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HIV Elite Controllers are Hospitalized More Often Than Persons with Medically Controlled HIV

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Background

- Elite control is characterized by HIV suppression in the absence of antiretroviral therapy (ART)
- Elite control is associated with chronic inflammation, but data on clinical outcomes among elite controllers are scarce
- Chronic inflammation among non-elite controllers is associated cardiovascular and neurologic diseases
- We hypothesized that hospitalization rates and reasons might differ between persons with elite control and medical control of HIV

Methods

- Comprehensive demographic, laboratory, treatment and hospitalization data extracted from clinical records of patients engaged in outpatient care at 11 HIV Research Network (HIVRN) sites in 2005-2011
- Person-years excluded if they contained two consecutive CD4 measurements <350 cells/mm^3 or any CD4 <200 cells/mm^3
- HIV control status categorized for each remaining person-year
  - **Medical control**: ≥3 undetectable HIV-1 RNA values over ≥12 months in the presence of ART, with subsequent blips <1000 copies/mL allowed if <50% of measurements
  - **Elite control**: ≥3 undetectable HIV-1 RNA values over ≥12 months in the absence of ART, with subsequent blips <1000 copies/mL allowed if <50% of measurements
  - **Low viremia**: all HIV-1 RNA <1000 copies/mL, but not satisfying other criteria for medical or elite control
  - **High viremia**: any HIV-1 RNA ≥1000 copies/mL
- Negative binomial regression used to assess hospitalization rates by HIV control status and adjust for covariates
- Reasons for admission determined by primary ICD-9 codes and grouped into diagnostic categories using modified Clinical Classification Software (AHRQ)

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Table 1. Demographic and Clinical Characteristics at Study Entry by HIV Control Status

Characteristic	Medical Control N=4,704(%)	Elite Control N=149 (%)	Low Viremia N=7,975 (%)	High Viremia N=10,635 (%)
Age, 18-34 years	607 (13)	21 (14)	1544 (19)	3698 (35)
35 – 49	2619 (56)	76 (51)	4293 (54)	5075 (48)
50 – 64	1359 (29)	49 (33)	1968 (25)	1737 (16)
≥ 65	119 (2)	3 (2)	170 (2)	125 (1)
Race, White	1569 (33)	35 (24)	2391 (30)	2751 (26)
Black	1922 (41)	87 (58)	3367 (42)	5344 (50)
Hispanic	1096 (23)	25 (17)	1965 (25)	2244 (21)
Male	3502 (74)	74 (50)	5953 (75)	7430 (70)
HIV risk factor, Heterosexual	1698 (36)	59 (40)	2754 (34)	4086 (38)
MSM	2084 (44)	39 (26)	3609 (45)	4378 (41)
IDU	781 (17)	45 (30)	1241 (16)	1718 (16)
Other/unknown	141 (3)	6 (4)	371 (5)	453 (4)
CD4 count, 200-350 cells/mm^3	345 (7)	1 (1)	829 (10)	1647 (16)
351-500	2194 (47)	19 (13)	3028 (38)	4061 (38)
501-750	1409 (30)	45 (30)	2669 (34)	3360 (32)
>750	756 (16)	84 (56)	1449 (18)	1567 (15)
Insurance, Private	686 (15)	18 (12)	1160 (15)	1315 (12)
Medicaid	1313 (28)	69 (46)	2827 (35)	3592 (34)
Medicare/Dual eligible	996 (21)	12 (8)	1199 (15)	1086 (10)
Ryan White/Uninsured	1492 (32)	46 (31)	2537 (32)	4141 (39)
Unknown	217 (5)	4 (3)	252 (3)	501 (5)

