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Association of Partial Adherence to Antiretroviral Therapy with Hospitalizations and Healthcare Costs 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 in a Medicaid population

Objective

- To explore the frequency of partial adherence among United States Medicaid patients treated with different HAART regimens
  - 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 on hospitalization rates and healthcare costs

Methods

- Retrospective analysis of medical and pharmacy claims from Medicaid enrollees with HIV from multiple states (MarketScan Medicaid Multi-State Database)
- Information was available on patient diagnoses, dates of service, place of service, therapeutic procedures, and prescriptions filled

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

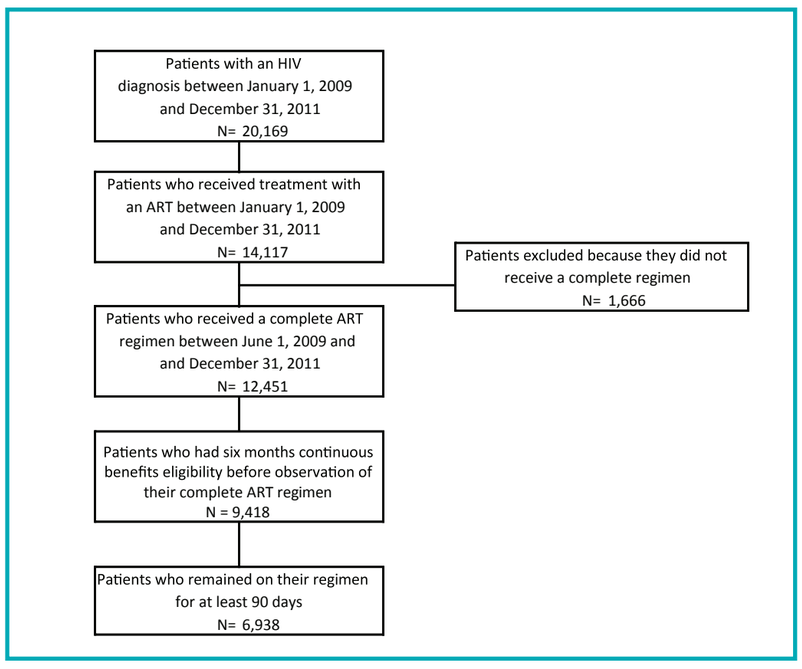
Study Measures

- 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 ART regimen - all components of the regimen
  - A partial regimen - some but not all components
  - No components available
- Number and percentage of patients with a hospitalization
- Average all-cause monthly costs

Data Analysis

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

Figure 1. Sample Population



Results

Table 1. Patient Characteristics

Characteristic	Raltegravir Based HAART	Boosted PI Based HAART	NNRTI Based HAART	STR
Total sample (N)	729	3,556	775	1,878
Mean (SD) age	44.6 (10.6)	43.2 (12.2)	47.5 (11.4)	43.8 (10.9)
Male	51.6%	50.1%	50.6%	52.5%
Race				
White	26.8%	19.1%	23.5%	24.3%
Black	60.1%	68.5%	64.1%	65.0%
Hispanic	1.9%	1.3%	1.2%	0.8%
Other/missing/unknown	11.3%	11.2%	11.2%	9.9%
Treatment naïve at index	13.6%	19.5%	8.3%	22.6%
Mean (SD) length of benefits eligibility post-index	379 days (220)	471 days (248)	503 days (251)	429 days (248)
Concomitant conditions				
Mental disorders	33.3%	29.4%	26.7%	24.5%
Drug or alcohol abuse	23.5%	22.3%	17.6%	18.9%

Table 2. Summary of Adherence to Complete ART Regimens

Adherence	Raltegravir Based HAART (N=729)	Boosted PI Based HAART (N=3,556)	NNRTI Based HAART (N=775)	STR (N=1,878)
ART regimen duration				
Average days (SD)	314 (202)	391 (246)	440 (255)	363 (239)
Adherence to ART regimen:				
Partial adherence				
% of ART duration (SD)	12.1% (21.0)	6.6% (12.9)	6.9% (12.8)	0.0% (--)
Non adherence				
% of ART duration (SD)	14.0% (15.9)	15.5% (15.1)	13.5% (16.4)	14.3% (13.0)
Overall adherence				
% of ART duration (SD)	73.9% (25.8)	77.9% (19.7)	79.6% (20.9)	85.7% (13.0)

