Decreasing Adherence to Antiretroviral Therapy over 4 years of Follow-up in a Commercially-Insured Population of Patients with HIV

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Introduction

- Improvement in antiretroviral therapy (ART) has transformed HIV to a chronic condition requiring lifelong therapy
- To achieve durable viral suppression, maintaining high adherence to daily ART is essential[1]
- ART has evolved from multi-tablet regimens (MTRs, consisting of two or more pills) to single-tablet regimens (STRs) and research has shown STRs lead to better medication adherence and viral suppression[1-3]
- Current literature on long-term adherence to ART in the commercially-insured US population is limited
- Study objective: To compare yearly and longer term ARV adherence among HIV patients overall and by those treated with STRs vs. MTRs

Methods

Study Design

- Patient characteristics and adherence were assessed using a retrospective study design from the Optum Clinformatics US-based commercial claims data spanning January 2011 to December 2017
  - Index date was defined as the date of the first complete ART regimen during the study period with duration ≥60 days
  - Patients were followed from index until the end of eligibility or death
  - Adherence was examined in the 1-year observation period for the overall analysis, and yearly following index among patients with ≥4 years of follow-up
  - A subgroup analysis was conducted among patients with index year during 2014-2016 to evaluate adherence with more recent ART

Inclusion Criteria

- Pharmacy claims for a complete ART regimen with duration ≥60 days
- ≥1 medical claim with a diagnosis of HIV (ICD-9-CM: V08, 042; ICD-10-CM: Z21, B20) during 2011-2017
- ≥18 years of age on the index date
- Continuous eligibility in the data for ≥3 months before (baseline) and ≥12 months after (observation) the index date

Exclusion Criteria

- ≥1 medical claim with a diagnosis of HIV-2 at any time (ICD-9-CM: 079.53; ICD-10-CM: B97.35)

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Study Measures

- Demographic characteristics were assessed during the baseline period
- Adherence to complete STR or MTR was measured as the proportion of days covered (PDC), defined as the number of non-overlapping days in the period that were "covered" by a complete regimen of the index type (STR or MTR) divided by the number of days in a fixed period of 1 year
- Patients switching from an MTR to an STR (or vice versa) for ≥60 days were censored and excluded from the following years' PDC calculations
- Patients who switched for a duration of <60 days were included but these days did not count towards PDC
- PDC was examined in the 1-year observation period overall, and yearly following index among patients with continuous data

Statistical Analyses

- Means and standard deviations (SDs) were reported for continuous variables; frequencies and proportions for categorical variables
- Wilcoxon rank sum test and Chi-square tests were used to compare continuous and categorical variables, respectively

Results

Baseline Characteristics

- Among the 15,153 patients who met the study selection criteria, 58% (n = 8,715) received an STR and 42% (n = 6,438) an MTR at index
- Overall, median age was 45 years, the majority were male (88%), and 53% were in the South
- Compared to MTR patients, STR patients had more recent index dates (Table 1)

Table 1. Percentage of patients by index year

Index Year	Overall N = 15,153	STR N = 8,715	MTR N = 6,438
2011	6,146 (41%)	2,942 (34%)	3,204 (50%)
2012	2,154 (14%)	1,174 (14%)	980 (15%)
2013	1,539 (10%)	953 (11%)	586 (9%)
2014	1,629 (11%)	975 (11%)	654 (10%)
2015	1,929 (13%)	1,361 (16%)	568 (9%)
2016	1,756 (12%)	1,310 (15%)	446 (7%)

Adherence During 1 Year Follow-Up

- During year 1, the proportion of patients with PDC ≥0.90 was 63% overall (Table 2), and greater for STR than MTR (67% vs. 58%, p <0.001)
- In the subgroup of patients with index during 2014-2016, adherence was slightly lower with PDC ≥0.90 for 57% of patients overall and greater for STR than MTR (62% vs. 48%, p <0.001)

Table 2. Adherence during the first year

PDC during 1 year of follow-up	Overall	STR	MTR
All Patients Mean ± SD	N=15,153 0.87 ± 0.17	N=8,715 0.88 ± 0.15*	N=6,438 0.85 ± 0.18*
PDC ≥ 0.90, n (%)	9,517 (63%)	5,794 (67%)*	3,723 (58%)*
2014-2016 Subset Mean ± SD	N=5,314 0.85 ± 0.18	N=3,646 0.87 ± 0.16*	N=1,668 0.80 ± 0.21*
PDC ≥ 0.90, n (%)	3,052 (57%)	2,251 (62%)*	801 (48%)*

