

Association between Partial Adherence to Antiretroviral Therapy and Hospitalization Risk in an HIV Population

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Background

- Patients with HIV have a range of treatment options including three FDA approved single tablet regimens and several multi-pill drug regimens
- While all regimens are vulnerable to the consequences of missed doses, an intrinsic difference of a once daily single table regimen (STR) in HIV treatment is preventing partial adherence e.g. taking some but not all components in a regimen
- Several studies have evaluated overall adherence to antiretroviral therapy^{1,2,3,4}
- We are unaware of any study that evaluated the impact on partial and complete adherence associated with STRs compared with other regimens

Objectives

- To explore the frequency of partial adherence among commercially insured patients treated with different non-STR multi-pill HAART
 - Multi-pill HAART included regimens with NRTIs plus a boosted protease inhibitor (boosted PI), raltegravir, or a non-nucleoside reverse transcriptase inhibitor (NNRTI)
- To examine the impact of partial adherence and other factors on hospitalization rates

Methods – Data Source

- Retrospective analysis of medical and pharmacy claims from a large commercially insured population of treated HIV patients in the US (LifeLink database)
- Information was available on patient diagnoses, dates of service, place of service, therapeutic procedures, and prescriptions filled

Methods – Patient Selection

- Patients were required to meet the following selection criteria:
 - An HIV diagnosis (International Classification of Diseases, 9th Edition, Clinical Modification [ICD-9-CM] code 042.xx) between January 1, 2009 and December 31, 2011
 - Receipt of a complete HAART (i.e., 2 NRTIs plus a third agent consisting of an NNRTI, PI, or II) for at least 90 days as a STR or as 2+ tablets per day between June 1, 2009 and December 31, 2011
 - At least 6 months of continuous benefits eligibility before the later of either initiation of the complete HAART regimen or June 1, 2009

