

# Association between Daily Antiretroviral Pill Burden and Hospitalization Risk in a Medicaid Population with HIV

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## Background

- Patients with HIV are often treated with 3 or more antiretroviral agents in complex, multi-pill drug regimens.
- Previous studies have found that a high daily pill burden is associated with a decrease in adherence to antiretroviral treatment (ART)<sup>1-3</sup>
- Additionally, prior studies have evaluated the adherence impact of fixed-dose combinations (FDCs) that consolidate ART into 1 pill per day.<sup>4,6</sup> These studies have shown that ART as a once daily single tablet regimen (STR) significantly improves patient adherence and virologic outcomes.

## Objective

- This study explored whether the adherence effect of STR also mediates better downstream outcomes, specifically hospitalization risk in patients who received a STR versus 2 or more tablets per day (2+ TPD).

## Methods

### Data Source – MarketScan Medicaid Multi-State Database

- Includes detailed information about hospitalizations, diagnoses, therapeutic procedures, physician services, and prescriptions for 26 million Medicaid enrollees from multiple states.
- Patients tracked longitudinally via de-identified, unique patient numbers.
- Lab data on viral load and CD4 count were not available.

### Study Populations

- Patients were selected for inclusion in this analysis if they met the following criteria:
  - Had a diagnosis of HIV/AIDS (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code 042.xx) between 1/1/2005 and 12/31/2009.
  - Received a complete ART regimen, defined as 2 nucleoside/nucleotide reverse transcriptase inhibitors (NRTI) along with a third agent (i.e., a nonnucleoside/nucleotide reverse transcriptase inhibitor [NNRTI], protease inhibitor, CCR5 antagonist, or integrase inhibitor).
    - The date on which patients initiated their first-observed complete ART regimen defined the study index date.
    - Patients were required to remain on their index regimen for at least 60 days.
  - Had at least 60 days of post-index and 6 months pre-index Medicaid enrollment.
- Patients were grouped in the following cohorts according to their overall ART daily pill count:
  - Single tablet regimen (STR): patients who received a single tablet regimen at any point in time.
  - 2 or more tablets per day (2+ TPD): patients who received a 2 tablet per day regimen at any point in time without ever receiving a STR
- Patients were followed from their regimen index date to the earliest date of regimen discontinuation, disenrollment from the health plan, or end of the database (3/31/2009).
  - Patients receiving 2+ TPD were allowed to change medications, so long as they continued receiving a complete regimen.
  - Discontinuation of the index regimen was defined as 60 consecutive days in which no refills were observed for any component of the regimen.

## Methods (cont'd)

### Outcome Measures

- Patient demographics: age, sex, Charlson comorbidity index score calculated during the 6-month pre-index period, HIV/AIDS medication classes received at index, and ART-naïve status (i.e., a binary indicator for whether the patient received any ART therapy in the 6-month pre-index period).
- Adherence: based on pharmacy records, measured as the proportion of days between the regimen index date and regimen discontinuation date (or end of follow-up) in which the patient had drug supply on hand for all ART components (commonly termed the medication possession ratio [MPR]).
  - Assessed at various intervals (i.e., 95% to 100%, 80% to 95%, 60% to 79%, less than 60%).
- Mean number of hospitalizations. Hospitalizations were assessed only for the duration of patients' index follow-up.

### Data Analyses

- All analyses were reported for patients on STR or on 2+ TPD.
- Descriptive analyses of all outcome measures were undertaken.
- Multiple-event Cox models were estimated to assess hospitalization risk over time and were assessed with a Poisson model estimated to assess hospitalization rates as a function of the number of pills required per day.
  - Independent variables included patient demographics, comorbidities, the number of pills received per day (i.e., STR versus 2+ TPD), and ART-naïve (vs. experienced) status.
  - Dependent variables included a count of the number of hospitalizations and the days from index to hospitalization.
  - Sensitivity analyses were conducted excluding patients with a boosted PI during follow-up as they may be more treatment experienced and at a more advanced stage of HIV.
- All analyses were conducted using SAS version 9.1.

