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Relationship between single-tablet regimen and adherence to HIV and non-HIV medications

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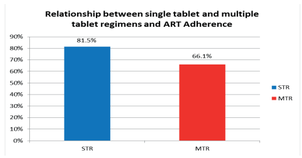
ABSTRACT

Background: Single tablet antiretroviral (ART) regimens (STR) are convenient and reduce pill burden compared to multiple tablet regimens (MTR). Improving convenience and pill burden can enhance medication adherence. The objectives of this study were to evaluate medication adherence to both ART and non-ART medications between STR and MTR recipients.

Material/methods: A retrospective cohort study, employing repeated subject sampling, was performed among HIV+ adults receiving care in Upstate New York Veterans' Healthcare Administration from 2000-13. Inclusion criteria: 1) receipt of ≥ 3 ART medications for ≥ 3 months and 2) availability of medication list and pharmacy refill records. Data collected included demographics, comorbidities, medications, and dispensing history. Medication adherence was defined using pharmacy refill records. Adherence to ART was defined as ≥ 3 ART agents in a patients' possession at any given time. Percent adherence was calculated by dividing the number of adherent days by the total days of therapy. Adherence to non-ART chronic medications was defined as having no medication in possession. Classification and regression tree used to identify breakpoints.

Results: Of the 1202 subjects, 165 (13.7%) were on STR and the remainder were on a MTR. Mean ± standard deviation (SD) age at start of regimens for STR and MTR recipients were 53.0 ± 9.0 and 50.3 ± 8.8 years, p< 0.001, respectively. Adherence to ART is displayed in Figure 1. Variables independently associated with optimal ART adherence (≥ 90%) were: use of STR (odds ratio, OR: 4.66; 95% confidence interval, CI: 3.18 – 6.82, p < 0.001), age ≥ 50 years (OR: 1.52; 95% CI: 1.08 – 2.15, p = 0.02) and use of ≥ 6 non-ART medications (OR: 0.46; 95% CI: 0.33 – 0.65, p < 0.001). For non-ART medications, mean ± SD adherence did not differ between STR (78.9 ± 13.8%) and MTR (81.1 ± 13.4%) recipients, p = 0.07. Variables independently associated with optimal non-ART adherence (≥ 90%) were use of ≥ 6 non-ART medications (OR: 0.46; 95% CI: 0.36 – 0.60, p < 0.001) and ART adherence ≥ 90% (OR: 2.84; 95% CI: 2.03 – 3.97, p <0.001).



Conclusions: Adherence to ART medications was significantly higher for STR versus MTR recipients. Adherence to non-ART medications was similar between STR and MTR recipients. Polypharmacy (use of ≥ 6 medications) was deleterious to optimal adherence (≥ 90%) to both ART and non-ART medications. Clinicians may opt to choose STR for HIV treatment to reduce the number of prescriptions and optimize adherence in HIV+ adults.

BACKGROUND

- Treatment of HIV infection requires the use of ≥ 3 antiretroviral (ART) medications in combination
- Advances have permitted coformulation of multiple ART medications into a single tablet regimen (STR)
- STR are perceived to be more convenient than multiple tablet regimens (MTR)
- It is unclear if medication adherence to both ART and non-ART medications differs between recipients of STR and MTR

OBJECTIVE

- Compare ART and non-ART medication adherence between STR and MTR recipients

METHODS

Setting and Study Population

- This study was performed among patients receiving care at one of the 5 sites in the Upstate New York Veterans' Healthcare Administration (VISN2)
- Study Design:
  - Retrospective cohort study utilizing repeated subject sampling among HIV-infected subjects receiving care between 2000 – 2013.
- Inclusion criteria:
  - Age ≥ 18
  - Documented HIV infection (ICD-9: 042 series)
  - Receipt of ≥ 3 ART medications for ≥ 3 months
  - Availability of medication list and pharmacy refill records
- Exclusion criteria:
  - Patients on incomplete ART regimens (monotherapy with fixed dose zidovudine/lamivudine/abacavir, etc.) were not included in these analyses.

Data Collection

Trained reviewers collected the following information from the patients' medical records:

- Demographics and comorbidities
- Year of HIV infection
- Medication history
  - Drug name, dose, and frequency
  - Number of drugs
  - Refill history
- Laboratory data
  - All CD4 and HIV RNA obtained were collected

Exposure Variable

- The exposure of interest in this study was the use of single tablet ART medication regimens (STR).
  - STR was defined as all components of the HIV treatment regimen coformulated into a single product (eg. fixed dose efavirenz/emtricitabine/tenofovir disoproxil fumarate)
  - All others were considered multiple tablet ART medication regimens (MTR).

Outcome Measures

- The primary outcome of this study was medication adherence
  - Medication adherence was evaluated separately for ART and non-ART medications
  - Adherence was defined using medication refill records and possession ratios were computed
- ART adherence was defined as possession of ≥ 3 ART medications at any given time
  - If patients were in possession of < 3 ART medications, it was considered a period of nonadherence.
- Non-ART medication adherence was restricted to medications that were used for chronic medical conditions
  - Non-ART medications used for as-needed indications were not evaluated
- Optimal adherence was defined as possession ratio !"90%.

