

# Employees Living with Human Immunodeficiency Virus (HIV): Impact of Disease and Antiretroviral Therapies on Healthcare Costs and Productivity

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## BACKGROUND

- New paradigms of antiretroviral (ARV) treatment have transformed HIV into a chronic disease with near-normal lifespan and social function.
- Possible regimens include "anchor" agents of several classes, such as the protease inhibitors (PI) atazanavir and lopinavir (with ritonavir boosting), or the non-nucleoside reverse transcriptase inhibitor (NNRTI) efavirenz.
- Anchor agents are always used along with "backbone" agents of several classes (DHHS Guidelines)<sup>1</sup>; however, anchors are usually the focus of efficacy and health economic comparisons.
- HIV patients may be employed in the workforce, where the costs of healthcare and productivity losses are the employer's burden through employee benefits.
- Nevertheless, HIV patients are often eager to maintain employment so as to ensure social status and preserve health benefits.
- Employers are the ultimate payers of healthcare for most commercially insured patients and provide more than just salary to their employees.<sup>2</sup>
- Health-related employer contributions include:
  - Medical service and prescription drug coverage.
  - Salary replacement payments for sick leave, short- and long-term disability absences.
- Evidence describing the cost impact of HIV can guide employers to better manage employee patient populations.
- Evidence describing the cost differences of ARV regimens will support rational benefit structures and formulary preferences for employees with HIV.
- Comparative health care and productivity costs associated with ARV anchor regimens utilized in employed HIV populations have not been published to date.

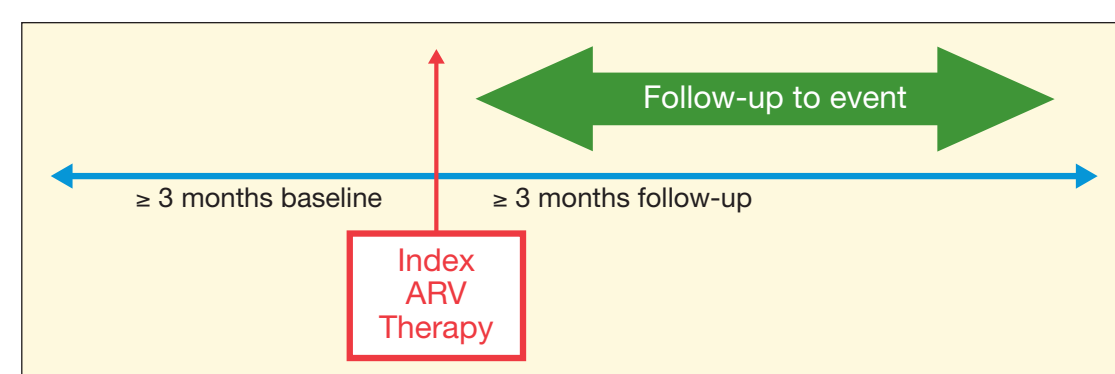
## OBJECTIVES

- Utilize "real world" claims data:
  - To characterize the healthcare costs and productivity of an ARV-treated (HIV-positive) employee cohort compared to an employee cohort not diagnosed with HIV and not treated with ARVs.
  - To examine the healthcare costs by Point of Service (PoS) for patients treated with lopinavir/ritonavir (LPV/r), efavirenz (EFV), or atazanavir/-ritonavir (ATV±RTV) based ARV regimens.
  - To examine productivity losses for patients treated with LPV/r, EFV, or ATV±RTV based ARV regimens.

## METHODS

- A retrospective analysis was performed on data extracted from employers' payroll records and claims originating from the Human Capital Management Services (HCMS) Research Reference Database consisting of over 900,000 employees representing the retail, service, manufacturing, and financial industries.
- Anonymity of person-level data was maintained according to the Health Insurance Portability and Accountability Act guidelines.
- Data were extracted for a post-index analysis of healthcare utilization, costs, and absenteeism (productivity), controlling for pre-index comorbidities and treatments.
- Index date was assigned at the first prescription claim for an identified study regimen.

