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

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Introduction

- Health care accounts for large (16%) and growing share of GDP
- Also of federal spending – Medicare & Medicaid projected to increase from 22 percent in 2005 to 35 percent by 2016 (CBO, 2006)
- Key driver of this – new and more expensive health care treatments and their diffusion to growing share of patients (Newhouse, 1992; Cutler, 2004)
- Are the benefits sufficiently large to justify costs?
  - Not obvious given demand and supply-side incentives, imperfect info, etc.
- Cost-effectiveness studies likely to become more important (Garber, 2004)
  - Possible lever for reducing growth rate of health care spending

Random Assignment Clinical Trials

- RACTs needed for FDA approval of treatments useful but have limitations
  - Do not consider health care expenditures
  - Idealized rather than real-world setting
  - Focus on average effects for certain subpopulations
  - Short time period and small sample sizes
- Can studies with observational data complement RACTs once the treatments have been approved?
  - Analogous to Lalonde's 1986 study of job training programs that used experimental data (though from opposite direction)

This Study – Focus on Impact of HIV Antiretrovirals (ARVs)

- RACTs suggested large benefits from some ARVs
  - Expedited FDA approval as a result
- Appear to have lowered mortality (from ~30% in 1993) – esp. from 1995-97
  - Followed approval of Epivir and three protease inhibitors
- Not representative of new treatments
- But good setting to test value of claims data in estimating impact
  - Sicker patients will take treatment – thus crucial to control for baseline health
  - Clinical data used to assign treatment but not observed in claims data