Statistical Analysis

- Categorical variables were compared using the Chi-square or Fisher's Exact test.
- Continuous variables were compared using the Student's T test or Mann Whitney U test.
- Classification and regression tree (CART) analyses were performed to identify breakpoints in continuous variables associated with dichotomous outcome variables.
- Multivariate logistic regression was used to determine variables independently associated with the outcomes of interest.
  - Two sets of regression models were performed
    - Optimal adherence to ART medications
    - Optimal adherence to non-ART medications
- A p-value < 0.25 in the bivariate analyses were included at model entry into the multivariate model and a backwards stepwise approach was used to identify the most parsimonious model that adjusted for confounding variables

RESULTS

Table 1: Bivariate Relationship between Clinical/Demographic Characteristics and Type of Antiretroviral Regimen

Covariate	Multiple tablet regimen recipients (n = 1037)	Single tablet regimen recipients (n = 165)	P-value
Age, mean (standard deviation, SD)	**50.3 ± 8.8**	**53.0 ± 9.0**	**<0.001**
Race			**0.95**
• **Caucasian**	**473 (45.6)**	**77 (46.7)**	
• **Black**	**519 (50.0)**	**80 (48.5)**	
• **Hispanic**	**33 (3.2)**	**6 (3.6)**	
• **Asian/Pacific Islander**	**3 (0.3)**	**1 (0.6)**	
• **Other**	**9 (0.9)**	**1 (0.6)**	
Sex, male (%)	**1010 (97.4)**	**158 (95.8)**	**0.24**
Risk behavior			**0.02**
• **MSM**	**252 (24.3)**	**37 (22.4)**	
• **MSM/IVDU**	**57 (5.5)**	**8 (4.8)**	
• **IVDU**	**299 (28.8)**	**31 (18.8)**	
• **Heterosexual sex**	**328 (21.6)**	**74 (44.8)**	
• **Female-female**	**2 (0.2)**	**0 (0)**	
• **Unknown**	**99 (9.5)**	**15 (9.1)**	
Median (inter-quartile range) years with diagnosed HIV infection	**21 (17 – 26)**	**15 (9 – 21)**	**<0.001**
Number of comorbidities, median (IQR)	**14 (8 – 21)**	**15 (9 – 21)**	**0.42**
ART regimen type			**<0.001**
• **NNRTI**	**287 (27.7)**	**162 (98.2)**	
• **PI**	**437 (42.1)**	**0 (0)**	
• **INSTI**	**35 (3.4)**	**3 (1.8)**	
• **Non-traditional/mixed class**	**278 (36.8)**	**0 (0)**	
Median (inter-quartile range) number of non-ART medications	**6 (3 – 10)**	**7 (4 – 11)**	**0.08**
Non-ART medication daily pill burden	**8 (4 – 14)**	**8 (5 – 14)**	**0.66**
***Use of ≥ 6 non-HIV medications**	**578 (55.7)**	**101 (61.2)**	**0.19**

All data presented as n (%) , mean (standard deviation), or median (inter-quartile range), unless otherwise noted.
* = classification and regression tree (CART)-derived breakpoint; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; INSTI = integrase strand transfer inhibitor.

Figure 1: Relationship between STR use and Adherence to ART and non-ART Medications

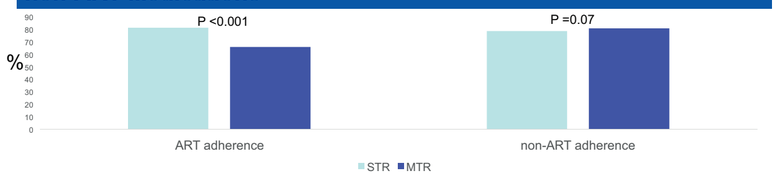


Figure 2: Adherence to ART & Non-ART Medications, Stratified by Number of Medications

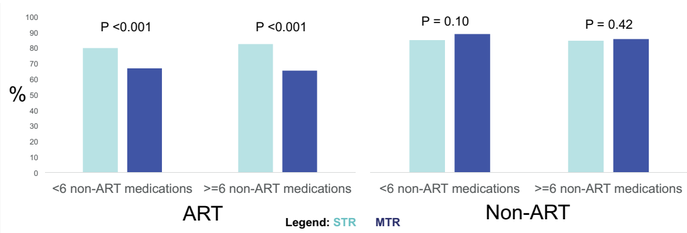


Figure 3: Mean Medication Adherence, Stratified by ART Regimen Type

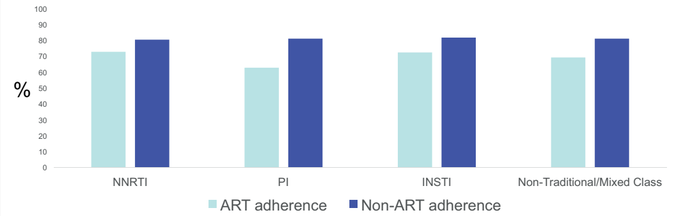


Table 2: Multivariate Analyses of Variables Independently Associated with Optimal (≥90%) Adherence to Antiretroviral Medications

Covariate	Adjusted odds ratio	95% confidence interval	P-value
Use of single tablet regimen	4.66	3.18 – 6.82	<0.001
Use of ≥ 6 non-ART medications	0.46	0.33 – 0.65	<0.001

Table 3: Multivariate Analyses of Variables Independently Associated with Optimal (≥90%) Adherence to Non-HIV Medications

Covariate	Adjusted odds ratio	95% confidence interval	P-value
Use of ≥ 6 non-ART medications	0.46	0.36 – 0.60	<0.001
ART adherence ≥ 90%	2.84	2.03 – 3.97	<0.001

CONCLUSIONS

- Adherence to ART medications was significantly higher for STR compared to MTR recipients
  - Optimal ART adherence predicted by use of STR and ≥ 6 non-ART medications
- Adherence to non-ART medications was similar between STR and MTR recipients
  - Predicted of non-ART adherence were ART ≥adherence 90% and use of ≥ 6 non-ART medications