Figure 1: Study Design



## Study Inclusion

- Employees > 18 years of age at index.
- At least 3 months baseline data prior to index date; at least 3 months follow-up data after index date.
- Patients were eligible for selected analyses only if record structures included those file types, for example, absence time and costs due to: Sick Leave (SL); Short-term Disability (STD); Long-term Disability (LTD); PoS Health Care.

## Study Cohorts

The following two cohorts were extracted:

- ARV Treated: Employees with an initial Rx claim for one of the following ARV study anchors with no claims for any ARV study anchor in the 3 months preceding index or any other study anchor thereafter: LPV/r, EFV, ATV±RTV.
- Non-HIV Controls: Employees without documented HIV<sup>1</sup> and with no claims for ARV therapies of any kind.

\*Patients with claims for multiple study anchors were excluded; <sup>1</sup>Indicated by International Classification of Diseases-9 Clinical Modification codes for HIV/AIDS (ICD-9-CM 042.xx)

Table 1: Study Design

Study Parameter	Description
Time Frame	Data from 2001 through 2nd Quarter 2010
Index Date	<ul style="list-style-type: none"> <li>ARV patients: the date of the 1st prescription claim for a study anchor ARV medication</li> <li>Non-HIV/ARV subjects: the average index date of the ARV subjects</li> <li>Initiation of ARV "backbone" medications was not monitored as part of index.</li> </ul>
Study Outcomes: Events and Costs	Total Healthcare Medical Healthcare by PoS * Physicians Office; Emergency Department; Inpatient (hospital); Outpatient (hospital or clinic); Laboratory; Other Prescription Drug * Study anchor ARVs + Backbone ARVs + All concomitant medications Absenteeism * Sick Leave; Short-term disability; Long-term disability
Study Comparisons	Employee cohorts * Combined study anchor ARV regimen cohort vs. non-HIV cohort * Between ARV treated cohorts defined by study anchor or regimen: LPV/r, EFV, or ATV±RTV
Analysis Data Sets	<ul style="list-style-type: none"> <li>Overall Data Set permitted analysis of all employees meeting study inclusion</li> <li>PoS Data Set (a subset of Overall Data Set) restricted to patients with PoS structured benefit reporting</li> </ul>

## Statistical Analysis

- Differences in descriptive characteristics between the study cohorts were compared using student *t* tests for continuous variables and chi-square tests for discrete variables ( $P < 0.05$  statistically significant).
  - Demographics and job-related variables
  - Charlson Comorbidity Index + Pre-Index Conditions
  - Post-Index ARV agents
- Adjustments for multiple comparisons between ARV cohorts were made using the Tukey-Kramer<sup>3</sup> procedure for continuous variables or the Marascuio<sup>4</sup> procedure for binary variables.
- Two Part Regression models (log link with gamma distribution) were utilized for all event, cost, and absenteeism dependent variables to yield estimates of monthly outcomes for employees:
  - Stage 1: Logistic regression to predict employees with any event/cost
  - Stage 2: Generalized linear models to predict amount of events/cost
- Models controlled for confounding factors, including: age, gender, marital status, race, exempt/nonexempt status, full-time/part-time status, salary, region (by first digit of ZIP code), baseline Charlson Comorbidity Index Score<sup>5</sup>, the number of months of data available, time of index, and baseline comorbidities and AIDS events.<sup>6</sup>

<sup>1</sup>International Classification of Diseases-9 Clinical Modification (ICD-9-CM 042.xx) or CPT-Code events

## Cost Adjustment

Costs were inflation adjusted to constant June 2010 US dollars using the US Bureau of Labor Statistics Consumer Price Index (CPI) factors for medical inflation, drug inflation, and all consumer goods.<sup>6</sup>

Table 2: Overall Data Set: Demographics, Pre-Index Conditions, and Post Index ARV Use

