers must therefore increasingly rely on non-experimental econometric methods to evaluate the effects of health care treatments. The methods utilized here suggest that one can use observational data from a real-world setting to estimate the effects on both expenditures and health outcomes, even without detailed clinical data. This is especially true if one has detailed information for the period both before and after the introduction of the treatments under consideration. Analyses that provide reliable estimates of the effect of alternative health care treatments could be an important input to efforts to increase the efficiency of the U.S. health care system.

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Figure 1: HIV/AIDS Cases in the 24% Medicaid Sample and # Living with AIDS in CA

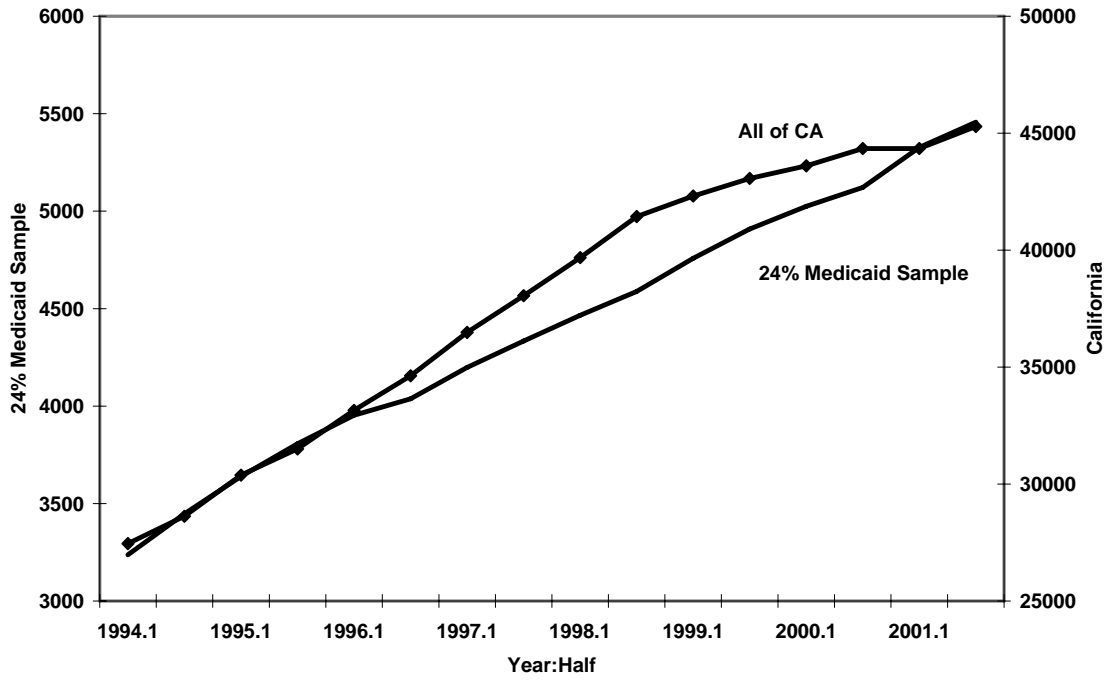


Figure 2: Half-Year Mortality Rate for AIDS Patients

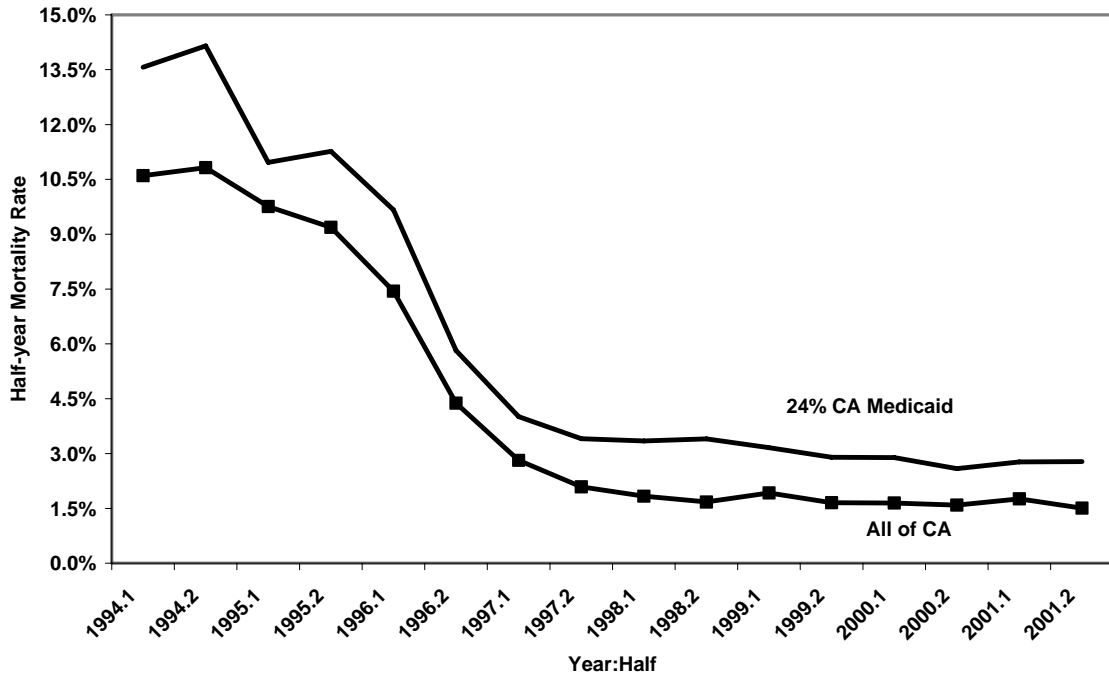


