Examining the Healthcare Burden of Antiretroviral Therapy Resistance Among People With HIV in the United States

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Conclusions

- Antiretroviral therapy (ART) resistance was associated with poorer clinical outcomes and increased healthcare use among people with HIV (PWH)
- Additionally, individuals with resistance were less likely to remain on their post-index HIV treatment for 12 months than those without known resistance
- These findings underscore the clinical and healthcare system burden of resistance and highlight the need for effective, durable regimens
- Key limitations of this study included potential residual confounders, missing clinical data (e.g., CD4, viral load) for some individuals, mis-classification of results, lack of secondary confirmation of no resistance for the non-resistance cohort, and identification of resistance in claims database even with lab data available

Plain Language Summary

- Drug resistance happens when HIV changes in ways that make some HIV medicines work less well
- This study looked at how HIV drug resistance is associated with people's health and their use of healthcare services
- In this study, people with HIV and drug resistance experienced more health complications and healthcare services than those without known drug resistance
- Additionally, individuals with resistance were less likely to remain on their prescribed HIV treatment for 12 months after testing confirmed that the virus is resistant to HIV medicines

Introduction

- ART has been pivotal in transforming HIV from a fatal diagnosis into a manageable chronic condition[1]
- However, resistance can reduce the effectiveness of ART and result in poorer clinical outcomes and downstream public health consequences
- The healthcare resource use associated with ART resistance in routine clinical practice is not fully understood and this study serves as a follow on to existing evidence examining resistance in specific populations[2]
- Given the low frequency of ART resistance, using a large real-world dataset can build our understanding of the burden of resistance in the United States

Objective

Evaluate clinical outcomes and healthcare resource utilization associated with primary resistance-associated mutations (RAMs) to ART among PWH in the United States

Methods

- This retrospective study utilized medical and pharmacy claims data from HealthVerity database
- Treatment-naïve or –experienced people with HIV with ≥1 confirmed primary RAM during 2023 were identified and matched 1:2 to PWH without suspected resistance or evidence of resistance testing (proxy for no resistance)
  - Lab tests of interest were identified using Logical Observation Identifiers Names and Codes (LOINC) within patient records; gene mutations conferring primary capsid (CA), protease (PR), reverse transcriptase (RT), and integrase (IN) RAMs were defined according to International AIDS Society-USA, as well as additional primary CA, PR, RT, and IN RAMs reported in the literature
  - Index date was defined as date of earliest primary RAM detection; matched non-RAM individual inherited the corresponding index date
- Matching variables included age, sex, payer type, treatment history, and Charlson Comorbidity Index (CCI)
- Continuous enrollment for ≥12 months pre- and post-index were required
- Baseline adherence was assessed during pre-index period; lab values assessed ± 90 days of index date
- Opportunistic infections and healthcare utilization were evaluated during the 12-month post-index period
- Differences between cohorts (primary RAM and non-RAM) were tested using generalized estimating equation method
- Time to nonpersistence (defined as the earliest of ART discontinuation, switch or add-on) was assessed through Kaplan Meier plot. Differences between the cohorts were compared by Log-Rank Test

Results

Table 1. Demographic and Clinical Characteristics

	Non-RAM N = 2660	Primary RAM N = 1330
Mean Age (SD)	45.7 (13.6)	44.5 (13.4)
Sex[a], n (%)		
Male	1878 (70.6)	939 (70.6)
Race/Ethnicity[a], n (%)		
Black	828 (31.1)	475 (35.7)
White	525 (19.7)	215 (16.2)
Hispanic	332 (12.5)	159 (12.0)
Asian	39 (1.5)	20 (1.5)
Region[a], n (%)		
Northeast	626 (23.5)	376 (28.3)
Midwest	450 (16.9)	91 (6.8)
South	803 (30.2)	554 (41.7)
West	664 (25.0)	253 (19.0)
Payer Type[a], n (%)		
Commercial	624 (23.5)	312 (23.5)
Medicare	168 (6.3)	84 (6.3)
Medicaid	1540 (57.9)	770 (57.9)
Mean Non-HIV CCI (SD)	0.9 (1.7)	1.0 (1.7)
Mean CD4 Cell Count (cells/μL)[b] (SD)	625.4 (346.2)	304.6* (311.1)
HIV Viral Load (copies/mL)[c], n (%)		
<200	146 (67.3)	207 (28.1)*
200-500†	8 (3.7)	48 (6.5)
500+	63 (29.0)	483 (65.4)*
On guideline recommended ART regimen 90 days pre-index	1560 (58.7)	691 (52.0)
On guideline recommended ART post-index	1486 (95.3)	625 (90.5)
	Non-RAM N = 1685	**Primary RAM N = 841**
Mean PDC During 12-month Pre-Index Period (SD)	0.75 (0.26)	0.64* (0.31)