Variable	LPV/r (N=159)	EFV (N=275)	ATV±RTV (N=74)	Non-HIV (N=381,821)
	Mean (S.E.) or Percent	Mean (S.E.) or Percent	Mean (S.E.) or Percent	Mean (S.E.) or Percent
Age (at index date)	41.11 (0.62)	40.36 (0.47)	43.36 (1.02)	41.21 (0.02)
Tenure (at index date)	7.08 (0.53)	5.87 (0.36)	7.23 (0.98)	9.27 (0.01)
Female	21.4%	17.5%	25.7%	43.9%
Married	44.5%	38.4%	43.5%	43.0%
Not married	55.9%	61.5%	56.4%	56.9%
Missing marital status	26.4%	38.2%	18.1%	21.2%
White	27.7%	21.5%	13.5%	41.7%
Black	27.0%	21.1%	23.0%	12.2%
Hispanic	7.5%	8.7%	6.8%	6.4%
Other race	3.8%	2.5%	0.0%	3.9%
Race missing	34.0%	46.2%	56.8%	35.7%
Exempt	27.0%	19.3%	23.0%	32.8%
Full-time	89.9%	96.0%	97.3%	89.8%
Annual salary	\$57,397 (\$4,975)	\$46,096 (\$1,670)	\$48,920 (\$3,794)	\$56,877 (\$134)
Months after Index	18.52 (0.79)	12.06 (0.84)	14.96 (1.59)	20.9 (0.02)
HIV diagnosis claim in study window	82.4%	81.5%	77.0%	0.0%
<b>Pre-Index Conditions</b>				
Modified Charlson Co-morbidity Index	0.26 (0.06)	0.31 (0.05)	0.11 (0.04)	0.08 (0.0)
Pre-index use of HIV-related agents	37.1%	26.2%	29.7%	0.0%
Any pre-index AIDS Health Care Event Diagnoses	11.9%	6.2%	2.7%	0.1%
Any additional conditions in the pre-index period	11.3%	11.6%	8.1%	9.3%
<b>Post-Index Backbone Therapy</b>				
Abacavir	15.7%	16.7%	25.7%	0.0%
Ampranavir	3.8%	1.5%	2.7%	0.0%
Darunavir	1.3%	0.7%	0.0%	0.0%
Didanosine	13.8%	7.3%	8.1%	0.0%
Emtricitabine	27.0%	54.5%	59.5%	0.0%
Etravirine	0.6%	0.70%	0.0%	0.0%
Fosamprenavir	0.0%	1.1%	2.7%	0.0%
Indinavir	1.9%	1.8%	0.0%	0.0%
Lamivudine	49.7%	43.6%	32.4%	0.0%
Neftinavir	2.5%	1.5%	0.0%	0.0%
Nevirapine	6.3%	5.8%	2.7%	0.0%
Raltegravir	1.9%	0.0%	2.7%	0.0%
Saqunavir	1.3%	0.4%	1.4%	0.0%
Stavudine	16.4%	8.7%	4.1%	0.0%
Tenofovir	47.2%	59.3%	68.9%	0.0%
Zidovudine	37.1%	27.3%	13.5%	0.0%

<sup>A</sup> $P < 0.05$  vs. ATV±RTV; <sup>B</sup> $P < 0.05$  vs. Non-HIV Cohort; <sup>C</sup> $P < 0.05$  vs. EFV; S.E.=Standard Error

Table 3: PoS Data Set: Demographics, Pre-Index Conditions, and Post Index ARV Use

