Persistence of Guideline-Recommended Antiretroviral Therapy Regimens Among Persons Living with HIV Newly Initiating Treatment in the US

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Introduction

♦ Discontinuation of antiretroviral therapy (ART) may lead to poor outcomes for persons living with HIV (PLWH)[1].
♦ While single-tablet regimens (STRs) have been associated with greater persistence compared to multi-tablet regimens (MTRs), few real-world studies have assessed persistence with current DHHS guideline-recommended ART regimens[2].

Objectives

♦ To assess persistence among treatment-naïve PLWH newly initiating ART, and measure risk of discontinuation for STRs vs MTRs, and across different STRs, backbones and third agents

Methods

Database Description

♦ The analysis used IQVIA longitudinal prescription claims database (LRx), which captures information on adjudicated dispensed prescriptions sourced from retail, mail, long-term care, and specialty pharmacies
♦ Claims captured in LRx represent prescriptions dispensed from 86% of US retail pharmacies, 55% of mail order pharmacies, and 40-70% of specialty pharmacies

Study Sample

Patients were included in the study if they met the following:
♦ Had ≥2 claims for ARV of interest (**Table 1**) during the index window of Jan 1, 2016 - Jul 31, 2019
  – For STRs, the date of the first ARV claim within this window was the index date
  – For MTRs, the fill date for the last component product/medication in the regimen was the index date (±5 day window between fills for component comprising the regimen is allowed)
♦ Index claim dispensed at a pharmacy that consistently submitted claims to the LRx database from 12 month prior to index to the end of the study period (Jan 31, 2020)
♦ Age ≥18 years as of the index date
♦ Had no evidence of ARV use in the 12 months prior to index
♦ Age, gender, and prescription information were not missing
♦ No evidence of ART use other than index drugs on the index date
♦ Excluded patients in DTG/3TC, DTG/RPV, EFV/3TC/TDF treatment groups due to small sample size

Statistical Analyses

♦ Persistence was assessed overall and by treatment regimen and was measured from the index date until treatment discontinuation (a ≥90 day gap between fills of initial regimen) of the initial regimen or the end of the data stream, whichever occurred first
♦ Kaplan-Meier curves with Log-rank test statistics were produced to compare time to discontinuation between the initial regimens
♦ Multivariate Cox proportional hazard models were constructed to compare adjusted persistence between STRs and MTRs, among the STRs, among the third agents comprising the regimens, and among the backbone regimens
  – Covariates included: age group, gender, US geographic region, insurance type, pre-index medications, and number of unique prescriptions on index date