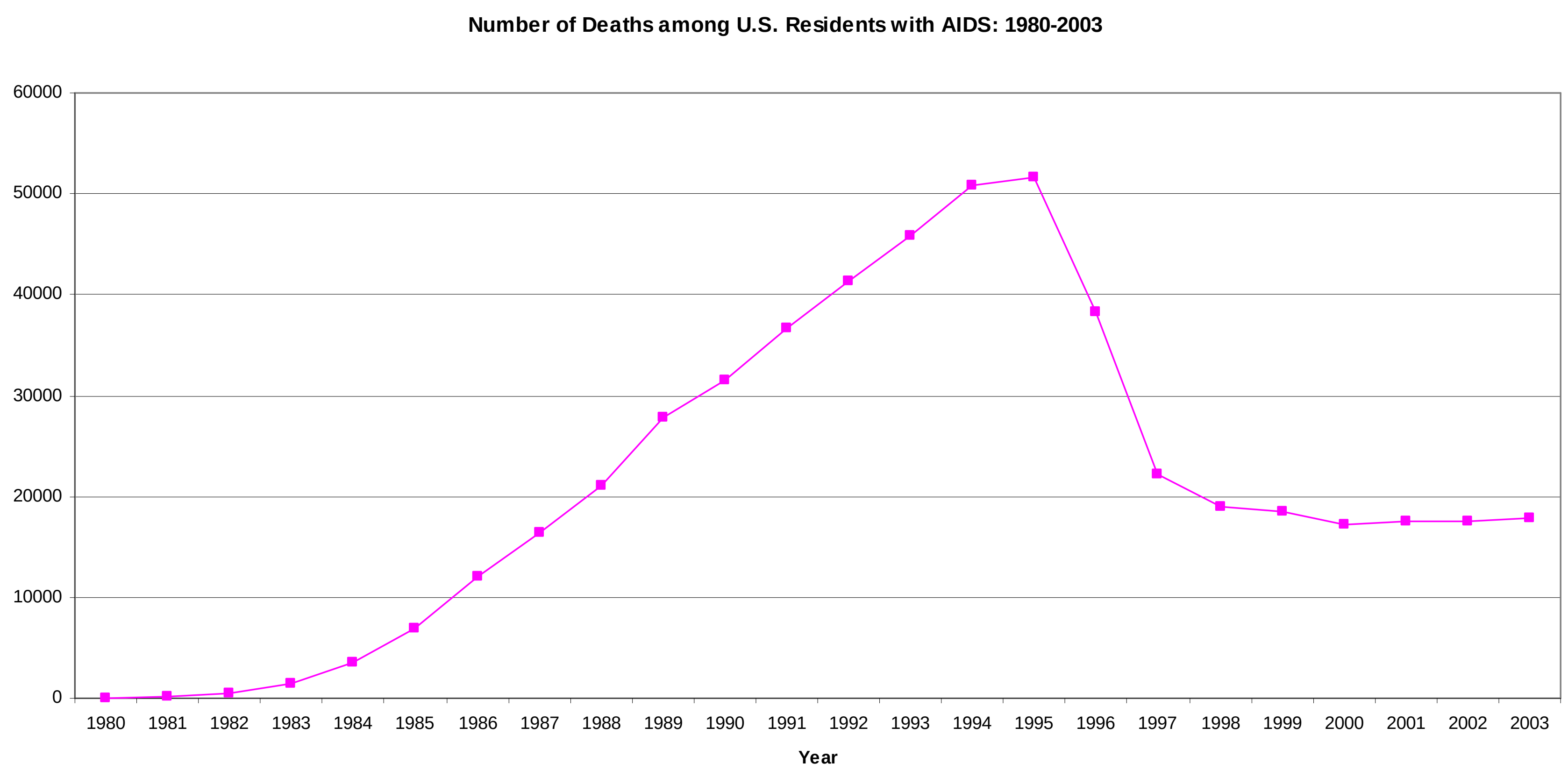

Number of Deaths among U.S. Residents with AIDS: 1980-2003
60000
50000
40000
30000
20000
10000
0
1980
1981
1982
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
Year

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

Estimating the Impact of ARVs

- Consider effect of treatment Z on person j in next period t+1

- Effect β likely to vary both across and within individuals

$$Y_{j,t+1} = \alpha_t + \beta_{jt} Z_{jt} + \mu H_{jt} + \theta X_{jt} + \varepsilon_{jt}$$

- Those in worse health likely to take treatment
  - Crucial to control for baseline health status H_{jt}

- Those with larger expected benefit β_{jt} likely to take treatment
  - Clinical evidence suggests $\beta_{jt} = f(H_{jt})$

Medicaid Claims and Mortality Data

- Claims & enrollment data for 24% sample of CA Medicaid recipients
  - Approx 50% with HIV/AIDS in U.S. are on Medicaid (Bhattacharya et al, 2003)
- Encrypted SSNs allow us to link data over time to form longitudinal data set
- Detailed information on health care utilization
  - Both before and after release of new treatments
  - Can construct (imperfect) measures of health status
  - Linked to mortality data for those with valid SSN through December, 2001
- 4.03 million individuals with 1+ months of eligibility between 1/93 and 12/03

Defining the Sample

- Select the 12,932 (out of 4.03 million) individuals with:
  - 2+ claims with primary or secondary diagnosis of HIV b/w 1/93 - 12/03
  - Consistent demographic data across years
  - Valid social security number (8 percent do not)
- Drop the 1063 who live in one of 8 COHS counties
- Drop the 1802 with 1+ Medicaid managed care months
- Final sample of 10,067 HIV/AIDS patients
- Individual enters sample in quarter of first HIV claim

The Impact of ARVs: Graphical Evidence

- Recall individual-level regression of effect of treatment Z

$$M_{j,t+1} = \alpha_t + \beta_{jt} Z_{jt} + \mu H_{jt} + \theta X_{jt} + \varepsilon_{jt}$$

- Treatment decision likely to depend on β_{jt} and H_{jt}
  - Makes identification at individual level difficult
- Start by aggregating across people to show trends in outcome variables of interest (mortality and expenditures)
  - Exploit rapid change in treatment patterns
  - 0 percent using PI/Epivir in 1995Q3, 60 percent by 1997Q1