Variable	LPV/r (N=102)	EFV (N=218)	ATV±RTV (N=74)	Non-HIV (N=195,956)
	Mean (S.E.) or Percent	Mean (S.E.) or Percent	Mean (S.E.) or Percent	Mean (S.E.) or Percent
Age (at index date)	41.27 (0.91)	40.23 (0.59)	43.36 (1.02)	41.91 (0.02)
Tenure (at index date)	15.15 (0.58)	15.03 (0.35)	7.23 (0.98)	7.87 (0.02)
Female	29.4%	17.0%	25.7%	48.8%
Married	47.7%	39.2%	43.5%	41.3%
Not married	52.1%	60.8%	56.4%	58.6%
Missing marital status	38.2%	45.4%	18.1%	29.7%
White	25.5%	22.0%	13.5%	45.5%
Black	25.5%	21.1%	23.0%	10.4%
Hispanic	9.8%	10.1%	6.8%	8.5%
Other race	4.9%	3.2%	0.0%	5.5%
Race missing	34.3%	43.6%	56.8%	30.2%
Exempt	30.4%	20.2%	23.0%	37.8%
Full-time	93.1%	96.8%	97.3%	95.6%
Annual salary	\$65,037 (\$7,575)	\$45,916 (\$1,982)	\$48,920 (\$3,794)	\$64,522 (\$117)
Months after Index	9.44 (1.17)	13.35 (1.03)	14.96 (1.59)	28.52 (0.03)
HIV diagnosis claim in study window	76.5%	80.7%	77.0%	0.0%
<b>Pre-Index Conditions</b>				
Modified Charlson Co-morbidity Index	0.32 (0.09)	0.33 (0.06)	0.11 (0.04)	0.10 (0.0)
Pre-index use of HIV-related agents	26.5%	23.4%	29.7%	0.0%
Any pre-index AIDS Health Care Event Diagnoses	12.7%	6.4%	2.7%	0.1%
Any additional conditions in the pre-index period	10.8%	11.0%	8.1%	10.5%
<b>Post-Index Backbone Therapy</b>				
Abacavir	10.8%	13.8%	25.7%	0.0%
Ampranavir	1.0%	1.4%	2.7%	0.0%
Darunavir	2.0%	0.9%	0.0%	0.0%
Didanosine	13.7%	5.0%	8.1%	0.0%
Emtricitabine	42.2%	68.8%	59.5%	0.0%
Etravirine	1.0%	0.9%	0.0%	0.0%
Fosamprenavir	0.0%	1.4%	2.7%	0.0%
Indinavir	1.0%	0.9%	0.0%	0.0%
Lamivudine	49.2%	43.4%	32.4%	0.0%
Neftinavir	2.9%	1.4%	0.0%	0.0%
Nevirapine	2.0%	5.0%	2.7%	0.0%
Raltegravir	2.9%	0.0%	2.7%	0.0%
Saqunavir	0.0%	0.0%	1.4%	0.0%
Stavudine	7.8%	3.7%	4.1%	0.0%
Tenofovir	57.8%	71.6%	68.9%	0.0%
Zidovudine	31.4%	19.3%	13.5%	0.0%

<sup>A</sup> $P < 0.05$  vs. ATV±RTV; <sup>B</sup> $P < 0.05$  vs. Non-HIV Cohort; <sup>C</sup> $P < 0.05$  vs. EFV; S.E.=Standard Error

## RESULTS

### Demographics, Pre-Index Conditions, and Post Index ARV Use

#### Overall Data Set:

- Employees using LPV/r had approximately 2-4 times greater pre-index AIDS Event Diagnoses compared to other study anchor cohorts.
- Employees using LPV/r had statistically more severe Charlson Co-morbidity scores at baseline compared to employees in the ATV±RTV and Non-HIV cohorts (Table 2).

#### PoS Data Set:

- Employees using LPV/r had statistically more severe Charlson Co-morbidity scores at baseline compared to employees in the ATV±RTV and Non-HIV cohorts (Table 3).

### Combined Study Anchor ARV Cohorts vs. Non-HIV Cohorts

#### Overall Data Set:

- Employees using ARVs exhibited statistically higher costs for Medical Healthcare, Drugs, "Total Health Cost," and Short-term Disability (Table 4).