Results

Baseline Characteristics

♦ A total of 90,949 STR and 20,737 MTR patients were included (**Figure 1**)
♦ Mean (SD) age was 42.5 (13.5) years for STR patients and 42.7 (13.2) for MTR patients (**Table 2**)
♦ Patients were predominantly male (76.3% for STR and 70.5% for MTR patients)
♦ Majority of patients were covered by commercial insurance (STR: 76.6%, MTR: 70.5%)
♦ In the 12-month pre-index period, the most commonly used drug classes were antibiotics (35.2%), antihypertensives (17.2%) and lipid-lowering therapy (6.7%)
♦ STR and MTR patients have similar post-index follow-up days (893.4 and 922.8 days)
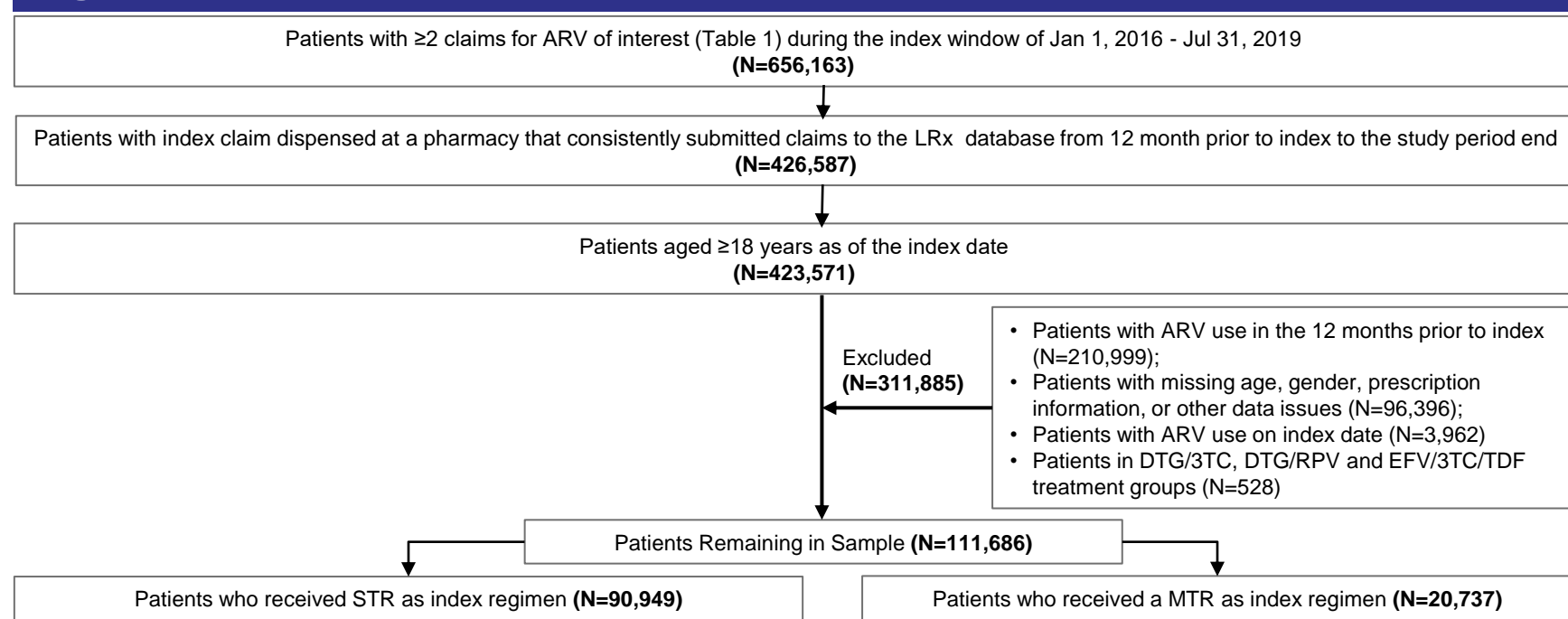
Figure 1. Sample Selection

Patients with ≥2 claims for ARV of interest (Table 1) during the index window of Jan 1, 2016 - Jul 31, 2019 (N=656,163)

Patients with index claim dispensed at a pharmacy that consistently submitted claims to the LRx database from 12 month prior to index to the study period end (N=426,587)

Patients aged ≥18 years as of the index date (N=423,571)

Excluded (N=311,885) | • Patients with ARV use in the 12 months prior to index (N=210,999); • Patients with missing age, gender, prescription information, or other data issues (N=96,396); • Patients with ARV use on index date (N=3,962) • Patients in DTG/3TC, DTG/RPV and EFV/3TC/TDF treatment groups (N=528)

Patients Remaining in Sample (N=111,686)

Patients who received STR as index regimen (N=90,949) | Patients who received a MTR as index regimen (N=20,737)

Table 1. Patient Distribution by DHHS-recommended Initial ART Regimens

	Regimen	N	
Single-tablet regimens (STRs) N=90,949	BIC/FTC/TAF	12,821	BIC: bictegravir
	EVG/c/FTC/TAF	27,059	EVG: elvitegravir
	EVG/c/FTC/TDF	8,390	FTC: emtricitabine
	ABC/3TC/DTG	21,575	TAF: tenofovir alafenamide fumarate
	RPV/FTC/TAF	5,953	TDF: tenofovir disoproxil fumarate
	RPV/FTC/TDF	4,698	DTG: dolutegravir
	EFV/FTC/TDF	10,453	ABC: abacavir
Multi-tablet regimens (MTRs) N=20,737	DTG + FTC/TAF	7,347	3TC: lamivudine
	DTG + FTC/TDF	5,560	RPV: rilpivirine
	DRV/r or DRV/c* + FTC/TAF	2,599	EFV: efavirenz
	DRV/r or DRV/c* + FTC/TDF	3,222	BIC: bictegravir
	ATV/r or ATV/c* + FTC/TAF	274	DRV: darunavir
	ATV/r or ATV/c* + FTC/TDF	1,557	ATV: atazanavir
	DRV or DRV/c* + ABC/3TC	178	c: cobicistat
			r: ritonavir
			* Boosted with cobicistat or ritonavir