*Indicates p<0.05 for group comparison;
[a]Other/unknown category not shown; [b]Among those with available CD4 results measured within 90 days of index date [N=85 non-RAM, N=39 primary RAM]; [c]Among those with available HIV viral load results measured within 90 days of index date [N=217 non-RAM, N=738 primary RAM]; †Among participants with at least one guideline-recommended ART during baseline period
CCI, Charlson Comorbidity Index; HIV, Human Immunodeficiency Virus; PDC, proportion of days covered; RAM, resistance associated mutation; SD, standard deviation

- Of those who met all inclusion criteria, 1330 had ≥1 primary RAMs and 2660 were matched to the non-RAM cohort (**Table 1**)
- Similar proportions in each cohort were reported in age, sex, payer type, treatment history, and CCI due to matched design
- Most resided in the South (41.7% and 30.2%, primary RAM and non-RAM, respectively)

Table 2. Opportunistic Infections During 12-month Follow-up

- Although incidence of any opportunistic infection during follow-up was low, it was more than twice as common in the primary RAM cohort vs non-RAM cohort (5.3% vs 2.5%, respectively) (**Table 2**)

	Non-RAM N = 2660	Primary RAM N = 1330
Any opportunistic infection, n (%)	67 (2.5)	71 (5.3)*
Pneumocystis, n (%)	19 (0.7)	27 (2.0)
Mycobacteria, n (%)	26 (1.0)	28 (2.1)
Cryptococcal meningitis, n (%)	11 (0.4)	18 (1.4)
Cytomegaloviral disease, n (%)	19 (0.7)	18 (1.4)
Mycobacterium tuberculosis, n (%)	19 (0.7)	19 (1.4)

*Indicates p<0.05 for group comparison

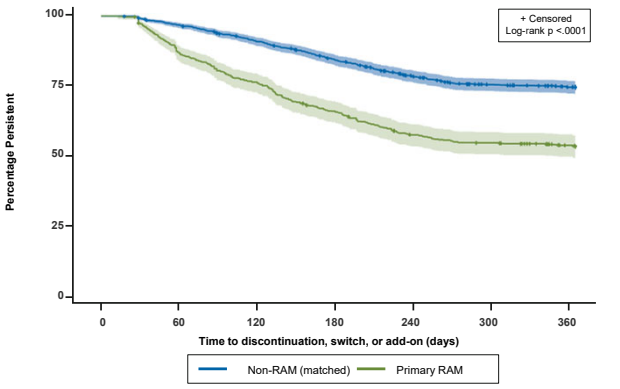
Table 3. HIV-related Healthcare Resource Utilization During 12-month Follow-up

	Non-RAM N = 2660	Primary RAM N = 1330
Any ED visit, n (%)	151 (5.7)	110 (8.3)*
Any inpatient visit, n (%)	378 (14.2)	258 (19.4)*
Mean length of stay, days	2.0	2.5
Any ambulatory visit, n (%)	2087 (78.5)	1120 (84.2)*
Any outpatient visit, n (%)	1185 (44.6)	511 (38.4)*
Any office visit, n (%)	1495 (56.2)	930 (69.9)*
Any other visit[a], n (%)	1665 (62.6)	1074 (80.8)*
Prescription claim count, mean (SD)	7 (6.3)	8 (6.2)*

*Indicates p<0.05 for group comparison;
[a]Labs, telehealth, home visits
ED, emergency department; RAM, resistance associated mutation; SD, standard deviation

- PWH with primary RAMs had higher emergency department, inpatient, and ambulatory visits compared to non-RAM cohort (p<0.05), but similar mean hospital length of stay (2.5 vs 2.0 days, p=0.16) (**Table 3**)

Figure 1. 12-month ART Persistence Among Treatment-experienced PWH on Guideline-Recommended ART Regimens Post-index



- Among treatment-experienced PWH who were on a guideline-recommended ART regimen within 90 days prior to index date, post-index ART regimen persistence at 12 months was significantly higher (p<0.0001) for non-RAM vs primary RAM cohort (**Figure 1**)

References: **1.** Deeks SG, et al. Lancet. 2013;382(9903):1525-1533. **2.** Sutton SS, et al. Open Forum Infectious Diseases. 2025;12(7): ofaf340.
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