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

C Cohen[1], KL Davis[2], JL Meyers[2]

[1]Community Research Initiative of New England, Boston, MA
[2]RTI Health Solutions, Research Triangle Park, NC

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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



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# 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



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# 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



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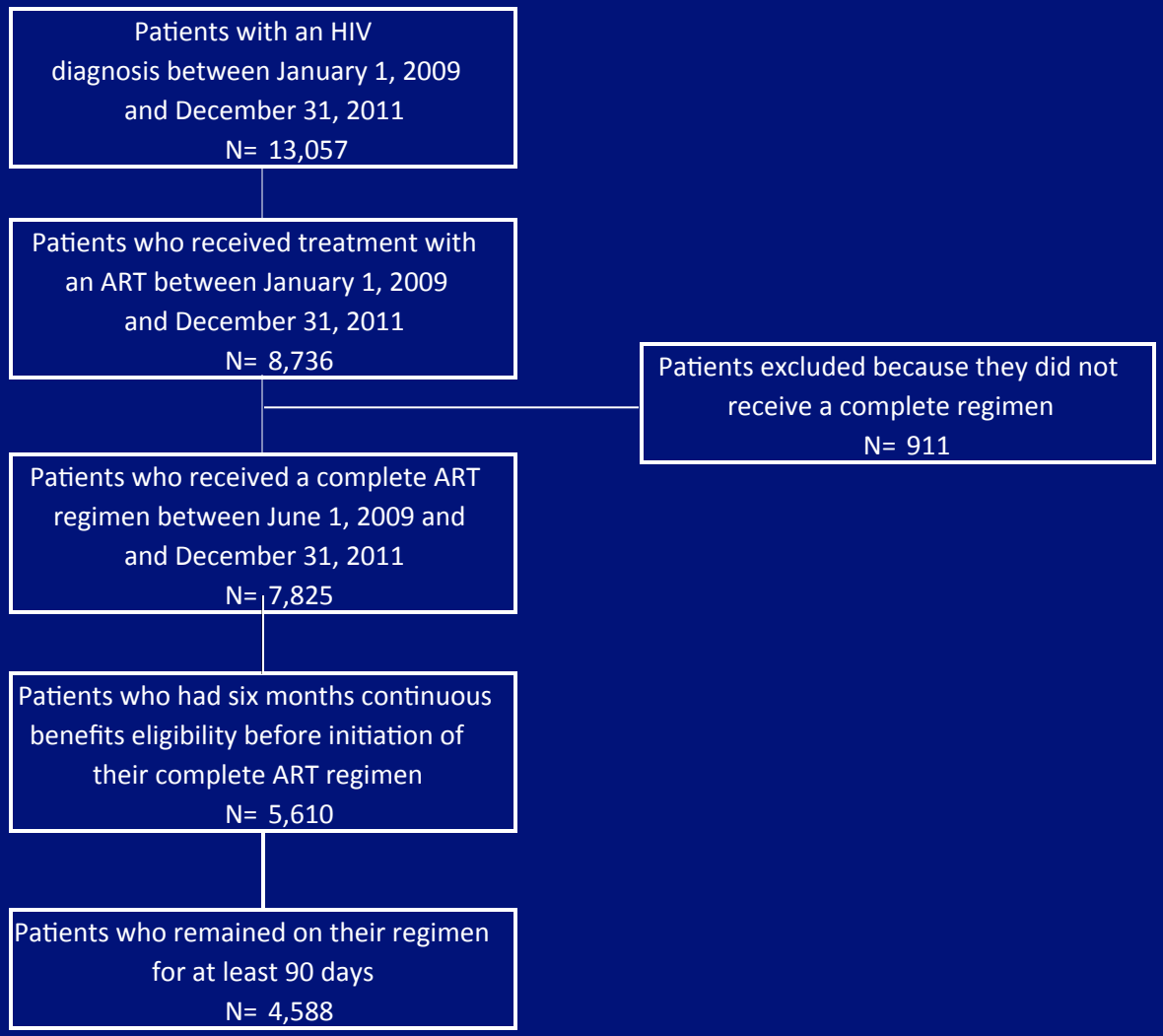
# Methods – Study Measures

- 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

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# 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% |

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# 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 ATR 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.