Figure 3: Fraction of CA Medicaid Sample Taking 1+ HIV Drugs in Each Quarter

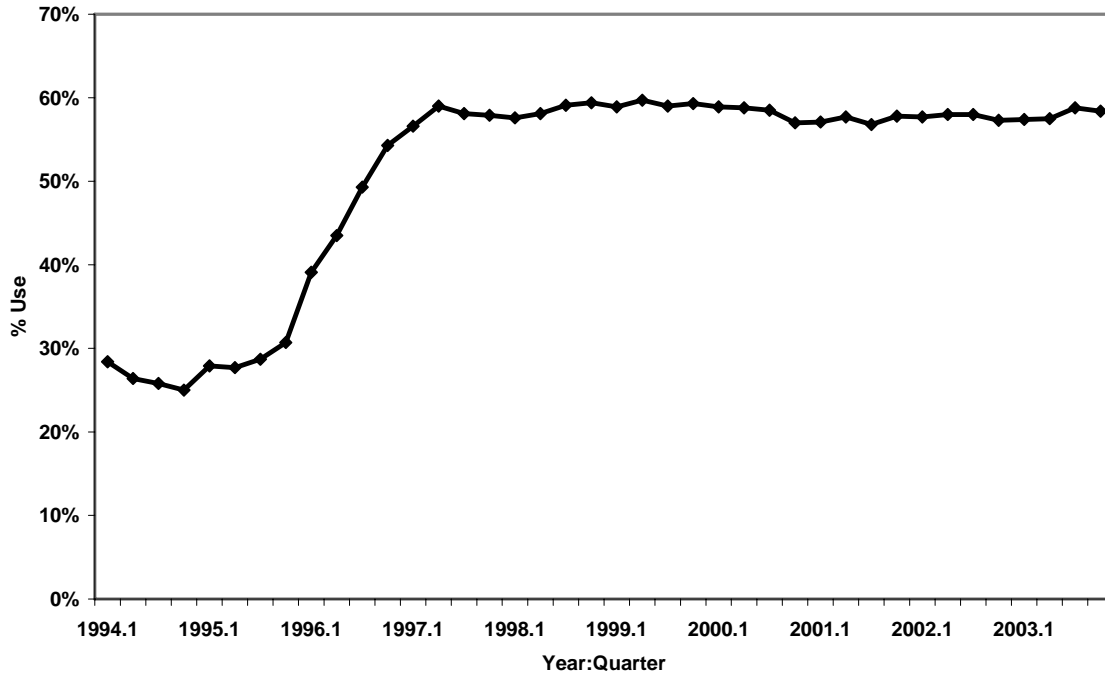


Figure 4: Diffusion of Efavir and Protease Inhibitors: 1994Q1 - 2003Q4

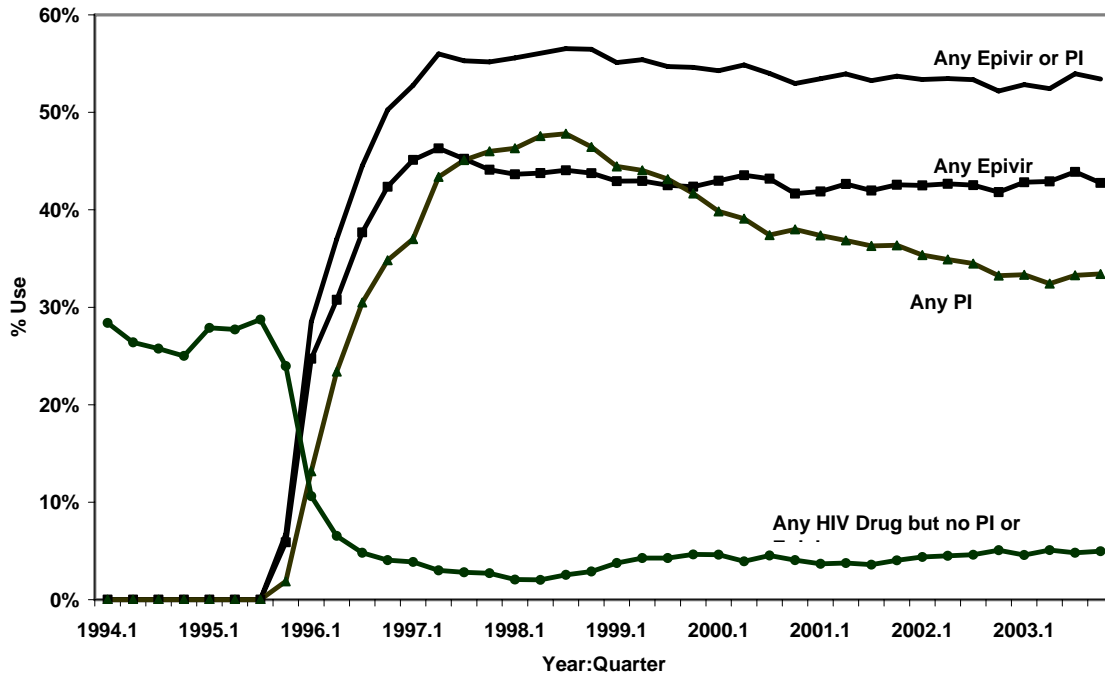


Figure 5: Quarterly Mortality Rate and Use of PI/Evir