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

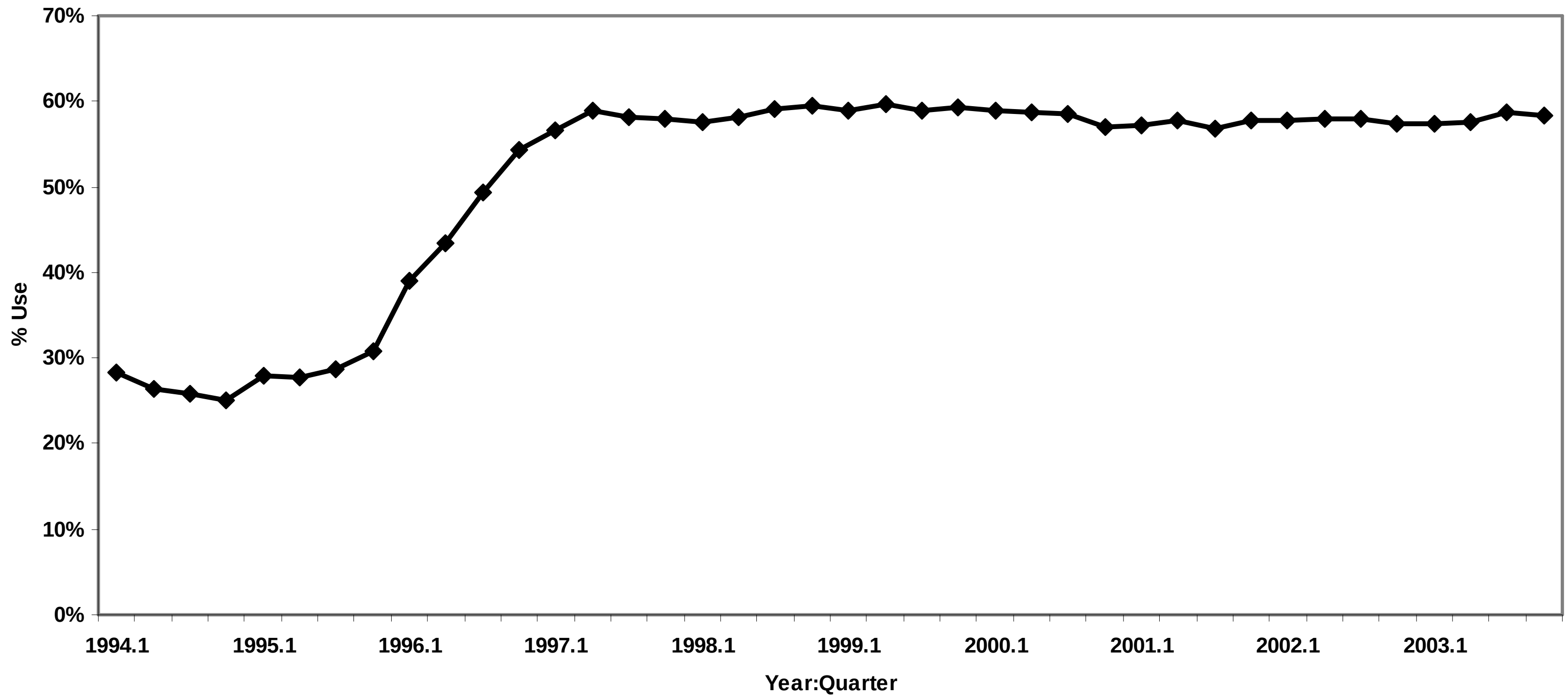
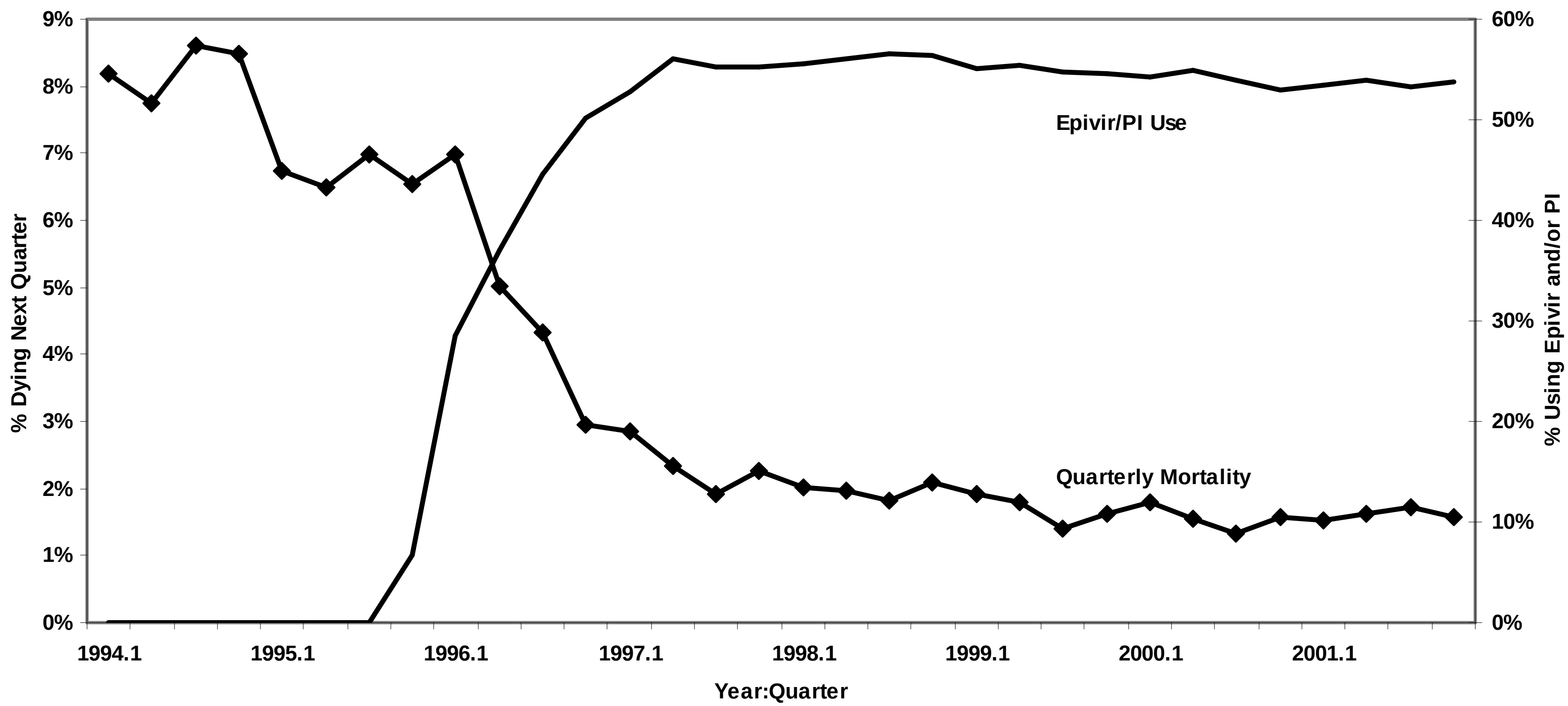


