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

Mark G. Duggan\*

William N. Evans†

\*University of Maryland, College Park, [duggan@econ.umd.edu](mailto:duggan@econ.umd.edu)

†University of Notre Dame, [wevans1@nd.edu](mailto:wevans1@nd.edu)

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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 (RCTs) 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 RCTs. We also find that the ARVs lowered short-term 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 an alternative method for estimating the real-world effects of new treatments that is especially well-suited to those treatments that diffuse rapidly following their approval.

**KEYWORDS:** HIV, AIDS, antiretrovirals, innovation, Medicaid

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## I. Introduction

During the 2004 calendar year, health care expenditures accounted for 16 percent of GDP in the U.S., with this share twice as large as the corresponding value in 1970 and predicted to exceed 20 percent by 2015. Previous research has suggested that a key contributor to rising health care costs is the introduction and diffusion of new and more expensive treatments (Newhouse, 1992; Cutler, 2004).<sup>1</sup> To the extent that these treatments provide health benefits that are sufficiently large to justify the cost increases, there may be little cause for concern. However, because most consumers of health care in the U.S. have health insurance, which partially or fully insulates them from price differences when choosing between alternative treatments, it is plausible that there is excessive use of certain treatments.<sup>2</sup> Similarly, health care providers may have incentives to advocate for certain treatments over others, which could exacerbate or attenuate this phenomenon.<sup>3</sup> Even absent these issues, 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 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. While these trials make important contributions to knowledge, they have a number of important limitations. Perhaps most importantly, they rarely consider the effect of a treatment on expenditures but instead focus only on health effects. Additionally, results from the trials 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).<sup>4</sup>

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<sup>1</sup> Of course, new treatments can lower health care spending as well through health improvements that reduce the demand for other types of medical care (Lichtenberg, 2001).

<sup>2</sup> See Garber, Jones, and Romer (2006) for an analysis of why for similar reasons health insurance and certain regulatory features can lead to excessive innovation in this sector.

<sup>3</sup> See Kessler and McClellan (1996) for one such example, in which physicians respond a greater threat of being sued for malpractice by providing more treatments than their counterparts at lower risk.

<sup>4</sup> 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).

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 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. They also have the advantage of capturing treatment patterns in the real world.

The key obstacle to obtaining reliable estimates when using claims data is that treatment is endogenous. Individuals who take a certain treatment may differ in important ways from their observably similar counterparts who do not. Previous researchers have accounted for this issue in a variety of ways. One prominent study used a patient's distance from a hospital as a source of variation in treatment (McClellan et al, 1994). In that study, the authors demonstrate that individuals who live closer to the hospital are more likely to receive intensive treatment, and use this variation to estimate the marginal effect of invasive treatments. However, as the authors note, this method is not well-suited to estimating the average effect of a health care treatment.

In this paper, we propose an alternative approach to estimating the effect of health care treatments that allows us to estimate the average effect of a new treatment soon after its introduction and how the effect varies across individuals. More specifically, we use several years of claims, eligibility, and mortality data from California's Medicaid program to estimate the effect of new HIV antiretroviral treatments (ARVs) on both health care spending and health outcomes.

We select these treatments as our case study for three 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), and thus our estimates are more likely to be reflective of overall impacts. Second, several RACTs have demonstrated the average health benefits of ARVs, and thus we have a baseline against which we can compare our estimates. To the extent that we replicate the RACT results for average health effects, we can be more confident that our estimates for spending and for how both health and expenditure effects vary across individuals are accurate.<sup>5</sup> And finally, because these treatments diffused rapidly, our estimates are less likely to be contaminated by changes in the population of individuals with HIV/AIDS.

We account for endogenous treatment decisions in two ways. First, we

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<sup>5</sup> It is important to note that here we do not consider producer surplus, which as Philipson and Jena (2006) point out can lead to underestimates of the benefits of new medical technologies. However, their estimates for ARVs suggest that the value of consumers' health benefits exceeded producer surplus by a factor of twenty, and thus at least for this category of treatments we are omitting only a small fraction of the social benefit.

utilize data from before and after the introduction of several new ARVs and exploit the fact that there were sharp changes in their use immediately following their approval. 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 comparing individuals who take the treatments 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 Epivir/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 outcomes are striking, they shed little light on the extent to which the effects 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 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 ARVs 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.<sup>6</sup> The new treatments reduced quarterly

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<sup>6</sup> 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

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 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.

The results from this study suggest an alternative method for utilizing claims data to evaluate the impact of new health care treatments on both spending and health. This method is most well-suited to evaluating the effect of treatments that diffuse rapidly such as the ARVs considered here.