Table 2. Baseline Demographic and Clinical Characteristics

Characteristics	Total N=111,686		STR N=90,949		MTR N=20,737		p value
Age, mean (SD)	42.5 (13.5)		42.5 (13.5)		42.7 (13.2)		0.023
18-34 years	37,322	33.4%	30,674	33.7%	6,648	32.1%	
35-49 years	37,045	33.2%	29,971	33.0%	7,074	34.1%	
50-64 years	31,774	28.4%	25,687	28.2%	6,087	29.4%	<0.001
≥65 years	5,545	5.0%	4,617	5.1%	928	4.5%	
Gender (n %)							
Male	83,998	75.2%	69,385	76.3%	14,613	70.5%	<0.001
Female	27,688	24.8%	21,564	23.7%	6,124	29.5%	
Geographic Region (n, %)							
Northeast	21,482	19.2%	17,082	18.8%	4,400	21.2%	
Midwest	17,124	15.3%	14,076	15.5%	3,048	14.7%	
South	55,343	49.6%	45,706	50.3%	9,637	46.5%	<0.001
West	17,737	15.9%	14,085	15.5%	3,652	17.6%	
Insurance Type (n, %)							
Cash	2,374	2.1%	1,844	2.0%	530	2.6%	
Commercial	84,250	75.4%	69,625	76.6%	14,625	70.5%	
Medicare	12,105	10.8%	9,456	10.4%	2,649	12.8%	<0.001
Medicaid	12,896	11.5%	9,971	11.0%	2,925	14.1%	
Unknown	61	0.1%	53	0.1%	8	0.0%	
Pre-index medication use (n, %)							
Antibiotics	39,259	35.2%	31,718	34.9%	7,541	36.4%	<0.001
Antihypertensives	19,188	17.2%	15,581	17.1%	3,607	17.4%	0.366
Antidiabetics	5,762	5.2%	4,711	5.2%	1,051	5.1%	0.512
Lipid-lowering therapy	7,479	6.7%	6,142	6.8%	1,337	6.4%	0.112
Anticoagulants	3,732	3.3%	2,937	3.2%	795	3.8%	<0.001
Antiarrhythmic drugs	71	0.1%	62	0.1%	9	0.0%	0.202
Respiratory drugs*	4,217	3.8%	3,361	3.7%	856	4.1%	0.003
≥1 non-ART on index date (n, %)	30,120	27.0%	23,022	25.3%	7,098	34.2%	<0.001
Post-index observation days, mean (SD)	898.9 (370.8)		893.4 (376.4)		922.8 (344.4)		<0.001

*includes lower and upper respiratory infections; **measured as number of days from index date until the end of study period (December 31, 2018)

Results, cont'd

Persistence Outcomes

♦ At 6 months, 71.4% of patients on STR were persistent, compared to 56.2% for MTRs (**Table 3**)
♦ Kaplan-Meier analyses showed that patients on STR had more days on therapy than those on MTR, overall and by individual regimen (**Figure 2 and 3**)
♦ Among all patients, persistence was highest with:
  – BIC/FTC/TAF   79.3% at 6 months   65.1% at 12 months
  – RPV/FTC/TAF   75.2% at 6 months   58.5% at 12 months
  – EVG/c/FTC/TAF   72.9% at 6 months   55.5% at 12 months

Table 3. Mean and Median Persistence by Treatment Regimen

Regimen	N	Median (days)	Mean (days)	% persistent at 6 months	% persistent at 12 months*
STR overall	90,949	326	425.4	71.4%	51.5%
BIC/FTC/TAF	12,821	303	311.6	79.3%	65.1%
EVG/c/FTC/TAF	27,059	373	470.7	72.9%	55.5%
RPV/FTC/TAF	5,953	380	469.6	75.2%	58.5%
DTG/ABC/3TC	21,575	356	473.4	71.4%	52.8%
EVG/c/FTC/TDF	8,390	246	359.6	62.4%	37.5%
RPV/FTC/TDF	4,698	240	354.3	61.9%	36.3%
EFV/FTC/TDF	10,453	292	408.1	67.1%	44.4%
MTR overall	20,737	213	307.8	56.2%	35.1%
DTG+FTC/TAF	7,347	326	396.7	69.4%	51.0%
DRV/r or DRV/c + FTC/TAF	2,599	243	330.5	63.3%	38.7%
ATV/r or ATV/c + FTC/TAF	274	240	297.9	60.2%	31.5%
DTG+FTC/TDF	5,560	102	219.1	37.8%	22.2%
DRV/r or DRV/c + FTC/TDF	3,222	193	275.7	54.2%	27.8%
ATV/r or ATV/c + FTC/TDF	1,557	184	247.6	52.5%	22.5%
DRV/r or DRV/c + ABC/3TC	178	162	204.7	48.3%	10.8%