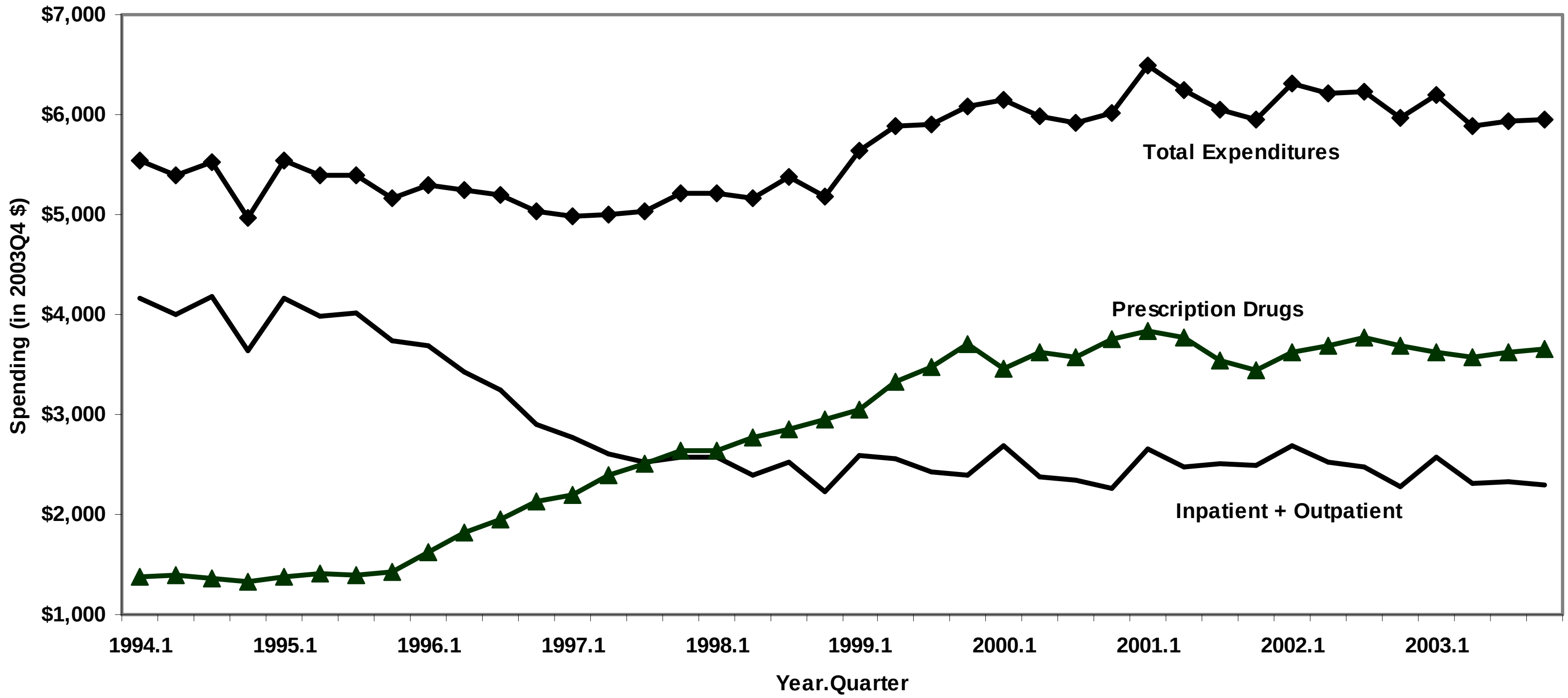
Figure 5: Quarterly Mortality Rate and Use of PI/Epivir