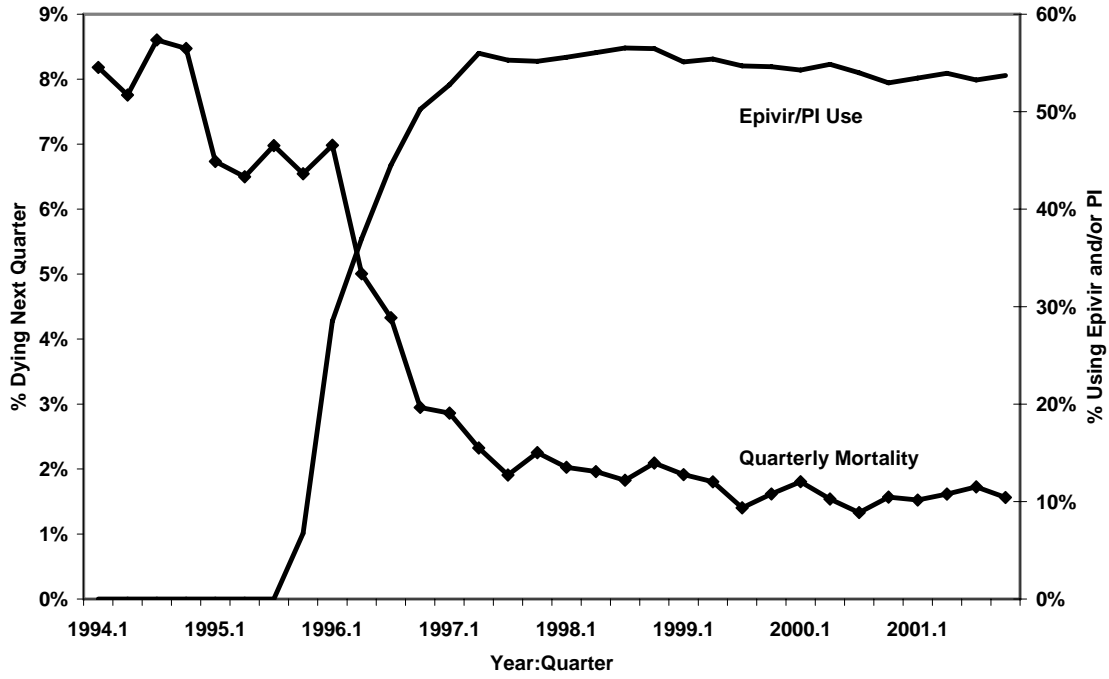


Figure 6: Average Quarterly Spending in the Medicaid HIV/AIDS Sample

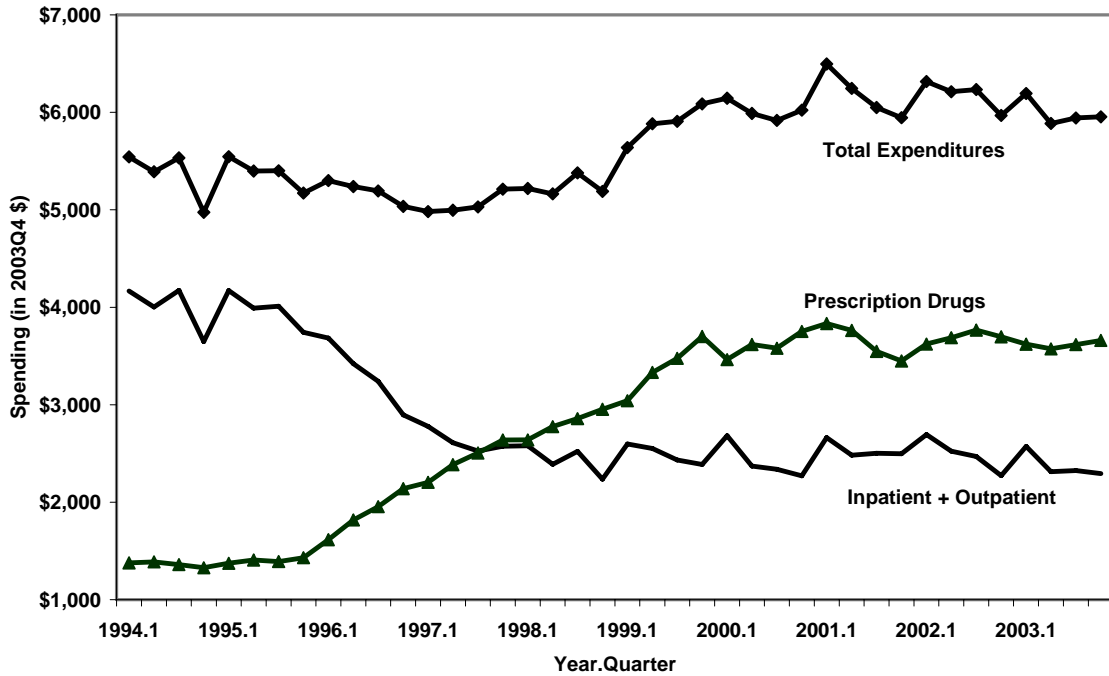


Figure 7: Quarterly Mortality Rates by HIV/AIDS Severity: 1995Q1 - 1997Q1

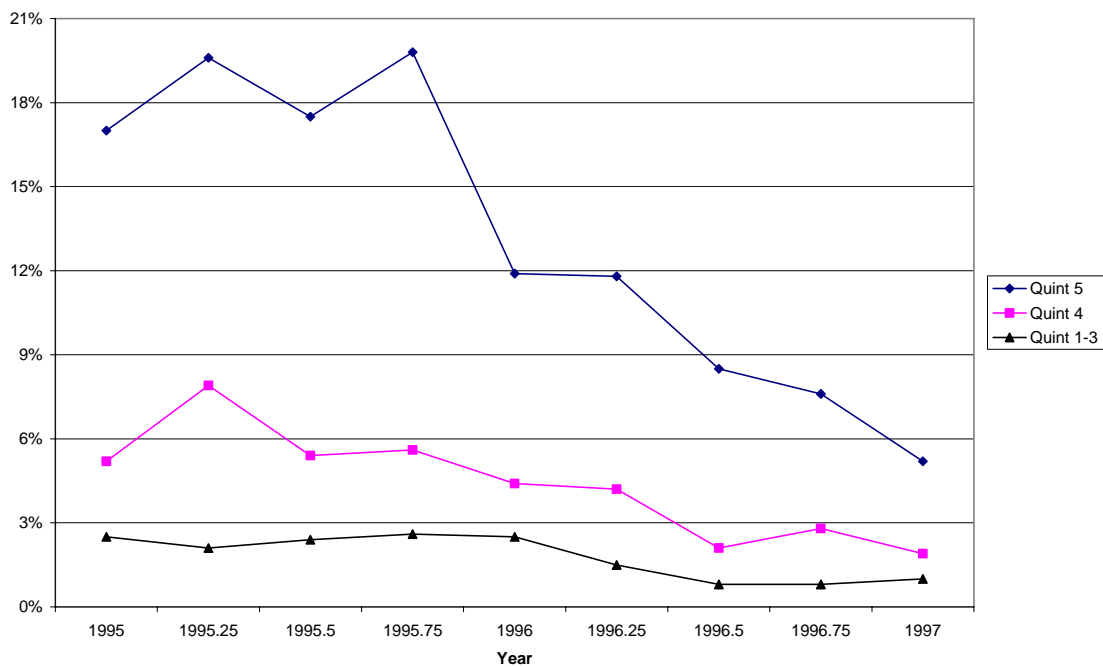
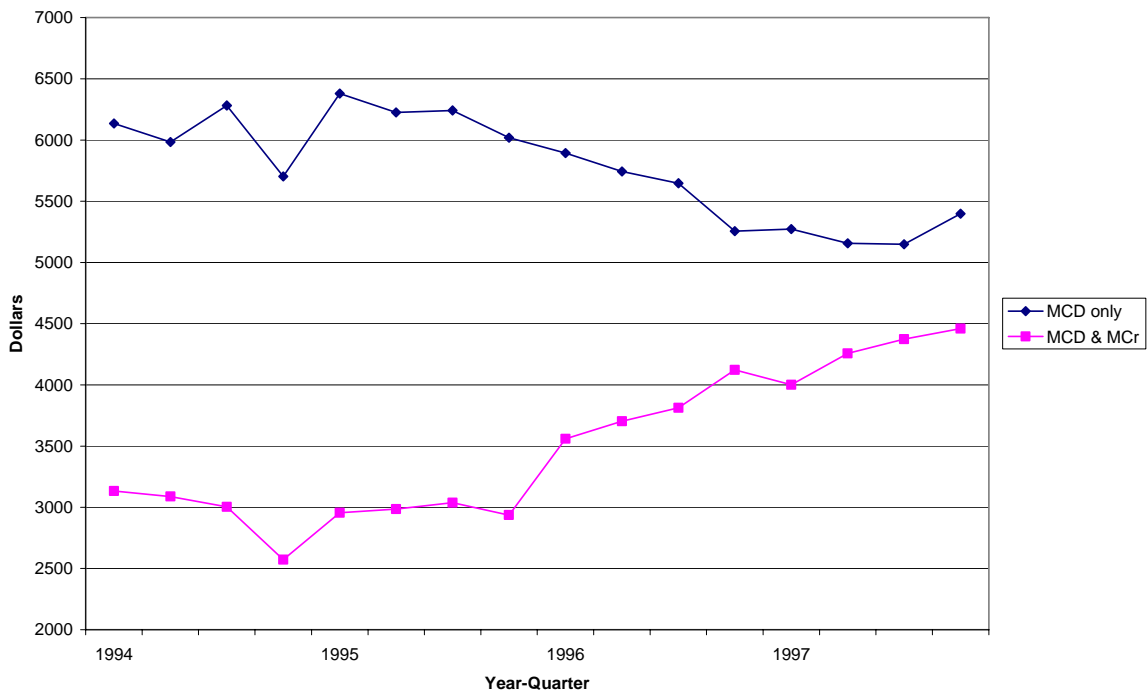


