



# A High Risk of Hospitalization Immediately Follows HAART Initiation

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## Abstract

**Background:** HAART decreases long-term morbidity and mortality; however its short term effect on hospitalization rates is unknown.

**Methods:** Hospitalizations among 1329 HAART-naïve subjects in an urban HIV clinic 1997–06 were examined for one year after HAART initiation. Rates were stratified by virologic responders ( $\geq 1$  Log<sub>10</sub> decrease in HIV-1 RNA within 6 months) and non-responders. Multiple negative binomial regression was used to assess factors associated with hospitalization.

**Results:** Responders (n = 965) were less likely than non-responders (n = 362) to be African American (75 vs. 87%, p < 0.001). Through 45 days after HAART, responders' mean hospitalization rate was similar to non-responders' (75.4 vs. 79.4 per 100 person years (PY)) and to pre-HAART rates (figure). Between 45 and 90 days, responders' rate decreased (p < 0.05 vs. baseline). After 90 days it settled near 45 per 100 PY (p < 0.01 both for decrease from baseline and vs. non-responders after 90 days). Findings were unchanged in multiple regression which included calendar time and in which women (IRR 1.39 [1.12, 1.72]), injection drug users (1.46 [1.19, 1.80]) and persons with baseline CD4 <100 cells/ml (2.20 [1.70, 2.84]) had higher rates.

**Conclusions:** For 90 days after HAART initiation, virologic responders remain at comparable hospitalization risk to non-responders and therefore warrant close clinical surveillance. Further studies will need to evaluate causes of hospitalization in this high risk time period.

## Background

In the short term after starting HAART, HIV-infected patients are at risk of immune reconstitution inflammatory syndromes, traditional opportunistic infections, and adverse drug reactions. While HAART decreases morbidity over the long-term, hospitalization risk immediately following initiation is unknown.

Our main objective was to measure the rates of all-cause hospitalizations stratified by virologic response over time in the year after HAART initiation.

## Methods

All HAART naïve patients in the Johns Hopkins HIV Clinical Cohort who initiated HAART 1997–2005 were considered for inclusion. Virologic response was defined as a decrease in HIV-1 RNA of 1 Log<sub>10</sub> or more or suppression below the detectable limit at 6 months after the HAART initiation date.

Hospitalization rates were calculated per 100 person years (PY) for the periods: 180 days prior to HAART initiation and days 1–45, 46–90, 91–180, and 181–365 after HAART. Analysis was performed with Chi<sup>2</sup> and Wilcoxon rank-sum tests and multivariate negative binomial regression using generalized estimating equations to estimate relative rates and standard errors.

TABLE 1. Baseline Characteristics

	Responders N = 965 (%)*	Non-Responders N = 362 (%)*	P
<b>Age at HAART Initiation (years)</b>			
18–29	109 (11.3)	48 (13.3)	<b>0.04</b>
30–39	387 (40.1)	169 (46.7)	
40–49	353 (36.6)	113 (31.2)	
≥50	116 (12.0)	32 (8.8)	
Median (IQR)	39.5 (34, 44.5)	38 (33, 43)	<b>&lt;0.01†</b>
<b>Gender</b>			
Women	328 (34.0)	141 (39.0)	0.09
Men	637 (66.0)	221 (61.1)	
<b>Racial / Ethnic Category</b>			
African American	722 (74.8)	314 (86.7)	<b>&lt;0.001</b>
White	221 (22.9)	42 (11.6)	
Hispanic	7 (0.7)	5 (1.4)	
Asian	4 (0.4)	0	
Other	11 (1.1)	1 (0.3)	
<b>HIV risk factors</b>			
IDU alone	196 (20.3)	89 (24.6)	0.21
IDU-Heterosexual	173 (17.9)	76 (21.0)	
IDU-MSM	41 (4.3)	12 (3.3)	
Heterosexual alone	284 (29.4)	102 (28.2)	
MSM alone	210 (21.8)	62 (17.1)	
Unknown/other	61 (6.3)	21 (5.8)	
IDU (alone or in combination)	410 (42)	177 (49)	<b>0.04</b>
<b>CD4 Count at HAART (cells/mm<sup>3</sup>)</b>			
<50	249 (25.8)	114 (31.5)	0.20
50–199	312 (32.3)	104 (28.7)	
200–349	235 (24.4)	87 (24.0)	
≥350	169 (17.5)	57 (15.8)	
Median (IQR)	156 (46, 297)	148 (29, 282)	0.09 †
<b>HIV-1 RNA at HAART (Log<sub>10</sub> copies/mL)</b>			
<4	174 (18.0)	75 (20.7)	0.32
4–5	372 (38.6)	145 (40.1)	
≥5	419 (43.4)	142 (39.2)	
Median (IQR)	4.9 (4.3, 5.4)	4.8 (4.1, 5.3)	0.08 †
<b>HAART Type</b>			
NNRTI (plus >2 NRTI's)	355 (36.8)	91 (25.1)	<b>&lt;0.001</b>
PI (plus ≥2 NRTI's)	497 (51.5)	230 (63.5)	
PI and NNRTI (plus ≥1 NRTI)	113 (11.7)	41 (11.3)	
<b>Calendar Era of HAART Initiation</b>			
1997–1998	383 (39.7)	217 (59.9)	<b>&lt;0.001</b>
1999–2002	384 (39.8)	105 (29.0)	
2003–2005	198 (20.5)	40 (11.1)	