Effects on Medicaid Expenditures

- New treatments much more expensive than predecessors
  - Quarterly ARV spending increased from $153 to $1275 from 95Q3 – 97Q3
- But may offset spending on other categories of medical care
  - Hospitalizations especially but also physician visits, etc.
- Effect may vary by severity of patient – possibility of offset is:
  - Greater for sicker patients
  - Lower for those also on Medicare (dual eligibles)
- Examine Δs for duals vs. non-duals and at different points of distribution

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



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

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

The Impact of PI and Epivir on Mortality and Expenditures

- Relationship between mortality (or spending) and treatment utilization

$$M_{j,t+1} = \alpha_t + \beta_{jt} Z_{jt} + \mu H_{jt} + \theta X_{jt} + \varepsilon_{jt}$$

- Allow treatment effect to vary with health status
  - Sicker patients likely to experience larger mortality reduction
  - Specifically assume $\beta_{jt} = \beta_0 + \beta_1 H_{jt}$
- Focus on 1995Q1-1996Q4 when treatments were rapidly diffusing
  - Treatment Z_{jt} will influence $H_{j,t+1}$ as well – thus likely to understate impact
  - OK if person's position in severity distribution does not change

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

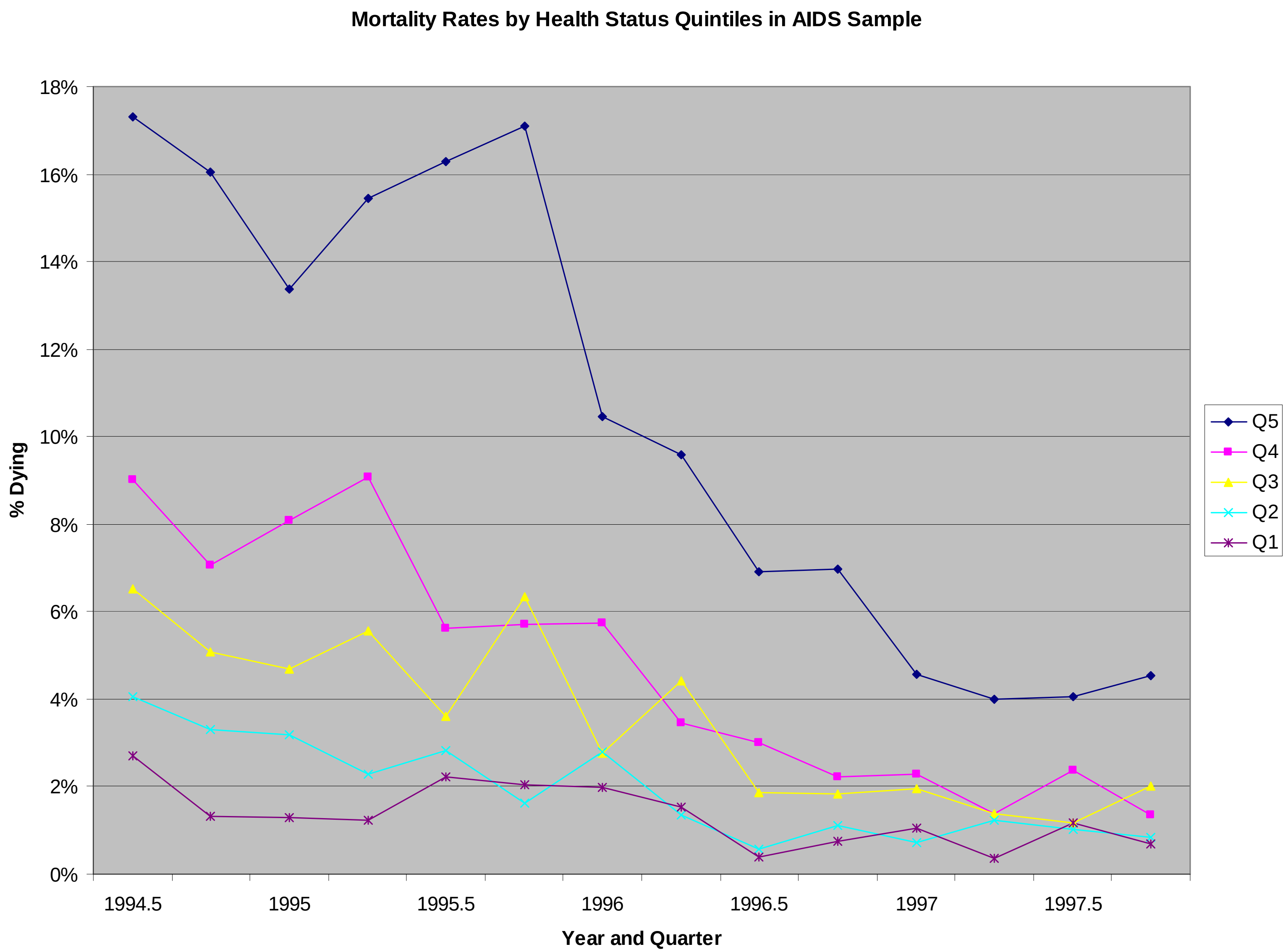
	(1)	(2)	(3)	(4)	(5)	(6)
Any PI or Epivir	-.0101***	-.0126***	-.0394***	-.0461***	.0102*	
	(.0035)	(.0036)	(.0039)	(.0039)	(.0061)	
HIV Severity Percentile			.1370***	.1026***	.1203***	.1185***
			(.0062)	(.0063)	(.0073)	(.0070)
Any PI or Ep * HIV Severity					-.0959***	-.0825***
					(.0120)	(.0068)
Female		-.0218***	-.0112***	-.0156***	-.0141***	-.0144***
		(.0035)	(.0034)	(.0034)	(.0034)	(.0034)
Black		0.0015	0.0024	0.0028	0.0029	0.0028
		(.0038)	(.0036)	(.0036)	(.0036)	(.0036)
Medicare		-.0095***	0.0028	-0.0035	-0.0043	-0.0040
		(.0034)	(.0033)	(.0033)	(.0033)	(.0033)
Quarters Included	95Q1-96Q4	95Q1-96Q4	95Q1-96Q4	95Q1-96Q4	95Q1-96Q4	95Q1-96Q4
# Observations	20235	20235	20235	20235	20235	20235
Quarter Effects?	Yes	Yes	Yes	Yes	Yes	Yes
R-squared	0.0060	0.0095	0.0393	0.0607	0.0630	0.0629
Age Controls?	No	Yes	Yes	Yes	Yes	Yes
Other Utilization Controls?	No	No	No	Yes	Yes	Yes
# Individuals	4152	4152	4152	4152	4152	4152