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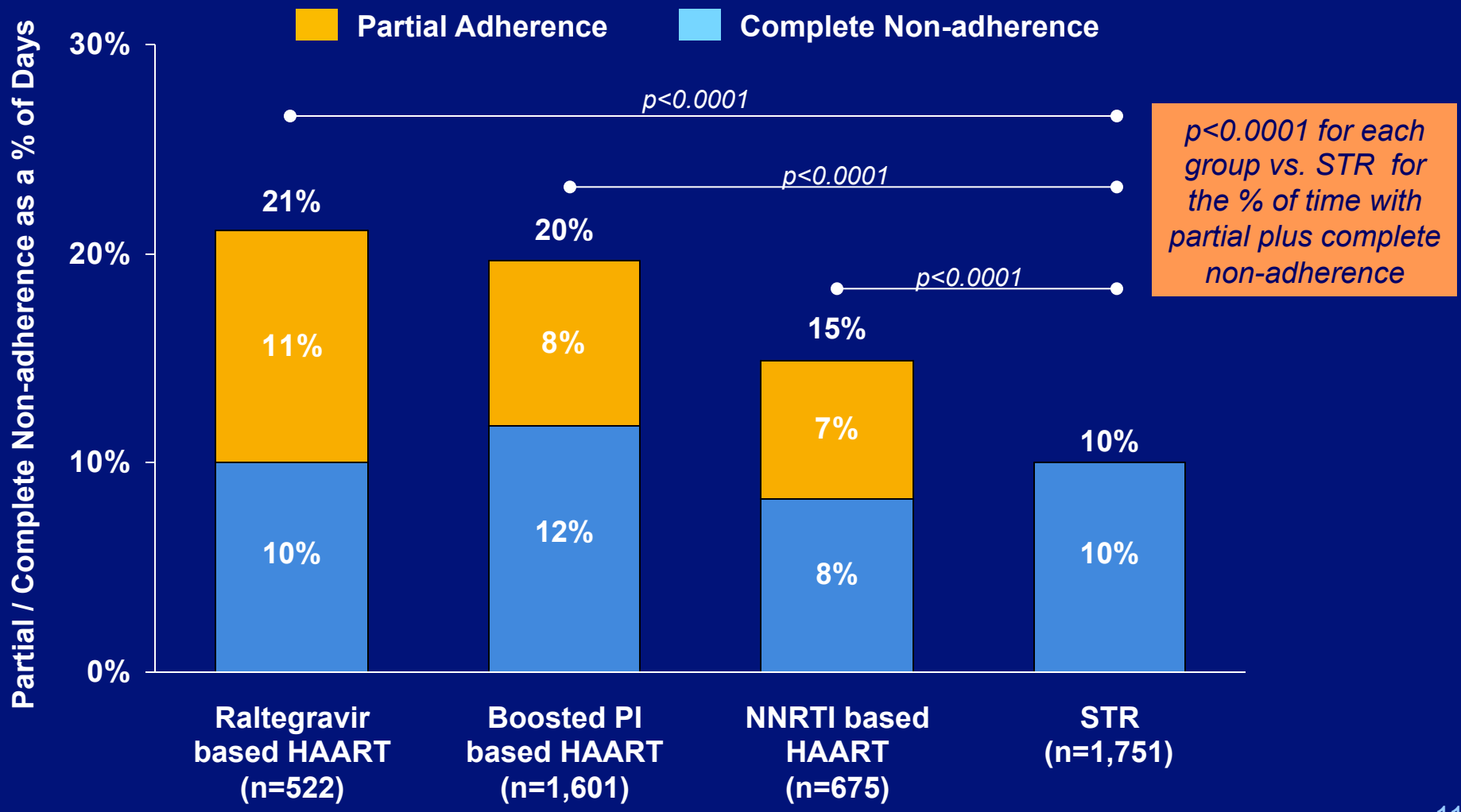
# Partial and Complete Non-Adherence to ART