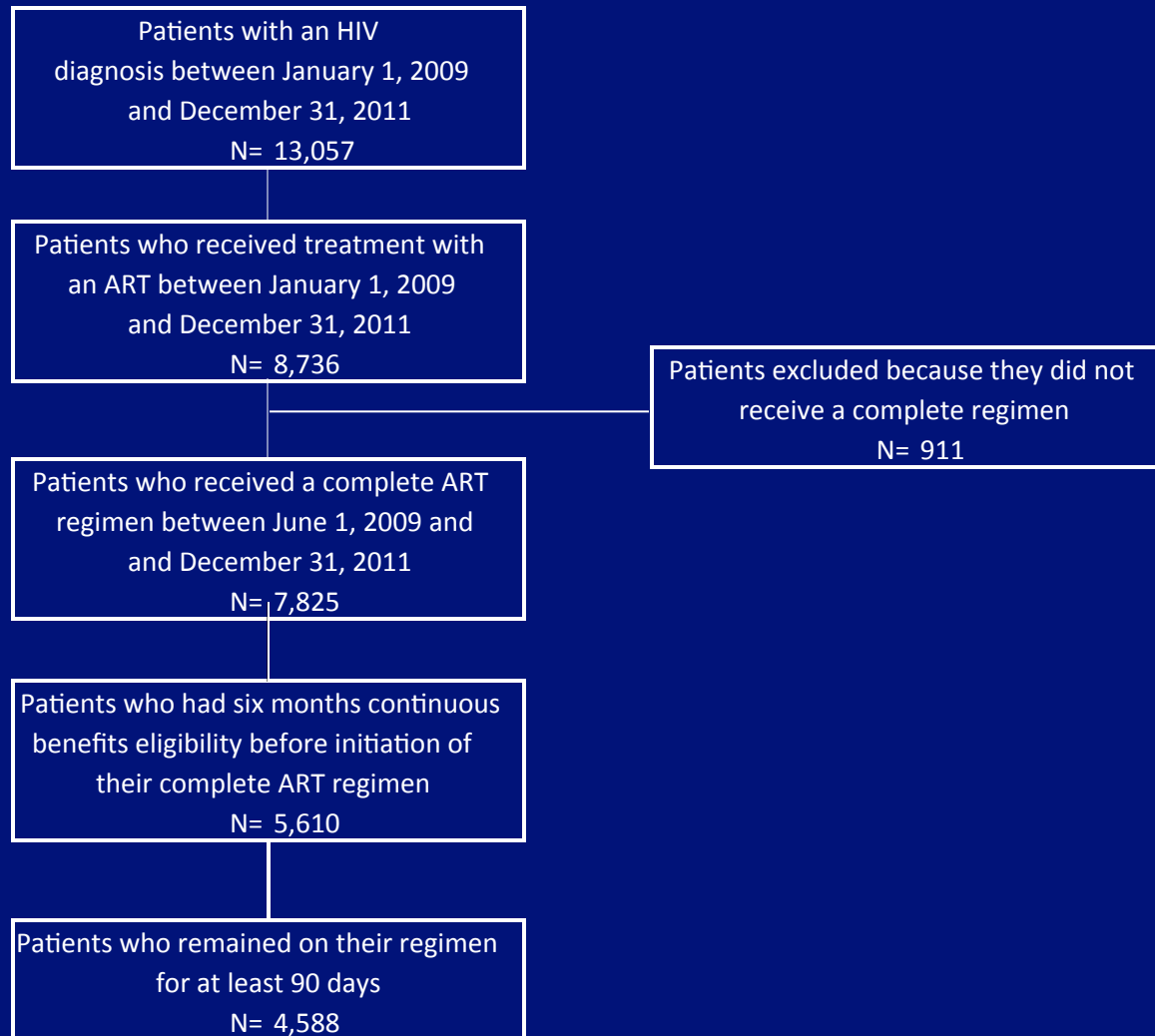
Methods – Study Measures

- All study measures were observed from ART initiation to discontinuation of the entire regimen, switching of third component classes, or end of the database
- Adherence was reported as the percent of days (using pharmacy refill data) that the patient had:
 - A complete regimen - all components of the regimen
 - A partial regimen - some but not all components
 - Complete non-adherence - no components available
- Number and percentage of patients with a hospitalization

Methods – Data Analysis

- Descriptive analyses of all outcomes were reported by third component class received
- Logistic regression models were estimated to assess hospitalization risk
 - Independent covariates included complete and partial adherence, demographics, and prior ART experience