## Results

Figure 1. Patient Selection

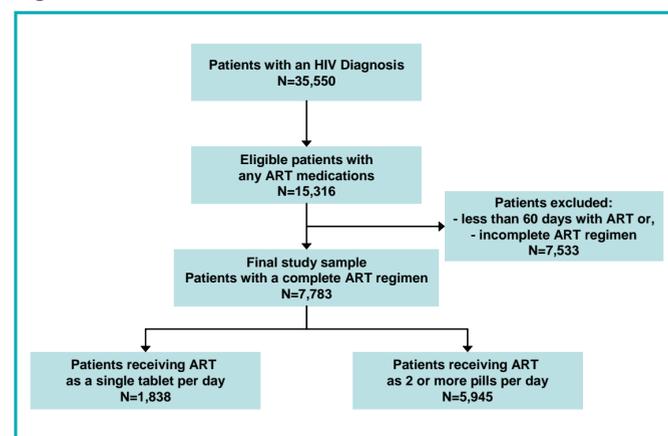
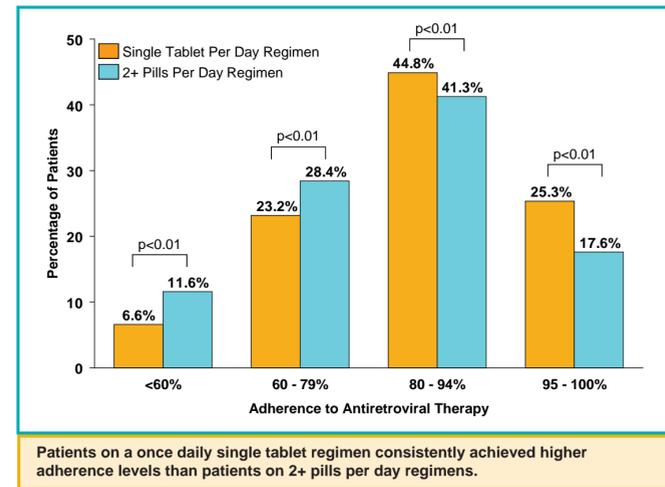


Table 1. Patient Demographics

Characteristic	Single Tablet Per Day Regimen	2+ Tablet Per Day Regimen	Overall
N	1,838	5,945	7,783
Female	48.6%	48.7%	48.7%
Age			
<35 years	23.5%	22.7%	22.9%
35-44 years	34.3%	34.3%	34.3%
45-54 years	32.4%	31.8%	31.9%
55+ years	9.8%	11.1%	10.9%
Mean (SE)	41.4 (0.3)	41.5 (0.2)	41.5 (0.1)
Mean (SE) Charlson Comorbidity Index	0.7 (0.03)	0.6 (0.02)	0.6 (0.02)
Concomitant Mental Health/Substance Abuse			
Mental disorders	21.3%	23.7%	23.1%
Illicit drug or alcohol abuse	18.8%	14.9%	15.8%
Treatment naïve patients	47.0%	25.9%	30.9%
ART Classes Received			
NRTIs	100.0%	100.0%	100.00%
NNRTIs	100.0%	26.1%	43.54%
Protease Inhibitors	---	73.6%	56.24%
Pharmacokinetic enhancers	---	30.0%	22.91%
Others	---	1.5%	1.13%
Received a boosted Protease Inhibitor	6.3%	64.1%	50.47%
Mean (SE) treatment and follow-up duration (days)	347 (6.46)	428 (4.84)	409 (4.07)

Figure 2. Adherence to Antiretroviral Therapy by Number of Tablets Required per Day