## **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 Epivir 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 Epivir/PI spawned the use of highly active antiretroviral therapy (HAART), 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. 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.<sup>7</sup> According to data from the U.S.

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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.

<sup>7</sup> 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

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; Florida 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.<sup>8</sup> 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 Efavir, 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 demographic characteristics 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.<sup>9</sup>

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.

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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.

<sup>8</sup> Lichtenberg (2003) uses aggregate, national-level data for the U.S. to estimate the effect of ARV approvals.

<sup>9</sup> There are no RACTs of which we are aware that compare the use of both Efavir and PI with the use of neither.

**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

### 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. Individuals can qualify for the means-tested Medicaid program through several different channels, with the most common reasons in California being the receipt of Temporary Assistance to Needy Families (TANF) or Supplemental Security Income (SSI) benefits. 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.<sup>10</sup>

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 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 claims and eligibility data<sup>11</sup> 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).

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<sup>10</sup> 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.

<sup>11</sup> 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. There is a 24 percent sample because the 20 and 5 percent samples that the state provides partially overlap.

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.<sup>12</sup> 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.<sup>13</sup>

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.<sup>14</sup> Third, we do not know when patients were first diagnosed with HIV or AIDS but instead only the date of their first Medicaid 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.<sup>15</sup> And sixth, we have incomplete utilization data for patients enrolled in a Medicaid managed care plan and thus exclude them from our analyses.

One final limitation to our analysis sample that must be considered in the results that follow is that we only have data for Medicaid recipients. While Medicaid insured approximately half of all California residents with HIV/AIDS during our study period (Bhattacharya et al., 2003), our sample does not include individuals who are uninsured or receive health insurance from another source. Perhaps the most relevant source for a person prior to or immediately following his/her enrollment in Medicaid is the AIDS Drug Assistance Program (ADAP), which was introduced in 1996. This program subsidizes the purchase of ARVs for low-income individuals who are without another source of health insurance. Because the introduction of this program may have affected the entry to or exit from the Medicaid program, we estimate several specifications below that restrict

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<sup>12</sup> 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.

<sup>13</sup> 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.

<sup>14</sup> 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.

<sup>15</sup> Medicare did not cover prescription drugs for dual eligibles during our study period.

only to those enrolled in Medicaid and diagnosed with HIV in the year prior to the introduction of ADAP.<sup>16</sup>

### 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 California<sup>17</sup> 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,<sup>18</sup> 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 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.<sup>19</sup>

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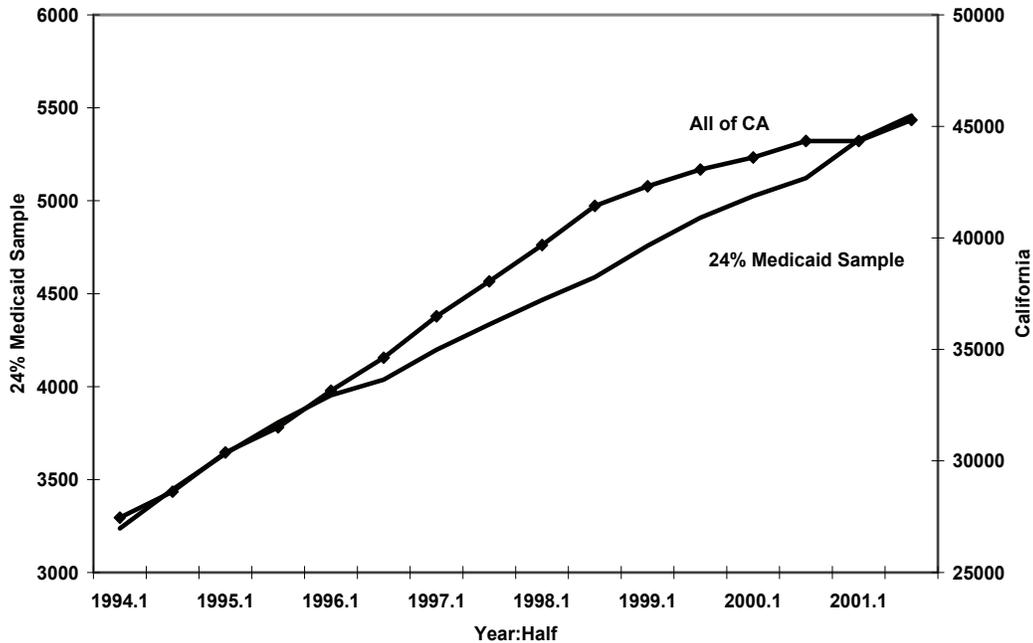
<sup>16</sup> The ADAP program gave some states an incentive to change the stringency of their Medicaid eligibility requirements. Recent research suggests that states with more stringent Medicaid eligibility thresholds had higher mortality rates among affected individuals with HIV/AIDS (Ghosh et al, 2007).