 - Dependent variable was a binary indicator for whether or not the patient had at least one hospitalization

Sample Population



Patient Characteristics

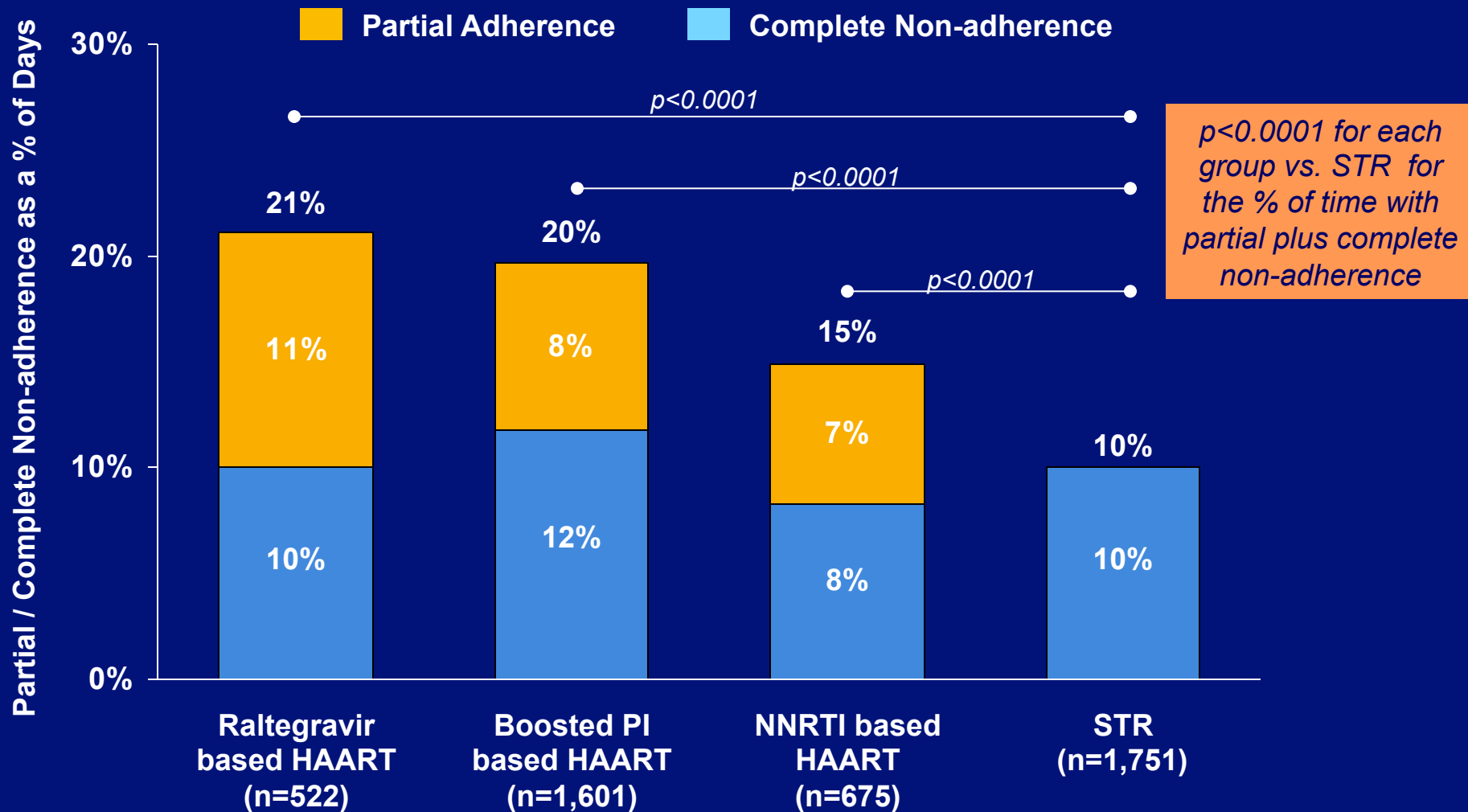
Characteristic	Raltegravir Based HAART	Boosted PI Based HAART	NNRTI Based HAART	STR
Total sample (N)	522	1,601	675	1,751
Mean (SD) age	47.1 (9.4)	45.9 (10.1)	48.0 (9.6)	44.4 (10.3)
Male	82.6%	79.7%	83.9%	84.2%
Geographic region				
East	4.4%	4.6%	4.9%	5.8%
South	45.4%	43.1%	41.2%	46.3%
Midwest	21.1%	21.0%	21.0%	24.7%
West	29.1%	31.3%	32.9%	23.2%
Treatment naïve at index	16.3%	13.9%	7.6%	26.7%
Mean (SD) length of benefits eligibility post-index	457 days (239)	566 days (237)	584 days (241)	554 days (252)
Concomitant conditions				
Mental disorders	25.1%	19.4%	16.7%	17.8%
Drug or alcohol abuse	10.2%	10.1%	5.0%	7.3%