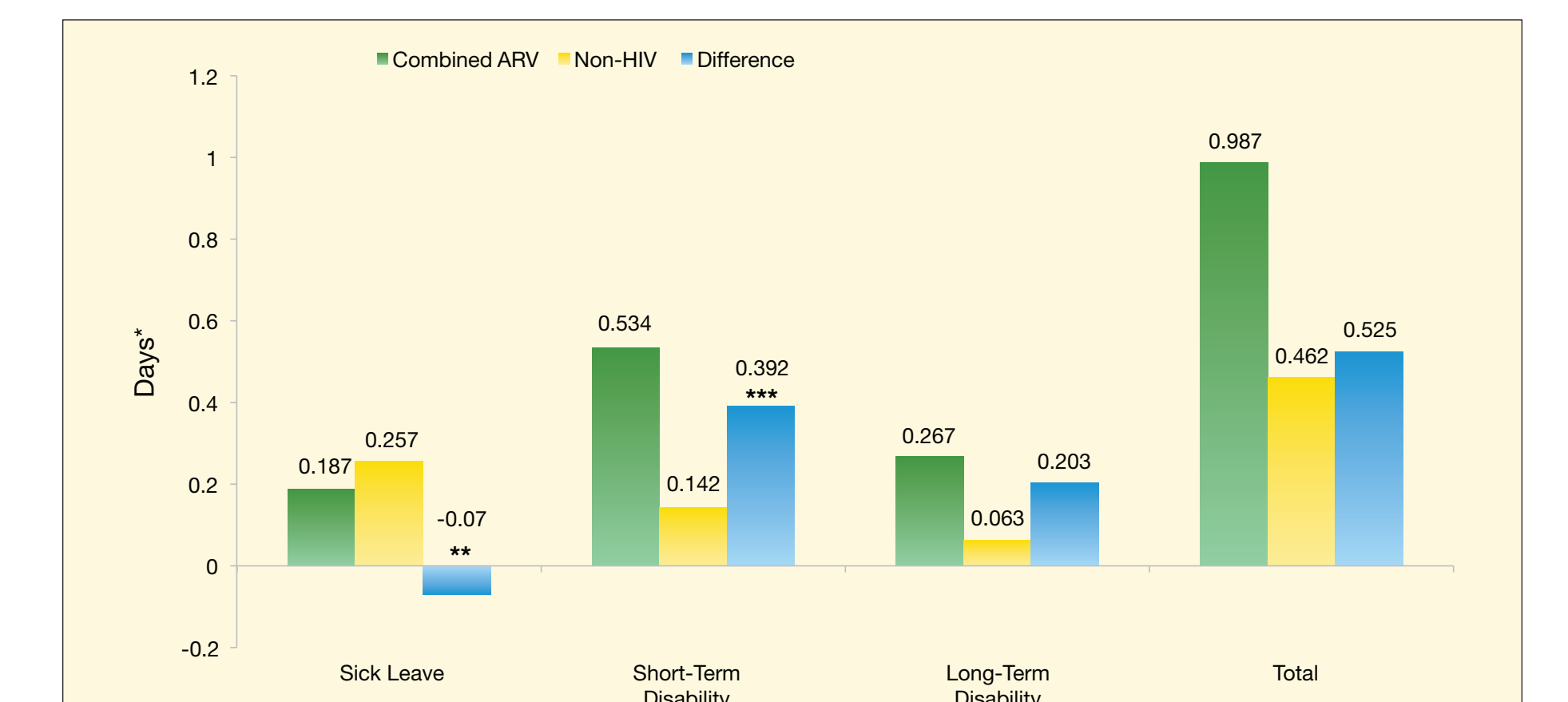
Table 4: Overall Data Set: Adjusted Monthly Health-Benefit Costs, Combined ARV vs. Non-HIV Cohorts

Cost Category	Combined ARV		Non-HIV		Between Cohorts	
	N	Costs*	N	Costs*	Difference	P-Value
Medical Healthcare	508	\$546	381,821	\$241	\$304	<0.0001
Drug (ARV+NonARV)	508	\$1,183	381,821	\$41	\$1,141	<0.0001
Total Health Cost	508	\$1,728	381,821	\$282	\$1,446	<0.0001
Sick Leave	161	\$29	149,241	\$32	(\$3)	NS
Short-term Disability	257	\$55	204,152	\$23	\$32	0.0162
Long-term Disability	345	\$15	276,407	\$4	\$11	NS

\*Regression Adjusted Monthly Costs, in June 2010 US \$; NS= $P > 0.05$

- Employees treated with ARVs used significantly more absence days for Short-term Disability than the non-HIV controls; however, the employees treated with ARVs had lower Sick Leave utilization (Figure 2).