<sup>17</sup> 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.

<sup>18</sup> 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.

<sup>19</sup> 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.

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



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.

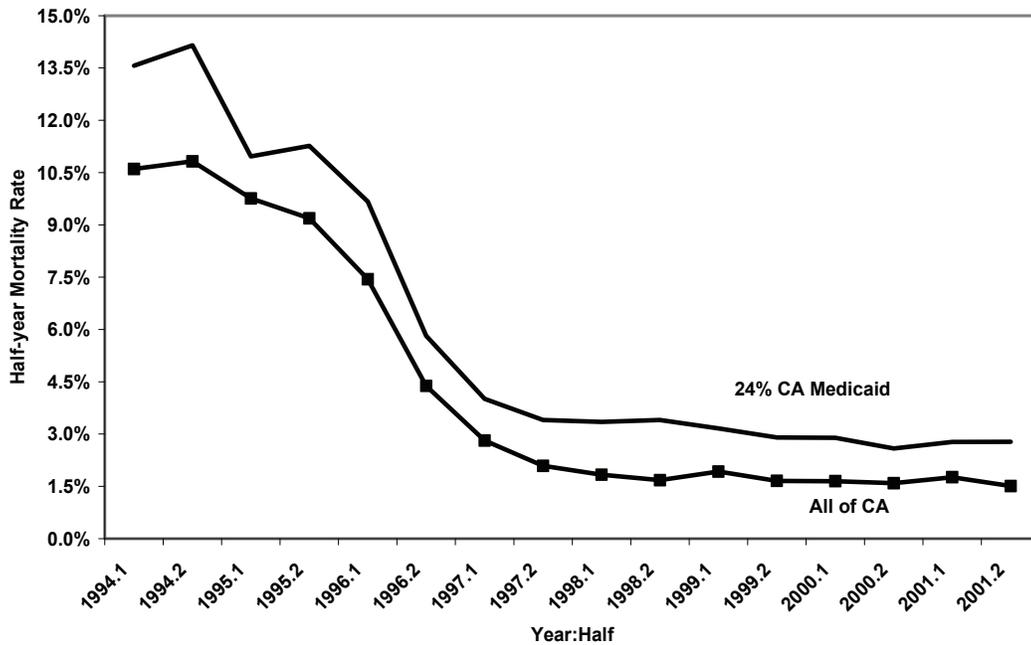
In Table 2, we report descriptive information for our sample in four years: 1994, 1997, 2000 and 2003. In constructing this sample we drop the 1,063 individuals who live in one of the eight counties that moved its Medicaid recipients into a county-organized health system during our study period because 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.<sup>20</sup> 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

<sup>20</sup> 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.

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 \$7125 to \$3510. In contrast, annual outpatient spending increased slightly while spending on prescription drugs tripled, driven primarily by the increased use of ARVs. Although average annual spending on prescription drugs increased by \$8,000 by the end of the study period in 2003, total annual spending increased by just \$4,800.<sup>21</sup> The fraction of HIV/AIDS patients who are 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.

Figure 2: Half-Year Mortality Rate for AIDS Patients



<sup>21</sup> 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).