Summary of Adherence to Complete ART Regimens

Adherence	Raltegravir Based HAART (N=522)	Boosted PI Based HAART (N=1,601)	NNRTI Based HAART (N=675)	STR (N=1,751)
ART regimen duration				
Mean (SD) days	389 (231)	487 (252)	523 (255)	488 (256)
Adherence to ART regimen (as a % of ART duration)				
All ART medications available (SD)	78.9% (24.9%)	80.4% (19.4%)	85.0% (17.1%)	90.0% (9.8%)
Only part of ART medications available (SD)	11.1% (21.7%)	7.87% (14.1%)	6.63% (13.0%)	0.0% (0.0%)
No ART medications available (SD)	10.0% (13.1%)	11.8% (13.1%)	8.3% (10.7%)	10.0% (9.8%)
Days with only part of ART medications available (SD)	42 (92)	36 (70)	36 (78)	---
Days with no ART medications available (SD)	34 (51)	52 (61)	40 (52)	45 (48)

Patients receiving STR had the highest percentage of days in possession of a complete ART regimen. While days with no ART medications was similar across all regimens, patients with non-STR regimens also had days with only part their ART medications.

Partial and Complete Non-Adherence to ART



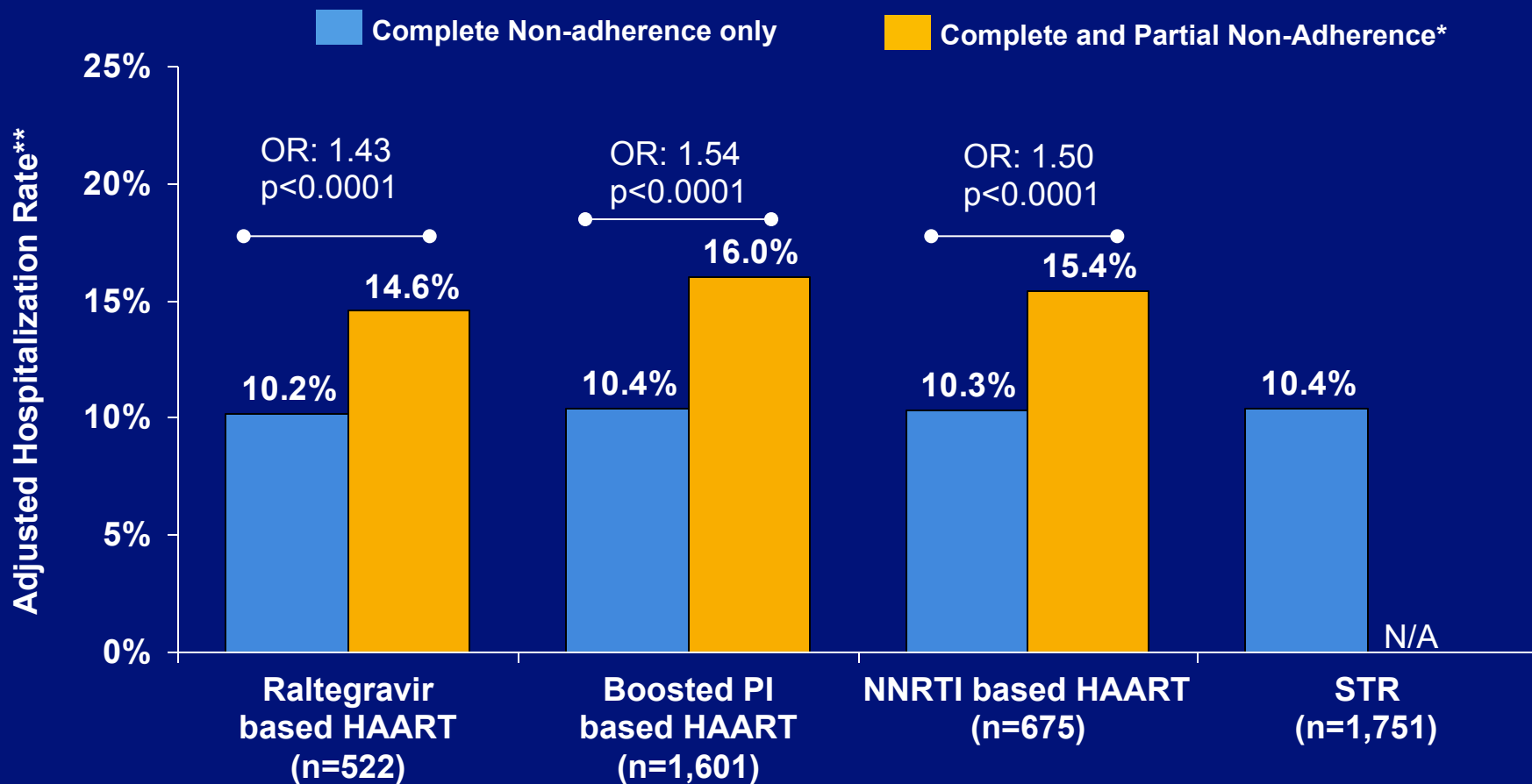
Logistic Regression Results Assessing Partial and Complete Non-Adherence and Risk of Hospitalization

Variable	Odds Ratio	P-Value	Lower 95% CI	Upper 95% CI
Partial adherence (vs. less than 20 days)				
20 to 40 days	1.497	0.0183	1.071	2.094
40 to 60 days	1.687	0.0215	1.08	2.636
Greater than 60 days	1.574	0.0009	1.204	2.058
Complete non-adherence (vs. less than 20 days)				
20 to 40 days	1.481	0.0025	1.149	1.91
40 to 60 days	1.492	0.0078	1.111	2.003
Greater than 60 days	1.946	<.0001	1.527	2.481
Treatment naïve at index	1.512	0.0009	1.185	1.93
Age (vs ≥ 65)				
Less than 35	0.363	0.0003	0.209	0.631
35-44	0.411	0.0005	0.25	0.676
45-54	0.492	0.0038	0.305	0.795
55-64	0.853	0.5262	0.522	1.394

Additional covariates included geographic location, plan and payer types

The risk of a hospitalization increased with partial and complete non-adherence to any HAART regimen. Additional significant risk factors included being treatment naïve, and age 65 or more.

Association of Adherence Rates and Rate of Hospitalization



Patients with complete and partial non-adherence to their medication were significantly more likely to be hospitalized than to patients with complete non-adherence only.

* Partial Adherence: Patients with at least 5% of days with either no NRTIs or no 3rd agents.

** Adjusted for differences between groups including complete non-adherence, treatment status at index, age, geographic location, plan and types.

Limitations

- Adherence was measured based on filled prescriptions, not the number of tablets ingested.
- There are no lab test results available to assess the impact of the different patterns of adherence observed on laboratory values of response.
- As these are observational data, patients are not randomized to the different treatments. We cannot exclude unmeasured confounding factors that influenced observed outcomes.
- A proportion of HIV treated patients (10.4%) were excluded from the analysis due to receiving incomplete ART regimens

Conclusions

- These data demonstrate that non-STR combinations have *twice the risk* of incomplete daily dosing vs. an STR
 - Patients on an STR had significantly better complete adherence to their HIV regimen
 - The risk of complete non-adherence is similar across regimens – supporting the similarity of the populations getting each type of regimen
- However – the *additional* risk for partial adherence is *only* seen with non STRs
 - This risk is in addition to the risk associated with complete non-adherence
 - Partial adherence was observed with all multi-pill non-STR regimens
- Partial adherence was associated with an additional statistically significant risk of hospitalization *in addition to* the risk associated with complete non-adherence
 - Additional risk of hospitalization ranged from 43 – 54%
- These data support the use of STRs to prevent the occurrence of partial adherence, and suggest a potential approach to prevent the adverse consequences associated with partial adherence

References

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