Figure 8: Average Medicaid Expenditures: Dual Eligibles vs. Medicaid Only



Appendix Figure 1: Rate of Non-Mortality Exit for Medicaid HIV/AIDS Sample

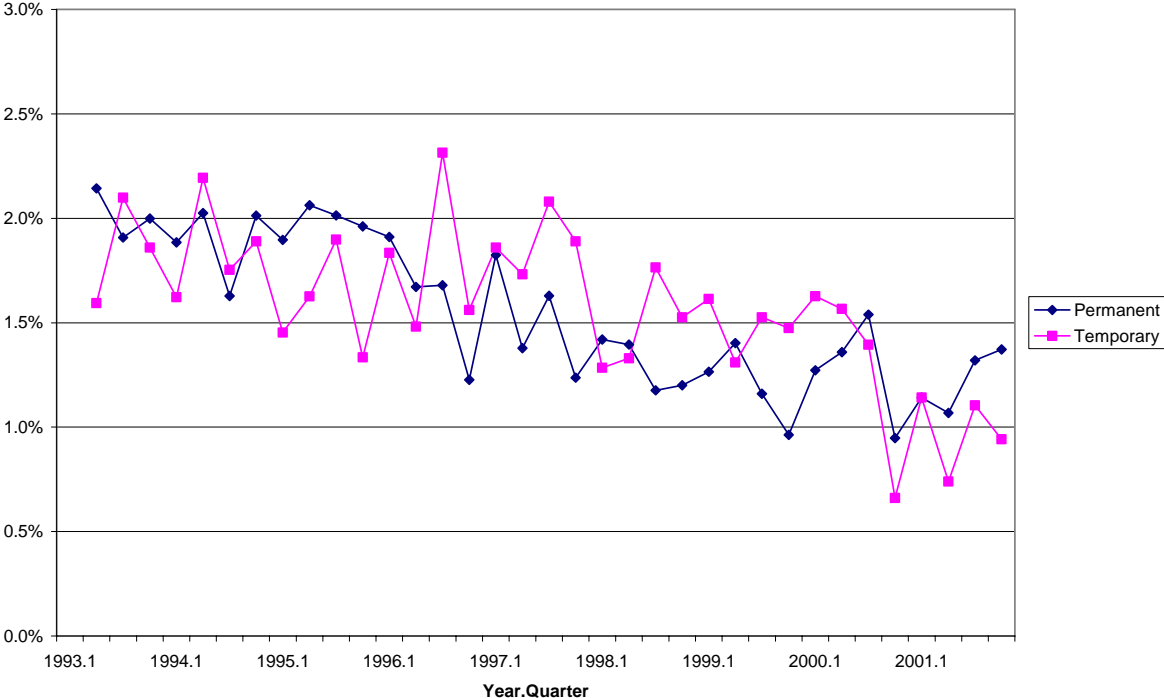


Table 1: Prescription Drugs Approved for Treatment of HIV Infection by 12/31/03

Class	Brand Name	FDA Appr. Date	First script in claims data	Ingredients
NRTI	Retrovir	3/19/1987	1/2/1993	zidovudine
NRTI	Videx	10/9/1991	1/4/1993	didanosine
NRTI	Hivid	6/19/1992	1/4/1993	zalcitabine
NRTI	Zerit	6/24/1994	8/6/1994	stavudine
NRTI	Epivir	11/17/1995	11/27/1995	lamivudine
NRTI	Combivir*	9/27/1997	10/17/1997	lamivudine, zidovudine
NRTI	Ziagen	12/17/1998	12/18/1998	abacavir
NRTI	Trizivir**	11/14/2000	12/1/2000	abacavir, zidovudine, lamivudine
NRTI	Viread	10/26/2001	11/1/2001	tenofovir disoproxil fumarate
NRTI	Emtriva	7/2/2003	7/16/2003	emtricitabine
PI	Invirase	12/6/1995	12/11/1995	saquinavir mesylate
PI	Norvir	3/1/1996	3/7/1996	ritonavir
PI	Crixivan	3/13/1996	3/26/1996	indinavir
PI	Viracept	3/14/1997	3/19/1997	nelfinavir mesylate
PI	Fortovase	11/7/1997	11/18/1997	saquinavir
PI	Agenerase	4/15/1999	4/26/1999	amprenavir
PI	Kaletra	9/15/2000	9/20/2000	lopinavir and ritonavir
PI	Lexiva	10/20/2003	11/11/2003	fosamprenavir calcium
NNRTI	Viramune	6/21/1996	8/10/1996	nevirapine
NNRTI	Rescriptor	4/4/1997	4/25/1997	delavirdine
NNRTI	Sustiva	9/17/1998	9/23/1998	efavirenz
FI	Fuzeon	3/13/2003	4/8/2003	enfuvirtide

Source for drug list and approval dates: US FDA at <http://www.fda.gov/oashi/aids/virals.html>

* Combivir is a combination of Epivir and Retrovir

** Trizivir is a combination of Epivir, Retrovir, and Ziagen

Table 2: Summary Statistics for the Medicaid HIV/AIDS Sample

	1994	1997	2000	2003
Average Age	38.4	40.7	43.0	45.1
% Ages 0-17	2.5%	2.6%	2.5%	2.2%
% Ages 18-29	12.0%	8.5%	4.4%	3.8%
% Ages 30-39	44.1%	38.7%	32.0%	21.9%
% Ages 40-49	29.3%	33.1%	37.7%	41.8%
% Ages 50-64	10.0%	13.4%	19.2%	25.3%
% Ages 65+	2.1%	3.8%	4.3%	4.9%
% Black	21.1%	23.4%	24.5%	25.0%
% Female	15.2%	21.3%	21.8%	22.3%
Inpatient Spending	7125	4309	3900	3510
Outpatient Spending	5091	4870	5007	5455
RX Spending	4122	7769	11913	12120
Total Spending	16338	16948	20820	21084
% Die in Year	23.0%	7.5%	5.2%	-
% Any Inpatient	47.8%	39.8%	30.0%	27.9%
Eligible Months	8.9	10.1	10.4	10.8
% Medicare	28.0%	39.2%	43.3%	44.7%
# in Sample	3221	3687	4275	4976