**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.

#### 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, 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.

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

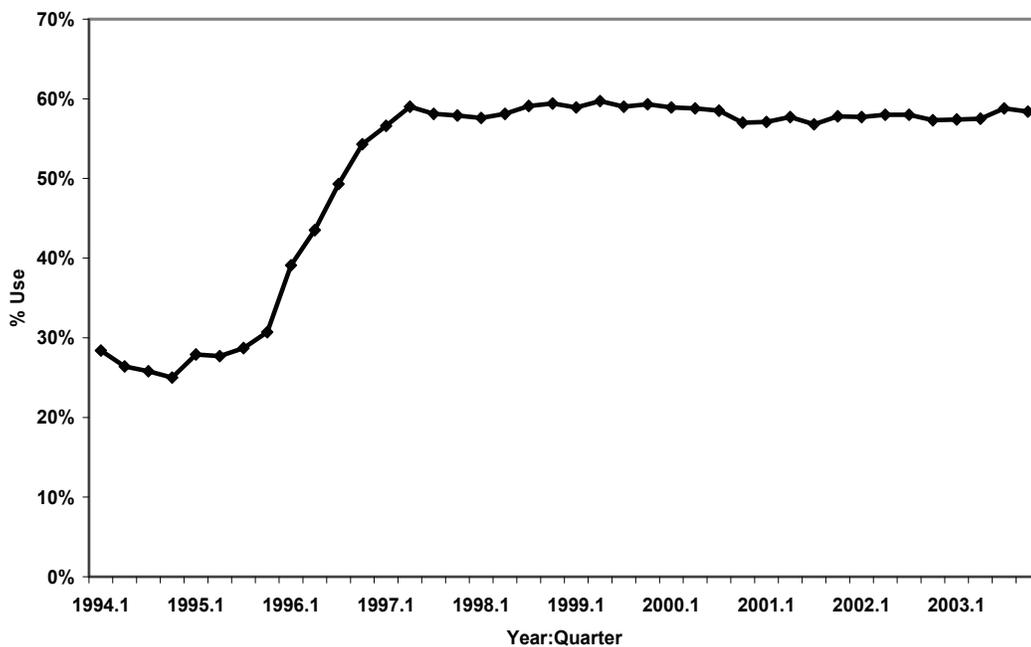


Figure 4: Diffusion of Epivir and Protease Inhibitors: 1994Q1 - 2003Q4

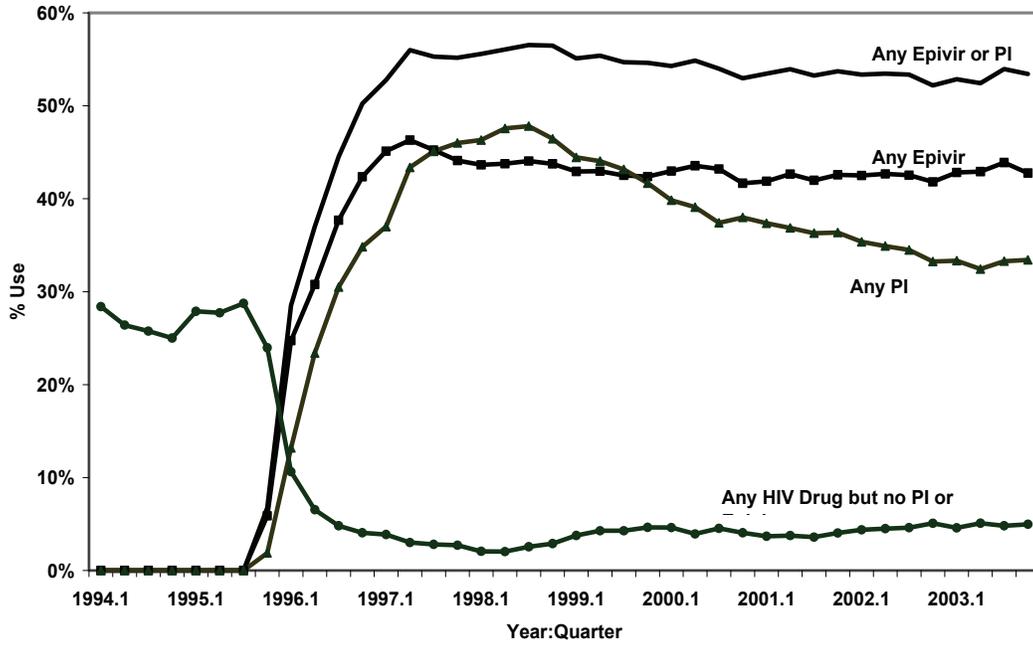
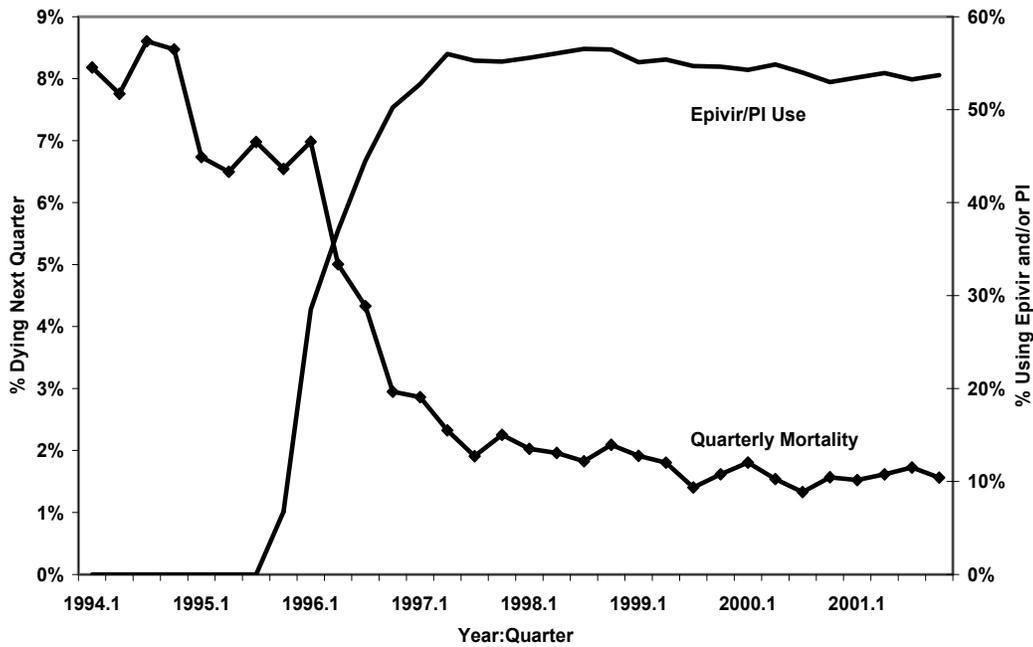