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 5: The Heterogeneous Impact of PI-Epivir on Medicaid Expenditures

	All Patients			Dual Eligibles Excluded		
	All	RX Only	IP-OP Only	All	RX Only	IP-OP Only
	(1)	(2)	(3)	(4)	(5)	(6)
Any PI or Epivir	967***	1473***	-505*	381	1039***	-658
	(377)	(225)	(306)	(705)	(365)	(608)
HIV Severity Percentile	5224***	289*	4935***	5332***	451***	4881***
	(596)	(150)	(564)	(675)	(157)	(635)
Any PI or Ep * HIV Severity	-1287**	428	-1715***	-1770*	698	-2468***
	(635)	(350)	(525)	(1074)	(541)	(917)
Female	-676***	-432***	-244	-944***	-449	-495
	(234)	(74)	(222)	(289)	(65)	(281)
Black	124	-358***	483***	332	-398	730***
	(200)	(74)	(186)	(258)	(61)	(252)
Medicare	-458	168	-626**			
	(324)	(119)	(302)			
Medicare * Percentile	-2544***	317	-2862***			
	(595)	(268)	(520)			
Quarters Included	95Q1-96Q4	95Q1-96Q4	95Q1-96Q4	95Q1-96Q4	95Q1-96Q4	95Q1-96Q4
# Observations	19448	19448	19448	12626	12626	12626
Quarter Effects?	Yes	Yes	Yes	Yes	Yes	Yes
R-squared	0.2157	0.3680	0.1480	0.1935	0.3587	0.1299
Age Controls?	No	Yes	Yes	Yes	Yes	Yes
Other Utilization Controls?	No	No	No	Yes	Yes	Yes
# Individuals	4048	4048	4048	3014	3014	3014

The dependent variable in columns 1 and 4 is equal to Medicaid spending in the next quarter. The other columns differentiate between spending on prescription drugs and all other services. Sample in specifications 1, 2, and 3 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. The last three specifications exclude individuals with one or more months of Medicare enrollment. Unit of observation is the person-quarter. All specifications include quarter fixed effects. Standard errors are clustered by individual.