Includes Medicaid-eligible individuals in the 24 percent CA sample with 1 or more HIV/AIDS claims in current or previous year. Excludes those with one or more months in a Medicaid managed care plan or in one of the eight counties with a county-organized health system.

Table 3: Determinants of Mortality and of Epivir/PI Utilization

	Mortality (1)	PI-Epivir (2)
HIV Severity	1.042*** (0.093)	0.979*** (0.129)
Female	-1.557** (0.658)	-0.124*** (0.019)
Black	-0.113 (0.675)	-0.126*** (0.018)
Age 15-24	-2.621** (1.050)	-0.198*** (0.043)
Age 25-34	-1.385** (0.663)	-0.021 (0.018)
Age 45-54	1.515* (0.886)	0.002 (0.022)
Age 55-64	1.141 (1.464)	-0.074** (0.035)
Age 65+	-1.312 (1.358)	-0.302*** (0.042)
Medicare	0.812 (0.635)	0.126*** (0.017)
Quarters Included	95Q1-95Q3	96Q1-96Q4
# Observations	6504	10523
Quarter Effects?	Yes	Yes
R-squared	0.0779	0.0986
Mean of Dep Var	0.062	0.428
# of Individuals	2711	3280

Sample includes all individuals with one or more HIV/AIDS claims in the quarter or in a previous quarter and who are eligible for Medicaid and still alive at the end of the quarter. Unit of observation is the person-quarter. All specifications are estimated as linear probability models and include quarter fixed effects. Standard errors are clustered by individual.

Table 4: The Heterogeneous Impact of Epivir/PI on Mortality

	(1)	(2)	(3)	(4)	(5)	(6)
Any Epivir/PI	-.0085** (.0038)	-.0113*** (.0039)	-.0280*** (.0039)	-.0285*** (.0039)	-.0360*** (.0040)	.0115 (.0076)
HIV Severity			.9731*** (.0658)	.9166*** (.0742)	.7819*** (.0753)	.9438*** (.0822)
Any Epivir/PI * HIV Severity						-.6387*** (.1092)
Previous HIV Severity				.1051 (.0665)	.0400 (.0658)	.0489 (.0639)
Female		-.0202*** (.0038)	-.0126*** (.0036)	-.0123*** (.0036)	-.0141*** (.0037)	-.0130*** (.0037)
Black		-.0015 (.0041)	-.0023 (.0036)	-.0024 (.0039)	-.0012 (.0038)	-.0012 (.0038)
Age 15-24		-.0505*** (.0061)	-.0362*** (.0065)	-.0358*** (.0066)	-.0332*** (.0077)	-.0326*** (.0079)
Age 25-34		-.0182*** (.0053)	-.0189*** (.0050)	-.0190*** (.0050)	-.0174*** (.0050)	-.0179*** (.0049)
Age 35-44		-.0088* (.0051)	-.0106** (.0048)	-.0107** (.0048)	-.0090 (.0048)	-.0093** (.0048)
Age 55-64		-.0082 (.0086)	-.0054 (.0087)	-.0054 (.0088)	-.0069 (.0086)	-.0062 (.0083)
Age 65+		-.0083 (.0098)	-.0019 (.0102)	-.0017 (.0102)	0.0005 (.0099)	.0021 (.0101)
Medicare		-.0085*** (.0037)	.0058 (.0033)	.0063* (.0036)	.0010 (.0036)	.0011 (.0035)
# Other RX Claims					.0016*** (.0002)	0.0016*** (.0002)
# Other Outpatient Claims					.0002** (.0001)	.0002*** (.0001)
# Other Inpatient Claims					.0005 (.0008)	.0006 (.0008)
Quarters Included	95Q1-96Q4	95Q1-96Q4	95Q1-96Q4	95Q1-96Q4	95Q1-96Q4	95Q1-96Q4
# Observations	15882	15882	15882	15882	15882	15882
Quarter Effects?	Yes	Yes	Yes	Yes	Yes	Yes
R-squared	0.0057	0.0092	0.0779	0.0783	0.0919	0.0978
# Individuals	3413	3413	3413	3413	3413	3413

Sample includes all individuals with one or more HIV/AIDS claims in the quarter or in a previous quarter and who are eligible for Medicaid in all three months of this quarter, all three months of the previous quarter, and still alive at the end of the quarter. Unit of observation is the person-quarter. All specifications are estimated as linear probability models and include quarter fixed effects. Standard errors are clustered by individual and included in parentheses.