Figure 5: Quarterly Mortality Rate and Use of PI/Epivir



The potential importance of Efavir/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 Efavir/PI use among HIV/AIDS patients in our sample during the 1994-2001 period. The coefficient on the change in Efavir/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.<sup>22</sup> 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 Efavir/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 Efavir/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 quarterly spending declined by 8 percent (\$5401 to \$5030) from late 1995 to 1997. As we demonstrate below, this change in average Medicaid expenditures masks important changes in its overall distribution.

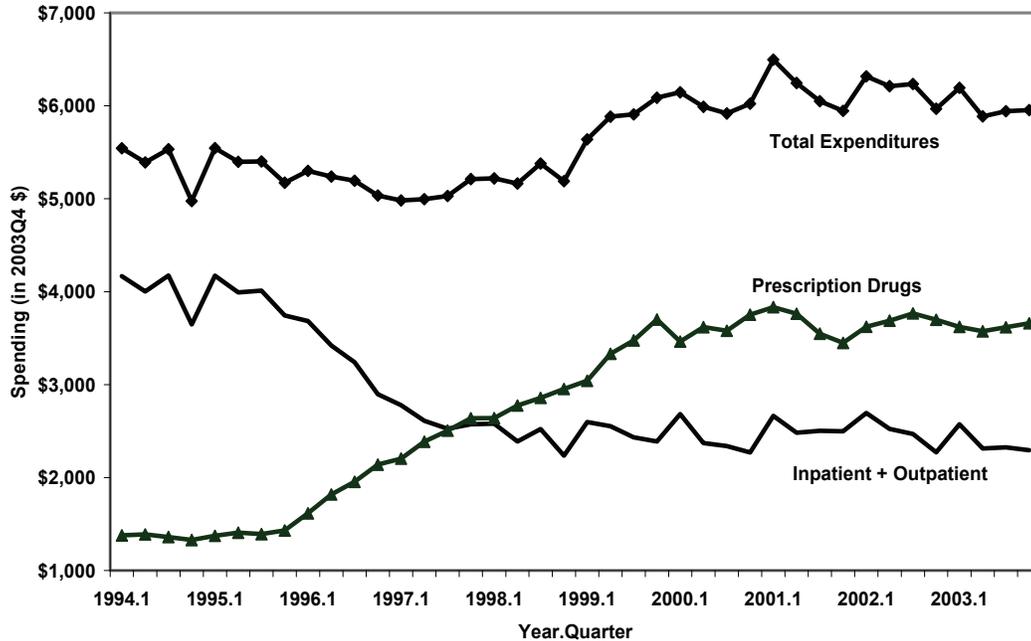
We also investigated whether the treatments affected the quarterly exit rate from the program for reasons other than mortality (e.g. return to work) and found little evidence to support this as shown in Appendix Figure 1. This is especially true in the two years just after the approval of Efavir-PI. This suggests that the composition of our sample is not changing too dramatically during the period that is the focus of our empirical analysis.<sup>23</sup>

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<sup>22</sup> It is worth noting that many taking Efavir 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.

<sup>23</sup> One noteworthy change shown in Table 2 is in the fraction of the sample that is female, which increased from 15 to 21 percent from 1994 to 1997. However, this fraction was already trending up prior to the approval of Efavir-PI.

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



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

In this section we estimate the impact of Efavir/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  $\gamma(H_{jt})$ <sup>24</sup>. Other background

<sup>24</sup> We define this function below to include both a "main effect" and an effect that varies linearly with health status.

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 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:

$$(2) D_{j,t+1} = \beta_0 + \beta_1 * HIV\_IP_{jt} + \beta_2 * HIV\_OP_{jt} + \beta_3 * HIV\_PAID_{jt} + \omega_{t+1} + \varepsilon_{j,t+1}$$

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.<sup>25</sup>

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 the number of observations is

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<sup>25</sup> 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.