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# 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.**



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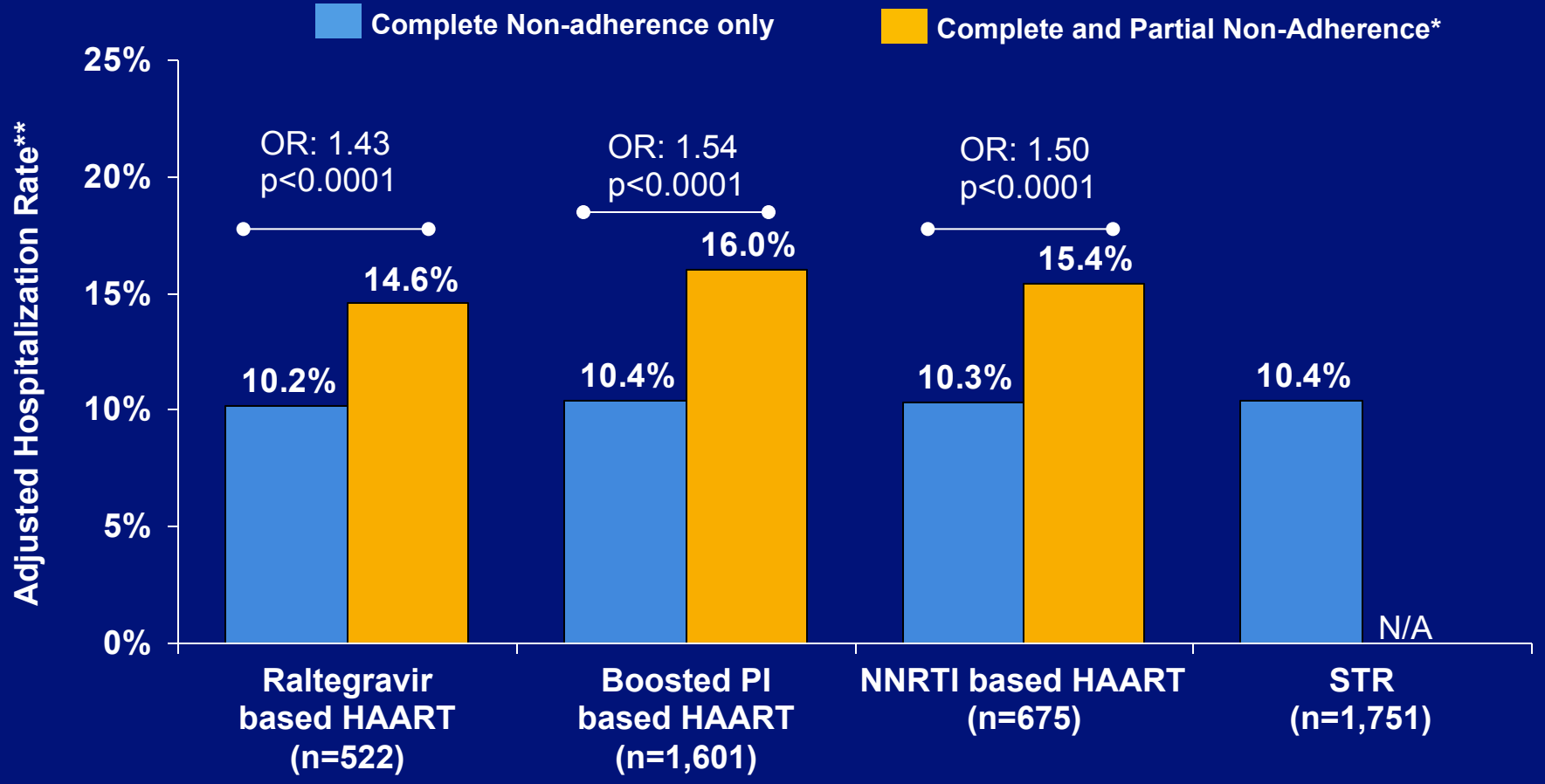
# Association of Adherence Rates and Rate of Hospitalization




**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.**

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* 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



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