Mortality Rates by Health Status Quintiles in AIDS Sample
18%
16%
14%
12%
10%
8%
6%
4%
2%
0%
% Dying
1994.5
1995
1995.5
1996
1996.5
1997
1997.5
Year and Quarter
Q5
Q4
Q3
Q2
Q1

Summary of Individual-Level Results

- Effect of new treatments on mortality varies across patients
  - Controlling for baseline health status is crucial
  - Sicker patients experience larger reduction in mortality
  - Estimate of 70% is close to RACTs
- Short-term expenditure effects also vary with health status
  - Offset of spending for sickest patients leads to reduction
  - Little utilization to offset for healthy patients
  - Increase in Medicaid spending on dual eligibles

The Impact on Long-Term Medicaid Spending

- Increase in life expectancy has increased time on the program
  - Little evidence of change in exit rate for other reasons (e.g. return to work)
  - Median # eligible months over 6-yr period increased from 21 to 68 from 1994-98
- Quarterly $ declines for those only on Medicaid
- Six-year spending up by 87 percent and median increased by 126 percent
- Misleading estimate of effect on lifetime costs because
  - Censoring (only 6 years considered)
  - Many other factors changing over time
  - Includes individuals not taking PI-Epivir

Estimating the Cost per Life-Year Saved

- Epivir/PI reduced quarterly Medicaid spending
  - From $6636 to $5920 for the median ARV patient not on Medicare
- Increased life expectancy and thus long-term spending increased
  - Reduced mortality rate from 8.3 to 3.2 percent for median ARV patient
- Assuming constant quarterly expenditures & mortality rate and that r=r
  - Present value of Medicaid $ increases from $80,242 to $187,937
  - Life expectancy increases by 4.9 years – approx. $22K per life year saved
  - Little further decline in mortality in 10 years since despite 14 new treatments

Discussion

- Use longitudinal claims data from before and after new treatment introductions
  - Provides a plausibly exogenous source of available treatments
  - Utilization varies over time and across groups
- Can shed light on return to medical innovations – true despite:
  - Limitations of claims data (e.g. no clinical data, other measures of health, etc.)
  - Endogenous treatment decisions
- Effects vary substantially across patients
  - Not "flat of the curve" for this treatment but perhaps for others
- Similar studies rarely done for Medicaid despite $39 billion in RX spending
  - $650 billion total for Medicare + Medicaid – possible to increase programs' efficiency?

Medicaid Spending on Prescription Drugs: 1993-2004

		All Prescription Drugs			HIV Antiretrovirals		
	% of MCD	Total $ (billions)	Scripts (millions)	Cost Per (dollars)	Total $ (billions)	Scripts (millions)	Cost Per (dollars)
1993	8.4%	10.628	343.3	30.96	0.022	0.11	198.23
1994	7.9%	10.758	332.9	32.32	0.018	0.09	198.09
1995	7.4%	11.156	330.1	33.79	0.063	0.27	236.89
1996	8.3%	12.786	339.8	37.63	0.149	0.48	307.31
1997	8.5%	13.653	340.9	40.05	0.384	1.04	370.62
1998	9.4%	15.796	351.3	44.96	0.710	1.99	357.33
1999	10.2%	18.368	368.6	49.83	0.815	2.17	375.41
2000	11.3%	21.929	405.2	54.12	0.878	2.35	373.93
2001	12.6%	27.039	476.9	56.70	0.820	2.11	389.45
2002	12.8%	31.322	524.1	59.76	1.043	2.43	429.59
2003	13.5%	35.501	576.9	61.54	1.221	2.80	435.55
2004	13.7%	38.940	607.2	64.13	1.347	2.93	459.32

Data on Medicaid prescription drug expenditures were obtained from the state drug utilization data on the CMS website at http://www.cms.hhs.gov/MedicaidDrugRebateProgram/. The data on total Medicaid spending was obtained from the publication 2005 CMS Statistics, which is also available on the CMS website at http://www.cms.hhs.gov/MedicareMedicaidStatSupp/.