7854.<sup>26</sup> The estimates for  $\beta_1$ ,  $\beta_2$ , and  $\beta_3$  using 1994 data are .0332 (se = .0126), .0027 (se = .0003), and .0034 (se = .0015), respectively, with the estimate for  $\beta_0$  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.  $\pi_{t+1}$  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  $\lambda$  is 1.042 (t-statistic of 11.2) and is not significantly different from 1. 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.

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<sup>26</sup> 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.

**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.

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 Epivir/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.

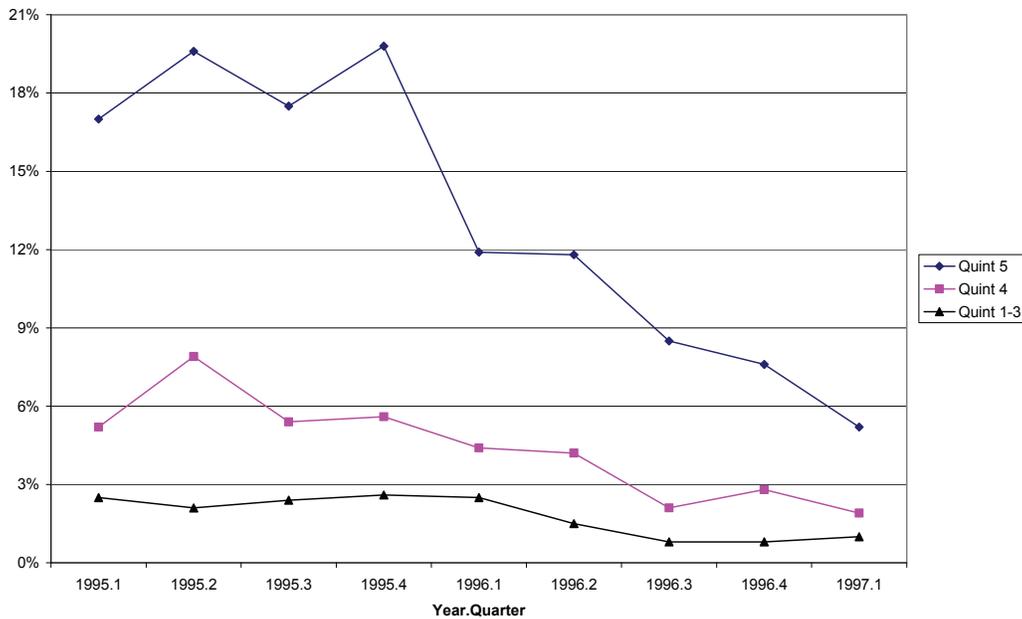
To estimate the effect of Epivir/PI on mortality, we estimate specifications that allow the effect of the treatment to vary across individuals as a function of the predicted mortality probability  $\hat{D}_{j,t+1}$ . Specifically, we assume that the treatment effect  $\gamma$  from equation (1) above 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  $\theta_1$  and the interaction of this effect with health status by  $\theta_3$ .<sup>27</sup> The vector of indicator variables  $\omega_{t+1}$  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 Efavir/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 Efavir or protease inhibitors during this same quarter.

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



<sup>27</sup> Thus the treatment effect function  $\gamma$  from equation (1) is equal to  $\theta_1 + \theta_3 * \hat{D}_{j,t+1}$ .

Before proceeding to the results, it is worth considering two possible 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 variable 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 small increase in this coefficient estimate to  $-.0113$ .

**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-	95Q1-	95Q1-	95Q1-	95Q1-	95Q1-
# 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.

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  $\theta_3$  that is significant at the one percent level. Including this interaction term reduces the magnitude of our estimate for  $\theta_1$  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 Epivir/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  $\theta_1$  and  $\theta_3$ . 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.

With our assumption that the effect of the treatment is linearly related with an individual's predicted mortality probability, the estimates suggests an average mortality rate decline of approximately 68 percent (which is equal to the ratio

$\theta_3 / \theta_2$ ), which is similar to the results reported above for the RACTs<sup>28</sup> 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.<sup>29</sup> This is true despite the fact that sicker individuals clearly self-select into the 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