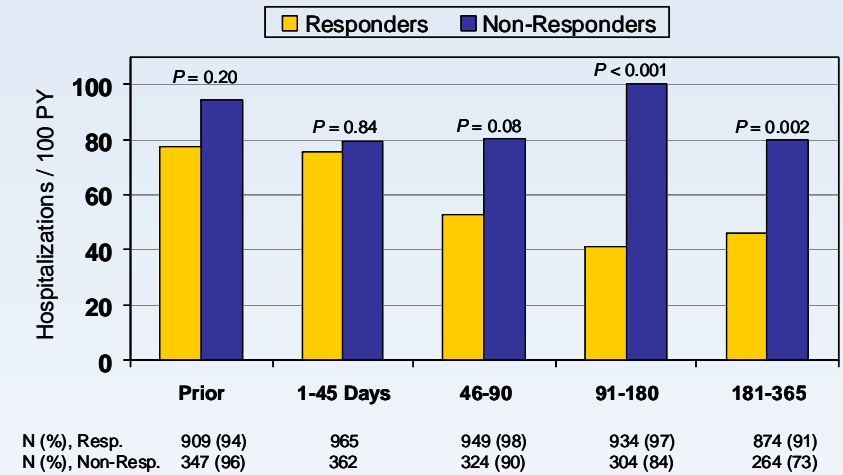
\* Values are Num (%) unless otherwise specified. Statistical comparisons made using Chi<sup>2</sup>-test except † indicates Wilcoxon rank-sum test. IDU, injection drug use; MSM, men who have sex with men; PI, protease inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor.

TABLE 2. Bivariate and Multivariate Relative Hospitalization Rates

	Bivariate Incidence Rate Ratio (95% CI)	P	Multivariate Incidence Rate Ratio (95% CI)	P
<b>Response Status by Time Periods</b>				
<b>Prior 6 mon</b>				
Responders	1.00	Ref	1.00	Ref
Non-Responder	1.22 (0.90, 1.65)	0.20	1.07 (0.80, 1.43)	0.67
<b>Days 1–45 After HAART</b>				
Responders	1.00	Ref	1.00	Ref
Non-Responder	1.05 (0.64, 1.72)	0.84	0.96 (0.59, 1.55)	0.86
<b>Days 46–90</b>				
Responders	1.00	Ref	1.00	Ref
Non-Responder	1.52 (0.95, 2.43)	0.08	1.42 (0.89, 2.28)	0.14
<b>Days 91–180</b>				
Responders	1.00	Ref	1.00	Ref
Non-Responder	<b>2.44 (1.59, 3.76)</b>	<0.001	<b>2.25 (1.48, 3.43)</b>	<0.001
<b>Days 181–365</b>				
Responders	1.00	Ref	1.00	Ref
Non-Responder	<b>1.74 (1.22, 2.48)</b>	0.002	<b>1.58 (1.11, 2.24)</b>	0.01
<b>Age at HAART Initiation (years)</b>				
18–29	1.00	Ref	---	---
30–39	0.98 (0.65, 1.48)	0.92		
40–49	1.18 (0.77, 1.80)	0.45		
>50	1.09 (0.68, 1.75)	0.71		
<b>Women</b>	<b>1.41 (1.14, 1.75)</b>	0.002	<b>1.39 (1.12, 1.72)</b>	0.002
<b>African American</b>	<b>1.86 (1.36, 2.54)</b>	<0.001	1.36 (1.00, 1.86)	0.05
<b>IDU</b>	<b>1.56 (1.25, 1.93)</b>	<0.001	<b>1.46 (1.19, 1.80)</b>	<0.001
<b>CD4 Count at HAART (cells/mm<sup>3</sup>)</b>				
<50	<b>2.80 (2.19, 3.59)</b>	<0.001	<b>2.49 (1.81, 3.42)</b>	<0.001
50–199	<b>1.56 (1.18, 2.06)</b>	0.002	<b>1.44 (1.07, 1.93)</b>	0.02
≥200	1.00	Ref	1.00	Ref
<b>HIV-1 RNA at HAART (Log<sub>10</sub> copies/mL)</b>				
<4	1.00	Ref	1.00	Ref
4–5	1.03 (0.74, 1.44)	0.87	0.88 (0.64, 1.22)	0.45
≥5	<b>1.75 (1.28, 2.40)</b>	<0.001	1.21 (0.85, 1.71)	0.29
<b>HAART Type</b>				
NNRTI (plus ≥2 NRTI's)	1.00	Ref	---	---
PI (plus ≥2 NRTI's)	1.05 (0.84, 1.32)	0.67		
PI and NNRTI (plus ≥1 NRTI)	1.12 (0.80, 1.56)	0.51		
<b>Calendar Era of HAART Initiation</b>				
1997–1998	1.00	Ref	---	---
1999–2002	1.11 (0.88, 1.40)	0.38		
2003–2005	1.05 (0.76, 1.45)	0.76		

--- Indicates not included in multivariate model because bivariate P > 0.20. PI, protease inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor.

Hospitalization Rates by Virologic Response over Time After HAART



## Conclusions

- Hospitalization rate remains high (comparable to the pre-HAART rate) for the first 45 days after HAART initiation for virologic responders and non-responders
- Responders' hospitalization risk falls significantly between 45 and 90 days after initiation until reaching a plateau of 45/100 PY
- In multivariate analysis, non-responders had no statistically significant change in hospitalization rate and had higher rates than responders after 90 days
- The rate of 45/100 PY for responders after 90 days is comparable to the overall hospitalization rate in our clinic population (44/100 PY) over the years in study
- Lower CD4, female sex, and IDU were associated with increased hospitalization risk but age, HAART type and calendar era were not

## Implications

- Providers should maintain close clinical monitoring through at least the first 90 days after HAART initiation
- Future studies should assess changes in diagnoses across time by responder status