Table 5: Trends in the Distribution of Medicaid Expenditures: 1994Q1-1997Q4

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
Quarter	Any Epiv/PI	Mean	Non-Duals	Duals	30th	50th	70th	90th	95th
1994Q1	0.0%	5330	6135	3133	648	1643	3792	14653	23623
1994Q2	0.0%	5183	5984	3088	584	1508	3554	14820	22610
1994Q3	0.0%	5320	6283	3004	617	1574	3698	15245	24546
1994Q4	0.0%	4783	5703	2572	604	1503	3627	13058	22039
1995Q1	0.0%	5331	6380	2955	695	1775	4100	14646	23059
1995Q2	0.0%	5190	6225	2986	652	1705	3998	14372	22581
1995Q3	0.0%	5193	6242	3037	637	1737	3939	13910	23658
1995Q4	6.7%	4973	6019	2937	651	1693	3895	13760	22893
1996Q1	28.5%	5096	5893	3560	788	2045	4209	13042	21622
1996Q2	37.0%	5037	5743	3703	889	2124	4450	13046	20835
1996Q3	44.5%	4994	5648	3812	924	2275	4345	12035	20049
1996Q4	50.2%	4841	5256	4122	1090	2473	4420	10679	18324
1997Q1	52.8%	4790	5273	4002	1149	2610	4369	10643	17888
1997Q2	56.0%	4803	5157	4257	1275	2775	4616	10459	16695
1997Q3	55.3%	4836	5149	4373	1257	2770	4715	10154	17814
1997Q4	55.2%	5011	5398	4460	1307	2860	4684	10164	19360

Table summarizes Medicaid expenditure data for individuals in the 24 percent CA sample with 1 or more HIV/AIDS claims in current or previous quarter and still alive at the end of current quarter. Excludes those with one or more months in a Medicaid managed care plan or in one of the eight counties with a county-organized health system. Column (1) lists the fraction of individuals in the sample with one or more claims for Epivir/PI in the quarter. Columns (2), (3), and (4) list average Medicaid spending for all individuals in the sample, those eligible for Medicaid only, and those eligible for Medicaid and Medicare, respectively. Columns (5) through (9) list expenditures at five different points in the quarter specific Medicaid expenditure distribution. Expenditures are inflation adjusted to November 2001 dollars.

Table 6: The Heterogeneous Impact of Epivir/PI on Medicaid Expenditures

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Any Epivir/PI	.834*** (.054)	.796*** (.054)	.682*** (.049)	.668*** (.049)	.633*** (.043)	.901*** (.058)	1.094*** (.049)
HIV Severity			7.371*** (.358)	5.782*** (.323)	3.411*** (.308)	4.192*** (.361)	4.262*** (.351)
Any Epivir/PI * HIV Severity						-3.345*** (.463)	-4.617*** (.435)
Previous HIV Severity				3.109*** (.390)	2.323*** (.369)	2.348*** (.359)	2.360*** (.333)
# Observations	8846	8846	8846	8846	8846	8846	14347
Quarter Effects?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
R-squared	0.0395	0.0510	0.1575	0.1677	0.2683	0.2723	0.2983
# Individuals	2265	2265	2265	2265	2265	2265	3196
Demographic Controls?	No	Yes	Yes	Yes	Yes	Yes	Yes
Utilization Controls?	No	No	No	No	Yes	Yes	Yes
Quarters Included	95Q1-96Q4	95Q1-96Q4	95Q1-96Q4	95Q1-96Q4	95Q1-96Q4	95Q1-96Q4	95Q1-96Q4

Sample includes all individuals with one or more HIV/AIDS claims in the quarter or in a previous quarter and who are eligible for Medicaid in all three months of this quarter, all three months of the previous quarter, and still alive at the end of the quarter. Unit of observation is the person-quarter. Dependent variable is the log of Medicaid spending in the next period. The key explanatory variable Any Epivir/PI is an indicator that equals one if an individual fills and Epivir or protease inhibitor prescription in the quarter and zero otherwise. Standard errors are clustered by individual and included in parentheses.