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Minimum adherence threshold necessary to achieve virologic suppression

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ABSTRACT

Background: Poor adherence (ADH) to antiretroviral therapy (ART) hinders the ability to achieve virologic suppression (VS). Study objectives were 1) quantify the minimum ADH threshold associated with achievement of VS and 2) determine if ADH is independently associated with VS.

Material/methods: A retrospective cohort study, with repeated subject sampling, was performed among HIV+ adults receiving care in Upstate New York Veterans' Healthcare Administration from 2000-2013. Inclusion criteria were: 1) receipt of ≥ 3 ART for ≥ 3 months, 2) availability of pharmacy refill records, 3) detectable pre-treatment (tx) HIVRNA and 4) ≥ 1 on-tx HIVRNA value. Data elements collected from medical records for each regimen included demographics, comorbidities, medications, dispensing history and lab values. Using pharmacy refill records, medication ADH was defined as possession of ≥ 3 ART agents at any time. Achievement of VS was defined as ≥ 1 undetectable on-tx HIVRNA. Classification and regression tree (CART) analyses were performed to identify breakpoints in ADH associated with VS.

Results: Of the 486 subjects, majority were tx-experienced (57.6%). Median (interquartile range, IQR) baseline HIVRNA was 15886 (1585 – 60052) copies/mL. The most common regimen types were NNRTI (38.5%), PI (37.7%), non-traditional/mixed class (21.6%) and INSTI (2.3%). VS occurred in 52.9% of subjects. Median (IQR) ADH was significantly higher for subjects achieving VS (71 [52 – 83%]) compared to those who did not (61 [42 – 76%]), p < 0.001. CART-derived ADH threshold associated with VS was 76.4%. When restricting to contemporary, traditionally-composed regimens, ADH threshold was 76.1%. Subjects with ADH ≥75% were significantly more likely (64.0%) to achieve VS compared to those <75% (46.4%), p < 0.001. Cumulative probability of achieving VS, stratified by ADH of 75%, is displayed in Figure 1. CART-derived ADH breakpoints for each regimen type were 76.1% (NNRTI-based), 75.9% (PI-based) and 78.8% (mixed regimen). Variables independently associated with VS were: ADH ≥ 75% (hazard ratio, HR: 1.70, 95% confidence interval, CI: 1.32 – 2.19, p < 0.001), use of a single tablet regimen (HR: 1.47, 95% CI: 1.04 – 2.08, p = 0.03), age ≥ 50 years (HR: 1.28, 95% CI: 1.00 – 1.65, p = 0.05), and use of once-daily non-HIV medications vs non-once daily non-HIV medications (HR: 1.35, 95% CI: 1.01 – 1.81, p = 0.04).

Conclusions: ADH ≥ 75%, age ≥ 50 years, single tablet regimen and use of once-daily non-HIV medications were independently associated with VS.

BACKGROUND

- Adherence to antiretroviral therapy (ART) is essential for achievment of virologic suppression (VS).
- Many newer ART agents are more potent than previous ART medications.
- The minimum adherence threshold necessary to *achieve* VS is not known.

OBJECTIVES

- Quantify the minimum adherence threshold associated with achievement of VS
- Determine if adherence threshold is independently associated with VS

METHODS

Setting and Study Population

- Patients receiving care in Upstate New York Veterans' Healthcare Administration (VISN2) from 2000-2013.

Study Design:

- Retrospective cohort study utilizing repeated subject sampling

Inclusion criteria:

- Age ≥ 18
- Documented HIV infection (ICD-9: 042 series)
- Receipt of ≥ 3 ART medications for ≥ 3 months
- Detectable HIVRNA at baseline
- Availability of HIVRNA on-therapy

Exclusion criteria:

- Incomplete ART regimens

Data Collection

- 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

Exposure Variable – Adherence to ART medication

- ART adherence defined as possession of ≥ 3 ART medications at any given time

Outcome Measure – Virologic Suppression (VS)

- Primary outcome was achievement of VS.
- VS defined as an undetectable HIVRNA value

Statistical Analysis

- Classification and regression tree (CART) analyses performed to identify breakpoints in ART adherence associated with achievement of VS.
- Multivariate logistic regression was used to determine if ART adherence was independently associated with achievement of VS.

RESULTS

Table 1: Clinical and demographic characteristics of study population

Covariate	Result (n = 486)
Age ± standard deviation	49.3 ± 8.3
Sex, male	466 (95.9)
Risk behavior • MSM • MSM/IDU • IDU • Heterosexual • Female-Female • Unknown	 120 (24.7) 38 (7.8) 142 (29.2) 157 (32.3) 2 (0.4) 27 (5.6)
Comorbidities, median (IQR)	15 (8 – 21)
Years of diagnosed HIV, mean ± SD	20.7 ± 6.7
Non-ART medications, median (IQR)	7 (4 – 13)
ART adherence, median (IQR)	66.3 (48.1 – 81.1)
Non-ART adherence, median (IQR)	82.3 (73.0 – 82.3)
Single tablet regimen	54 (11.1)
Treatment-naive	206 (42.4)
Contemporary ART regimen	260 (53.5)

Figure 1: Relationship between ART adherence and achievement of virologic suppression

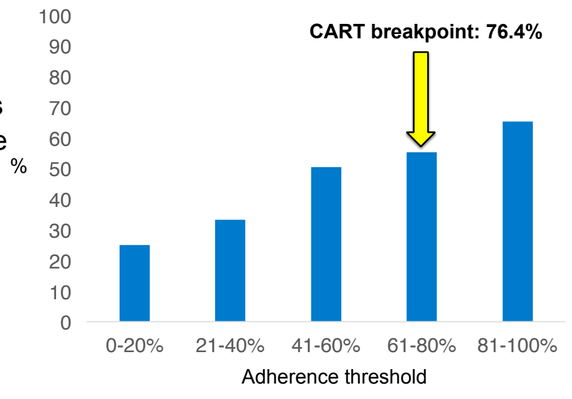

Figure 2: Cumulative probability of achieving virologic suppression ≥ 75%

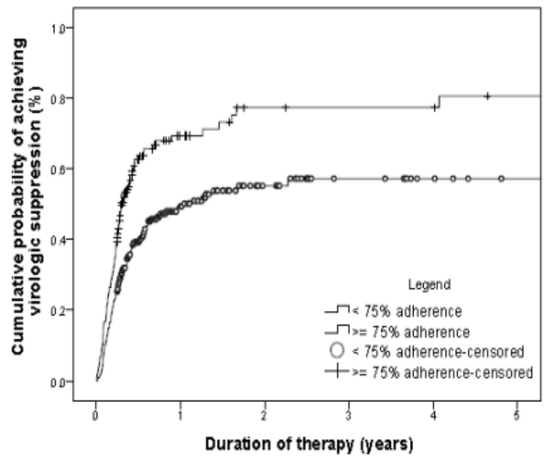

Table 2: Variables independently associated with achievement of VS

Covariate	Hazard Ratio	95% C.I.	P-value
Adherence ≥ 75%	1.70	1.32 – 2.19	<0.001
Single tablet regimen	1.47	1.04 – 2.08	0.03
Age ≥ 50	1.28	1.00 – 1.65	0.05
Once daily non-HIV medications	1.35	1.01 – 1.81	0.04

CONCLUSIONS

- Adherence to ART regimen of at least 75% is necessary to *achieve* virologic suppression
- Achievement of ART was predicted by adherence ≥ 75%, single tablet regimen, age ≥ 50 and use of once daily non-HIV medications
- Clinicians should continue to advocate for strong ART adherence