Figure 1. Unadjusted All-Cause Hospitalization Rates by HIV Control Status

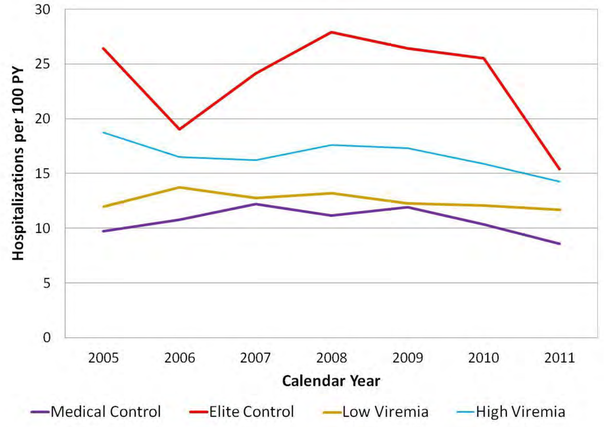
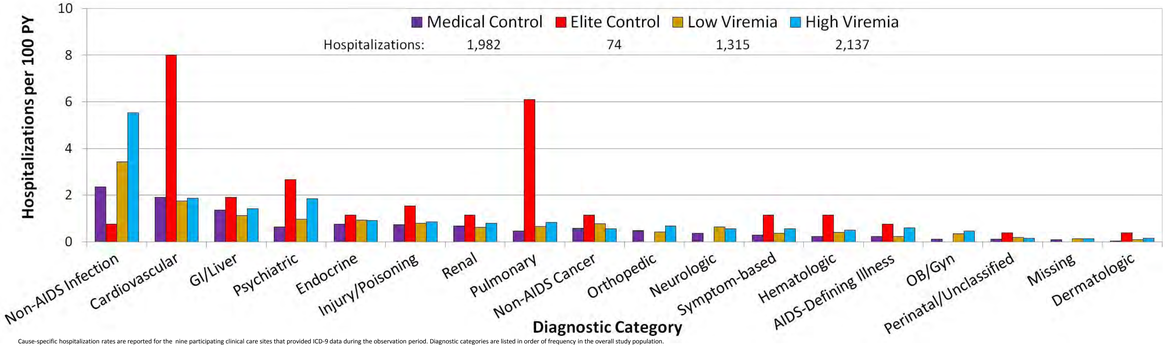


Figure 2. Cause-Specific Hospitalization Rates by HIV Control Status



Cause-specific hospitalization rates are reported for the nine participating clinical care sites that provided ICD-9 data during the observation period. Diagnostic categories are listed in order of frequency in the overall study population.

Table 2. Multivariable Analysis of Risk Factors for Hospitalization

Characteristic	Adjusted IRR (95% CI)
HIV control status, Medical control	1.0 (Ref)
Elite control	**1.66 (1.12-2.47)**
Low viremia	**1.29 (1.18-1.40)**
High viremia	**1.65 (1.51-1.80)**
Age, 18 -34 years	1.0 (Ref)
35-49	1.08 (0.97-1.21)
50-64	**1.40 (1.24-1.58)**
≥65	**2.32 (1.90-2.83)**
Race, white	1.0 (Ref)
Black	1.03 (0.93-1.15)
Hispanic	**0.84 (0.74-0.95)**
Gender, male	1.0 (Ref)
Female	**1.35 (1.22-1.49)**
HIV risk factor, Heterosexual	1.0 (Ref)
MSM	0.89 (0.79-1.00)
IDU	**1.39 (1.24-1.55)**
CD4 count, >750 cells/mm^3	1.0 (Ref)
501-750	**1.17 (1.08-1.28)**
≤500	**1.33 (1.21-1.46)**
Insurance, Private	1.0 (Ref)
Medicaid	**2.14 (1.88-2.44)**
Medicare/Dual eligible	**2.15 (1.87-2.48)**
Ryan White/Uninsured	1.14 (0.99-1.30)
Calendar year, 2005	1.0 (Ref)
2006	1.01 (0.90-1.13)
2007	1.03 (0.92-1.16)
2008	1.04 (0.92-1.16)
2009	1.04 (0.93-1.17)
2010	0.94 (0.84-1.05)
2011	**0.85 (0.76-0.95)**

IRR: incidence rate ratio; MSM: men who have sex with men; IDU: injection drug use
Model also included categorical indicator for clinical care site to control for site-specific variability in hospitalization rates. Results in **bold** are statistically significant (p≤0.05).

Conclusions

- Elite control is associated with higher risk of hospitalization than is medical control of HIV
- Cardiovascular and pulmonary diseases are the most common reasons for hospitalization among elite controllers
- Non-AIDS-defining infections are an uncommon reason for hospitalization among elite controllers

Strengths & Limitations

- Study includes one of the largest reported samples of elite controllers
- Selection bias may contribute to higher utilization by elite controllers who are engaged in care as compared to elite controllers not captured in our study
- ICD-9 codes may inaccurately describe hospitalization cause
- Hospitalizations may be incompletely captured

Implications

- Studies are needed to determine the reasons for high hospitalization rates among elite controllers, including the contribution of chronic immune activation and inflammation
- Whether ART and/or anti-inflammatory agents reduce hospitalization risk among elite controllers should be investigated prospectively
- The high rate of cardiovascular hospitalizations among elite controllers is consistent with studies showing increased risk of atherosclerosis