Figure 2. Percentage of Time with Complete and Partial Adherence, by Cohort

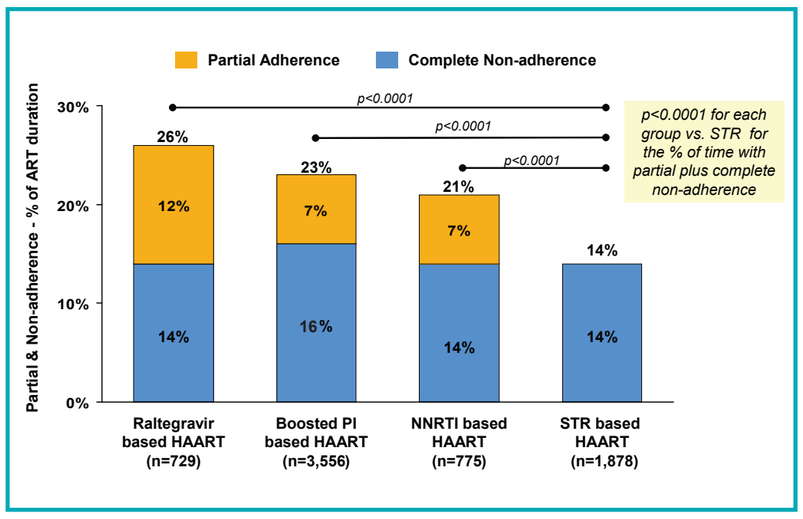
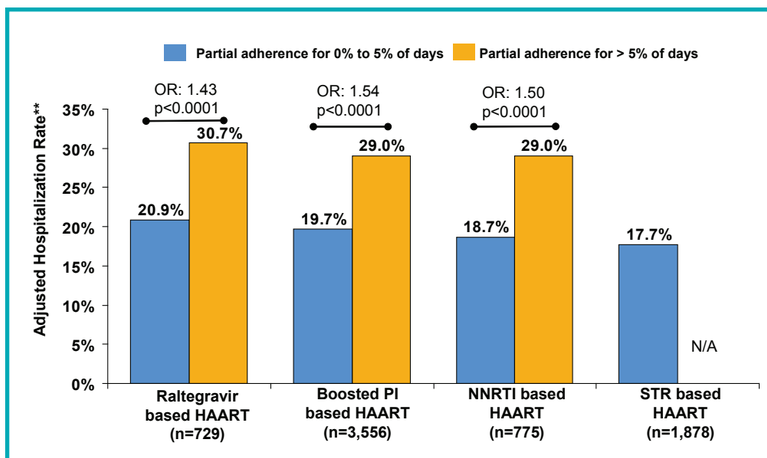


Table 3. Logistic Regression Results Assessing Partial and Complete Non-Adherence and Risk of Hospitalization

Variable	Odds Ratio	Lower 95% CI	Upper 95% CI	P-value
Partial adherence (vs. 0 to 10 days)				
10 to 20 days	1.056	0.791	1.411	0.7107
20 to 30 days	1.341	1.019	1.765	0.0361
30 to 40 days	1.612	1.164	2.232	0.0041
40 to 50 days	1.713	1.173	2.501	0.0053
Greater than 50 days	1.743	1.453	2.090	<0.0001
Complete non-adherence (vs. 0 to 10 days)				
10 to 20 days	1.249	0.995	1.568	0.0553
20 to 30 days	1.450	1.142	1.843	0.0023
30 to 40 days	1.478	1.155	1.892	0.0019
40 to 50 days	1.838	1.434	2.356	<0.0001
Greater than 50 days	1.995	1.658	2.401	<0.0001
Concomitant mental disorder (vs. no concomitant mental disorder)	1.449	1.268	1.655	<0.0001
Concomitant drug/alcohol abuse (vs. no concomitant drug/alcohol abuse)	2.361	2.052	2.717	<0.0001
Age (vs. ≥ 65)				
Less than 35	0.298	0.176	0.505	<0.0001
35-44	0.438	0.261	0.733	0.0017
45-54	0.575	0.346	0.957	0.0334
55-64	0.78	0.464	1.309	0.3462

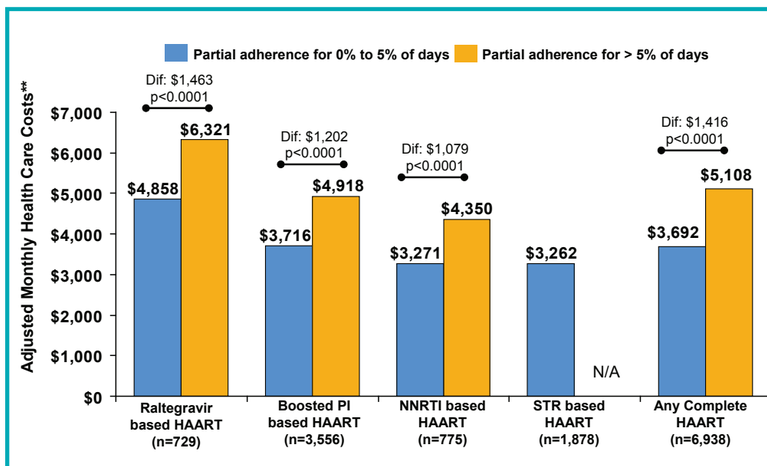
Additional covariates included race, gender, treatment naïve vs. experienced status, regimen length, and third component

Figure 3. Association of Partial Adherence Rates and Adjusted Rate of Hospitalization



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, and plan types.

Figure 4. Association of Partial Adherence and Adjusted Monthly Health Care Costs



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, and plan 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 (13.4%) were excluded from the analysis due to receiving incomplete ART regimens

Conclusions

- **These data demonstrate that non-STR combinations have *at least 1.5 times 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%**
- **Partial adherence was associated with a 38% increase in health care costs compared to patients who had partial adherence for less than 5% of follow-up**
- **These data support the use of STRs to prevent the occurrence of partial adherence, and supports complete adherence and suggest a potential approach to prevent the adverse consequences associated with partial adherence**

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