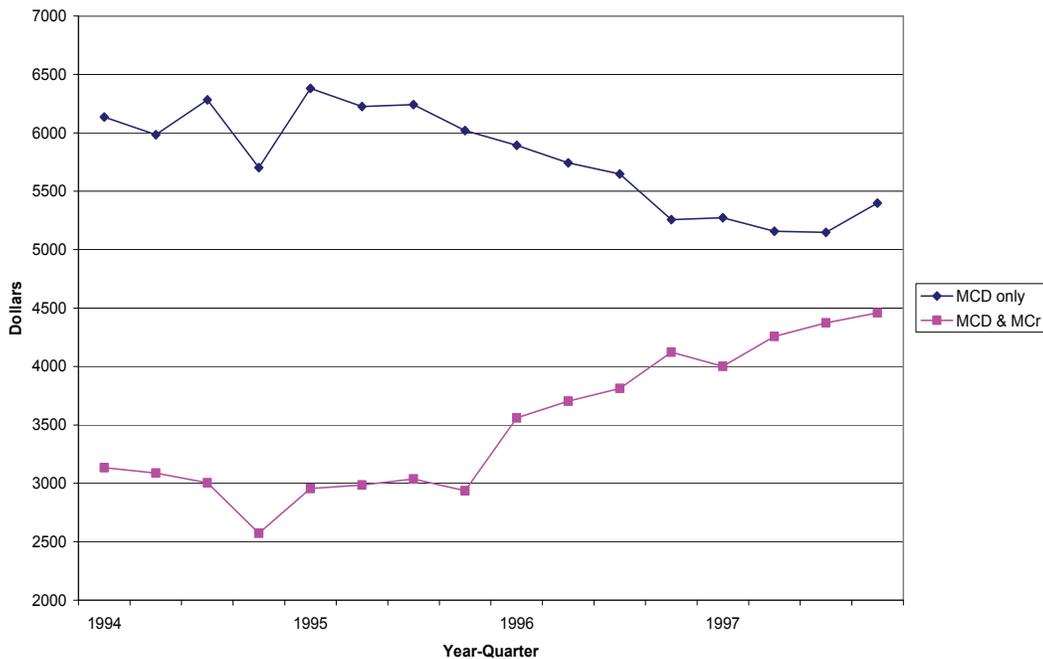
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<sup>28</sup> It is not strictly comparable to the RACT results because most of these studies considered the effect of just protease inhibitors when combined with AZT and Epivir. This underscores the point raised above that we are capturing the effect of a combination of treatments rather than of one specific pharmaceutical treatment.

<sup>29</sup> 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.

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.<sup>30</sup>

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



These trends in average spending may mask important changes in the overall distribution of spending. In Table 5 we list five different percentiles (30<sup>th</sup>, 50<sup>th</sup>, 70<sup>th</sup>, 90<sup>th</sup>, and 95<sup>th</sup>) in the distribution of Medicaid expenditures. If Epivir/PI

<sup>30</sup> The short-term spending declines suggested by this time series and estimated in the next section are qualitatively similar to the 10 percent average decline in spending estimated by Bozzette et al (2001) for a non-Medicaid population. In a related study, Goldman et al (2001) estimate an average expenditure reduction of 31 percent that is attributable to more generous coverage of ARVs by state AIDS Drug Assistance Programs.

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 30<sup>th</sup> and 50<sup>th</sup> 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 90<sup>th</sup> and the 95<sup>th</sup> percentiles declined by 24 percent. The change at the 70<sup>th</sup> 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.

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

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
Quarter	Any Epivir/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.

### 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.<sup>31</sup> We focus on individuals only eligible for Medicaid (thus excluding dual eligibles) 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  $\sigma_1$  and  $\sigma_3$ , which represent the main effect of Epivir/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 Epivir/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  $\sigma_1$  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  $\sigma_3$  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 similar in the final specification (7) in which we include both dual eligibles and individuals eligible only for Medicaid and therefore have a larger sample.<sup>32</sup>

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<sup>31</sup> The logarithmic transformation substantially reduces the skewness in the data that can produce biased estimates given the assumption of a normally distributed error term. 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.

<sup>32</sup> As was true for the mortality specifications, our results are qualitatively similar if we "freeze" each patient's predicted mortality probability at its level in the fourth quarter of 1995 for observations in 1996.

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

**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.

## 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.<sup>33</sup> 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  $\rho$  per quarter. Patients are assumed to die at a rate of  $\delta$  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:

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

For simplicity, assume that  $\rho$  is equal to  $r$ <sup>34</sup> and therefore, that discounted lifetime costs equal  $M_0/\delta$ . When Epivir/PI was introduced, assume baseline costs and the mortality rates changed to  $M_0^a$  and  $\delta^a$  respectively, and therefore, lifetime costs would then be  $M_0^a/\delta^a$ . 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

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<sup>33</sup> 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.

<sup>34</sup> 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.