* p-value <0.0001

Adherence During 4 Year Follow-Up

- PDC ≥0.90 decreased over time in the overall sample (year 1: 67%, year 2: 57%, year 3: 57%, year 4: 53%)
- The decreasing trend was observed in both groups but was greater in MTR group, p-value < 0.0001 for all years (Figure 1)
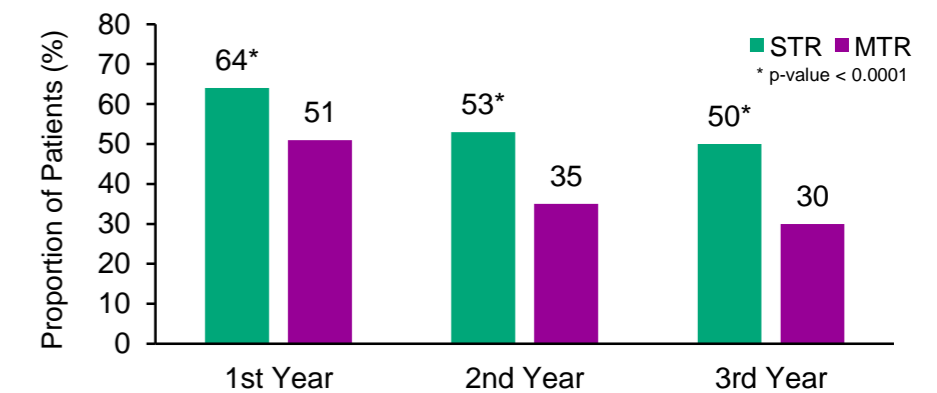
Figure 1. ≥ 90% Adherence over time for patients with ≥ 4 years
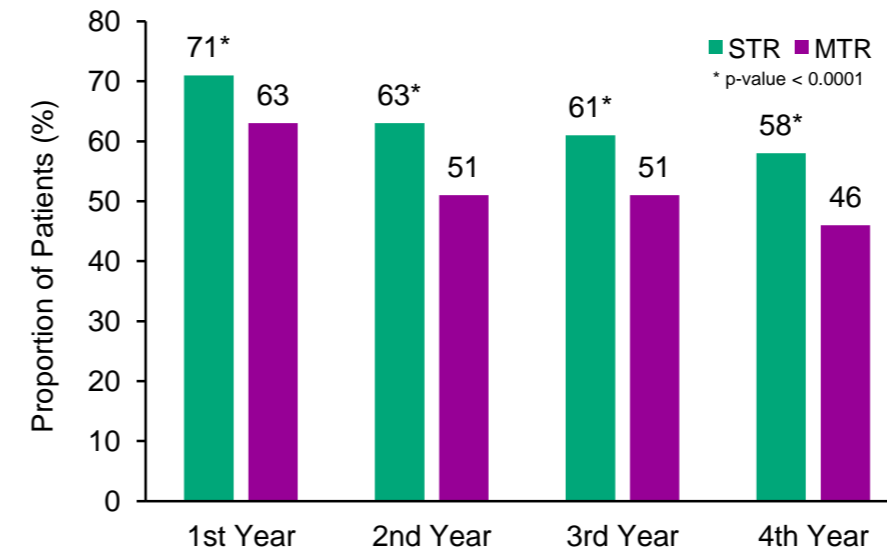
Adherence During 3 Year Follow-Up (Index Year 2014-2016 Subset)

- PDC ≥0.90 decreased over time in the overall sample (year 1: 59%, year 2: 46%, year 3: 42%)
- The decreasing trend was observed in both groups but was greater in the MTR group, p-value < 0.0001 for all years (Figure 2)

Figure 2. ≥ 90% Adherence over time by STR and MTR

Discussion

- Findings from this study are consistent with previous literature that reported higher adherence to ARV regimens of a single pill versus multiple pills per day, among US Veterans, Medicaid enrollees, and commercially insured populations[1-4]
- Analysis of yearly adherence demonstrated sub-optimal adherence overall and adherence decreased over time, but the drop was larger for MTR patients; STR patients maintained higher adherence compared to MTR patients at each year of follow-up
- The use of regimens with lower pill burden or less frequent dosing could improve sub-optimal adherence and achieve higher adherence over time

Conclusions

- Adherence showed room for improvement in the first year of observation overall and in the modern ARV era (i.e., index date between 2014-2016), with those receiving STRs having higher adherence as compared to those receiving MTRs
- Adherence tended to decrease year over year
- Maintaining high rates of ARV adherence is a critically important aspect of therapy for patients with HIV
- Interventions to facilitate long term high adherence should be explored

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