## Results (cont'd)

Table 2. Multivariate Analysis of Risk and Rates of Hospitalization

	Multiple-Event Cox Model		Poisson Count Model	
	Hazard Ratio	P-Value	Incidence Rate Ratio	P-Value
Received a Single Tablet Per Day Regimen (vs. a 2+ TPD)	0.753	<0.0001	0.705	<0.0001
Female (vs. male)	1.178	<0.0001	1.021	<0.0001
Age (vs. less than 35)				
35 to 44 years	0.907	0.0432	1.189	0.6685
45 to 54 years	0.979	0.6609	1.489	0.0003
55+ years	1.205	0.0012	1.164	<0.0001
Charlson comorbidity index (vs. index less than 1)				
Between 1 and 2	2.381	<0.0001	2.318	<0.0001
Greater than 2	2.761	<0.0001	2.529	<0.0001
Treatment naïve (vs. treatment experienced)	1.329	<0.0001	0.906	0.0062
Had a mental disorder diagnosis (vs. no mental disorder diagnosis)	1.301	<0.0001	1.348	<0.0001
Had a drug or alcohol abuse diagnosis (vs. no drug or alcohol abuse diagnosis)	2.052	<0.0001	1.812	<0.0001

Among other factors, patients on a once daily single tablet regimen had a 25% lower risk of hospitalizations compared to patients with 2 or more tablets per day regimen (hazard ratio=0.75; p<0.001).

Figure 3. Number of Hospitalizations: ART Naïve and Experienced Patients (Poisson Count Model)

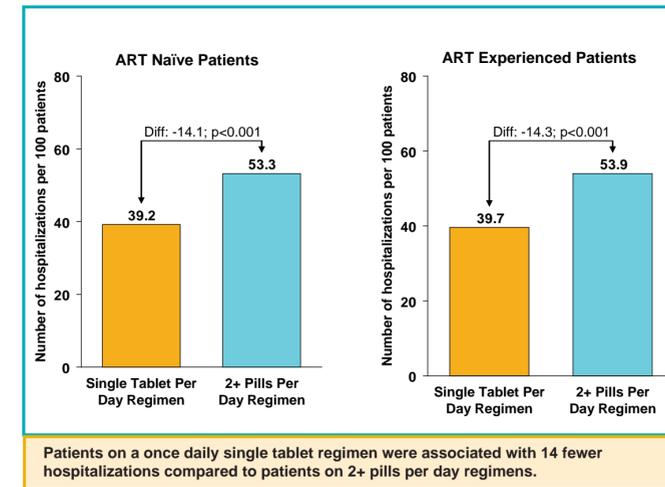
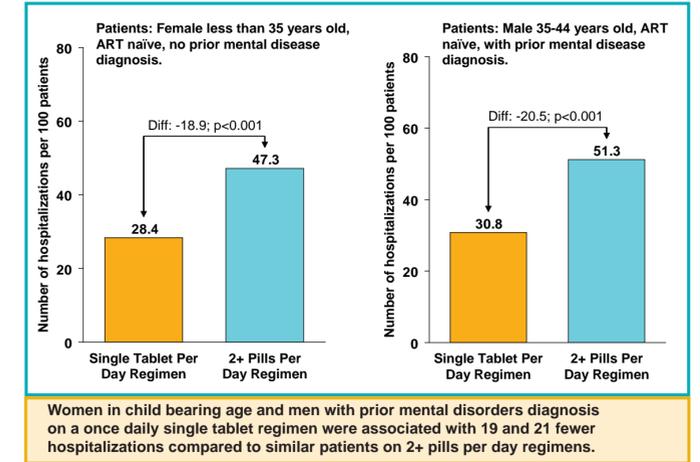


Figure 4. Number of Hospitalizations: Women of Child Bearing Age and Patients with Prior Mental Disease Diagnosis (Poisson Count Model)



## Limitations

- Since patients were not randomized to the different treatments and that information on CD4 and viral load were not available, we cannot exclude unmeasured confounding factors might influence outcomes.
- Results from this study may not be applicable to commercial, Medicare, or uninsured populations or to the general HIV/AIDS population in the United States.

## Conclusions

- After controlling for treatment experience and other available confounders, the use of a once daily single tablet antiretroviral therapy was associated with a 25% reduced risk of hospitalization. This was true even when limiting the analysis to treatment naïve patients.
- Analysis of a range of specific patient demographic and clinical profiles showed there were from 14 to 20 fewer hospitalizations per 100 patients on a once daily single tablet regimen compared to patients on 2 or more tablets per day.
- A higher observed adherence in this group may explain this association.

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