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.<sup>35</sup> 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  $M^a_0$ . 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.<sup>36</sup>

The estimates for this treatment do not apply to other ARVs or to other new health care treatments. Indeed as shown in Figure 5, since the utilization of Epivir/PI 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. However, before inferring anything about cost-effectiveness from these simple trends, there are two important issues to consider. First, mortality rates may have increased had it not been for the arrival of the new ARVs, as the virus could have become more resistant to a specific drug over time. Second, there may be other improvements in morbidity that are not captured by mortality rates alone.<sup>37</sup>

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<sup>35</sup> 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. The increase in life expectancy is just half as large as the 15 year impact simulated by Philipson and Jena (2006) using the results from previous studies. However, their estimate includes the increase in life expectancy from the time than an individual first contracts HIV. As noted above, when individuals are first observed in our sample they may already have had HIV for several years.

<sup>36</sup> Our results further assume that the short term mortality and expenditure effects that we estimate will persist in the long term. To the extent that the treatments become less effective over time, lead to complications from other health conditions, and so forth, this assumption will not be accurate.

<sup>37</sup> While we have in this study focused on mortality, one could use the claims data to construct measures of morbidity such as the presence of other conditions or time spent in inpatient care.

## **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 the use of individual-level administrative data from before and after the release of a new health care treatment can be used to obtain credible estimates of its effect on both health care spending and health outcomes and how this varies across individuals. Our findings for the average treatment effects are in line with those from previous studies that use randomized research designs or that have the benefit of 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 varies across individuals and how the effects of the treatments vary as well. Additionally, we can consider the effect on health care expenditures.

When interpreting the results from our empirical analyses, it is important to bear in mind a number of limitations. First, our model assumes that the effect of ARVs is linearly related with our measure of health status. Second, to the extent that unobserved factors are correlated with the ARV treatment decision, our estimates will be biased. Third, changes in the observable characteristics of those with HIV during our study period raise the possibility of composition bias. Fourth, our estimates do not account for possible changes in the effectiveness of ARVs over the long term. And finally, our estimates do not consider factors such as firm R&D costs or treatment-induced changes in risky behavior, which represent important components of a more comprehensive accounting of overall treatment benefits and costs.

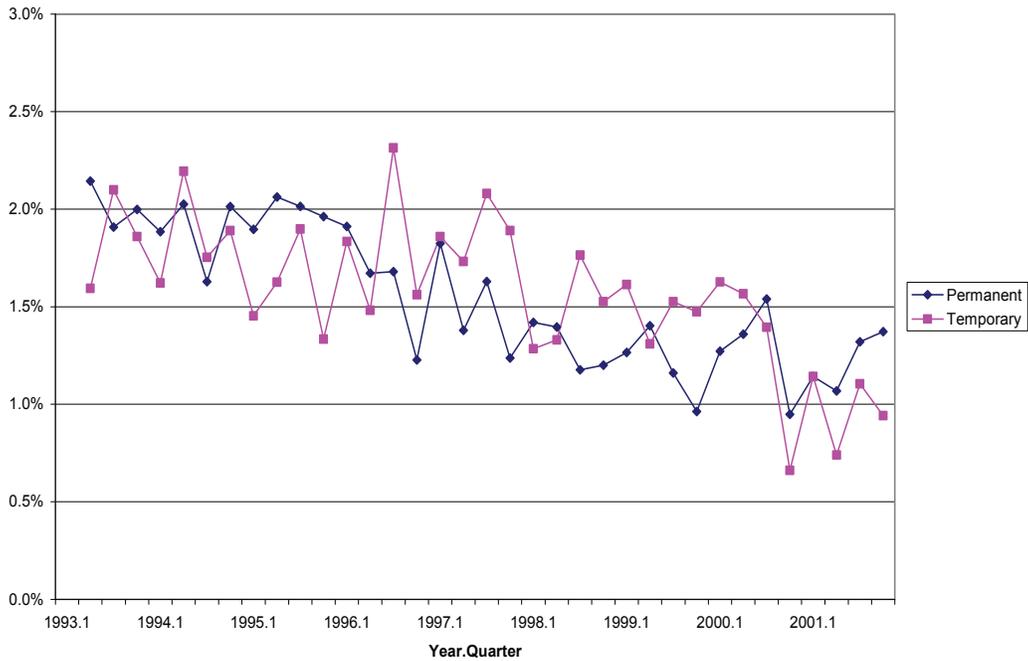
But the results from our primary specifications, combined with the trends in mortality and in the distribution of Medicaid spending, strongly suggest that one can use readily available administrative data from a real-world setting to

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There will inevitably be certain measures of health status that one cannot capture in claims data, and the importance of this limitation will depend on the treatment being considered.

obtain credible estimates of the effect of new treatments on both health care spending and health outcomes and how these effects vary across individuals. An important benefit of using data from before and after the introduction of new treatments 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. Our approach is most well-suited to the evaluation of treatments that diffuse rapidly and that are likely to affect health status primarily in ways that can be captured in administrative data.

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



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