Figure 2: Overall Data Set: Adjusted Monthly Days (Absenteeism), Combined ARV vs. Non-HIV Cohorts



\*Regression Adjusted Monthly Days; NS= $P > 0.05$ ; \*\* $P < 0.004$ ; \*\*\* $P < 0.0024$

#### PoS Data Set:

- The ARV cohort had statistically significantly higher costs at all PoS except the Emergency Department (Table 5).

Table 5: PoS Data Set: Adjusted Monthly Overall Costs, Combined ARV vs. Non-HIV Cohorts

Point of Service Category	Combined ARV (N=394)		Non-HIV (N=195,956)		Between Cohorts	
	Costs*	N	Costs*	N	Difference	P-Value
Physician's Office	\$117	57	\$57	57	\$60	<0.0001
Inpatient Hospital	\$138	94	\$94	94	\$44	0.0441
Outpatient Hospital or Clinic	\$131	73	\$73	73	\$58	<0.0001
Emergency Department	\$12	16	\$16	16	(\$4)	0.0221
Laboratory	\$9	8	\$8	8	<0.0001	
Other	\$10	9	\$9	9	\$1	NS
Drug (ARV+NonARV)	\$1,731	339	\$39	339	\$1,692	<0.0001
Total	\$2,149	3287	\$287	3287	\$1,862	<0.0001

\*Regression Adjusted Monthly Costs, in June 2010 US \$; NS= $P > 0.05$

### Comparison of Study ARV Anchor Cohorts: LPV/r vs. EFV vs. ATV ± RTV

#### PoS Data Set:

- LPV/r and EFV cohorts showed similar costs in all Service Categories.
- Driven by both ARV and Non-ARV drug costs, Total Healthcare costs were significantly greater for the ATV±RTV cohort compared with both the LPV/r and EFV cohorts, although ATV±RTV had lowest Physician Office and Emergency Department costs (Table 6).

Table 6: PoS Data Set: Adjusted Monthly 'Costs' Between Study Anchor Cohorts

Point of Service Category	LPV/r (N=102)	EFV (N=218)	ATV±RTV (N=74)	P-Value Between Cohorts		
	Costs*	Costs*	Costs*	LPV/r vs. EFV	LPV/r vs. ATV±RTV	EFV vs. ATV±RTV
Physician's Office	\$132	\$91	\$117	NS	NS	NS
Inpatient Hospital	\$148	\$82	\$167	NS	NS	NS
Outpatient Hospital or Clinic	\$104	\$123	\$133	NS	NS	NS
Emergency Department	\$17	\$12	\$2	NS	0.0011	<0.0001
Laboratory	\$7	\$8	\$9	NS	NS	NS
Other	\$23	\$3	\$0	NS	0.0447	0.0019
ARV Drug	\$1,205	\$1,174	\$1,489	NS	0.0276	0.0071
Non-ARV Drug	\$163	\$154	\$431	NS	0.0001	0.0001
Total Healthcare	\$1,799	\$1,674	\$2,322	NS	0.009	0.0013

\*Regression Adjusted Monthly Costs, in June 2010 US \$; NS= $P > 0.05$

- LPV/r and EFV cohorts demonstrated similar utilization of services, except ARV Drug category.
- ATV±RTV cohort utilized more Drug (ARV, Non-ARV) services than both the LPV/r and EFV cohorts (Table 7).

Table 7: PoS Data Set: Adjusted 'Number of Services' Between Study Anchor Cohorts

Point of Service Category	LPV/r (N=102)	EFV (N=218)	ATV±RTV (N=74)	P-Value Between Cohorts		
	Services*	Services*	Services*	LPV/r vs. EFV	LPV/r vs. ATV±RTV	EFV vs. ATV±RTV
Physician's Office	2.36	2.26	1.85	NS	NS	NS</