*Patients with 12 month persistence of those who had a start date 1 year prior to study end (January 31st, 2020)
No. of patients with at least 12 months follow-up: STR overall (91,077), BIC/FTC/TAF (7,055), EVG/c/FTC/TAF (25,320), RPV/FTC/TAF (5,402), DTG/ABC/3TC (20,316), EVG/c/FTC/TDF (8,229), RPV/FTC/TDF (4,564), EFV/FTC/TDF (10,191), MTR overall (19,365), DTG+FTC/TAF (6,872), DRV/r or c+FTC/TAF (2,418), ATV/r or c+FTC/TAF (257), DTG+FTC/TDF (5,117), DRV/r or c+FTC/TDF (3,180), ATV/r or c+FTC/TDF (1,545), DRV/r or+ABC/3TC (176)

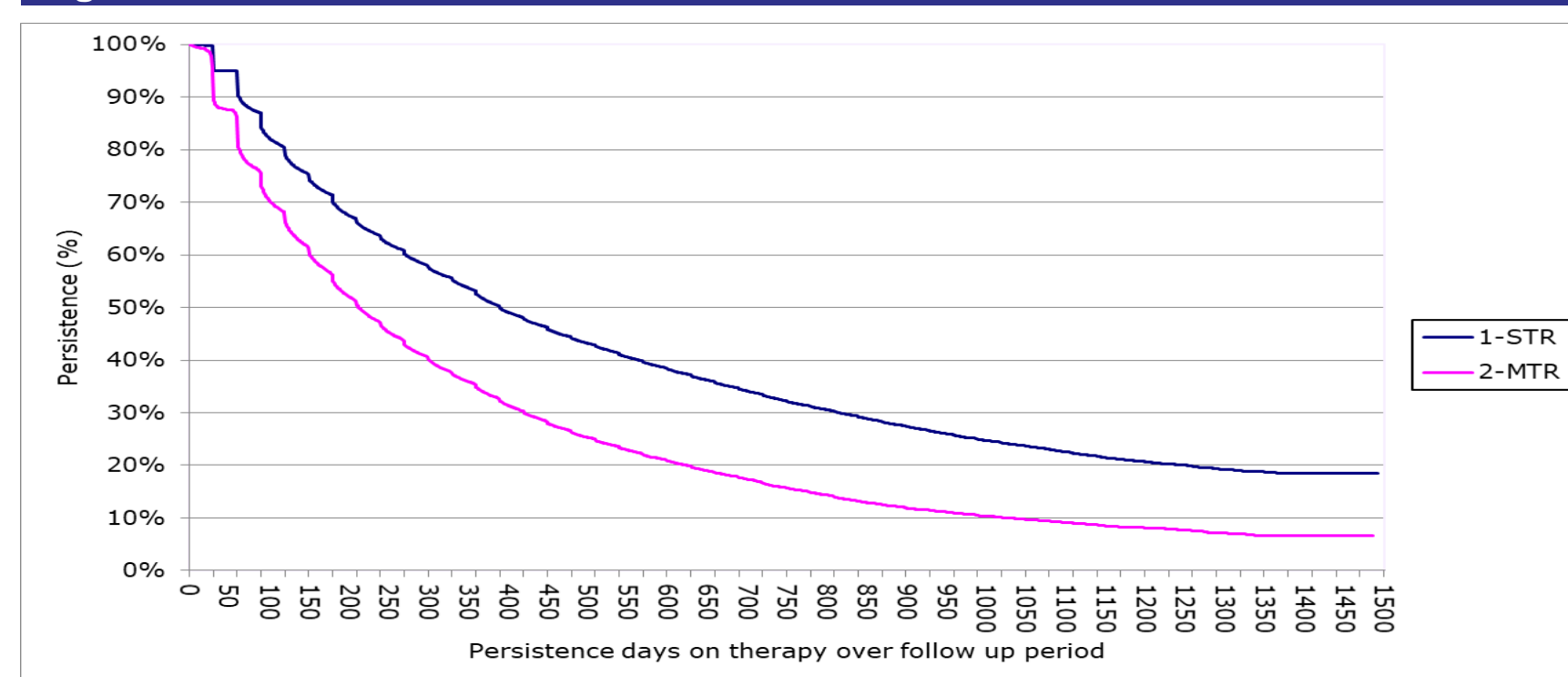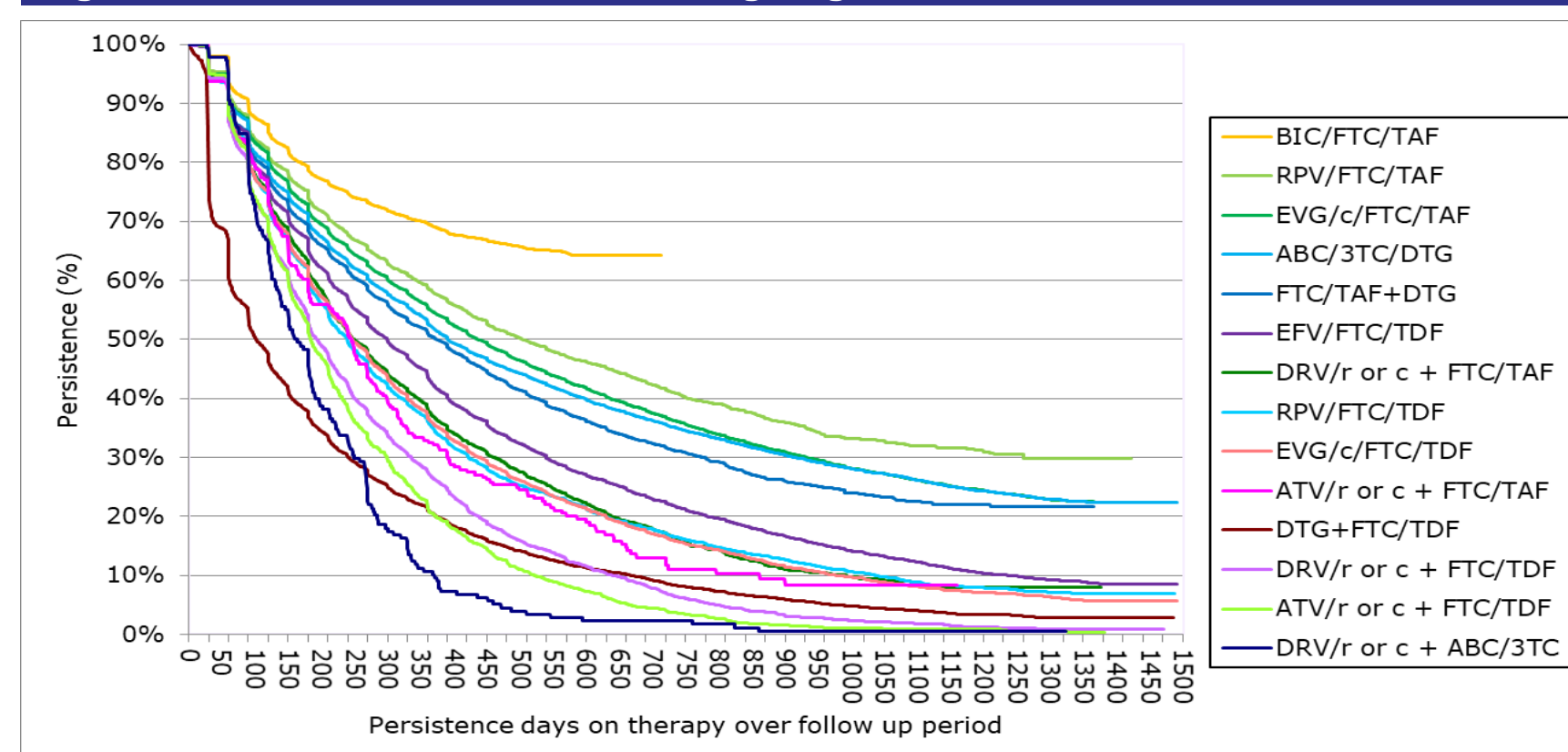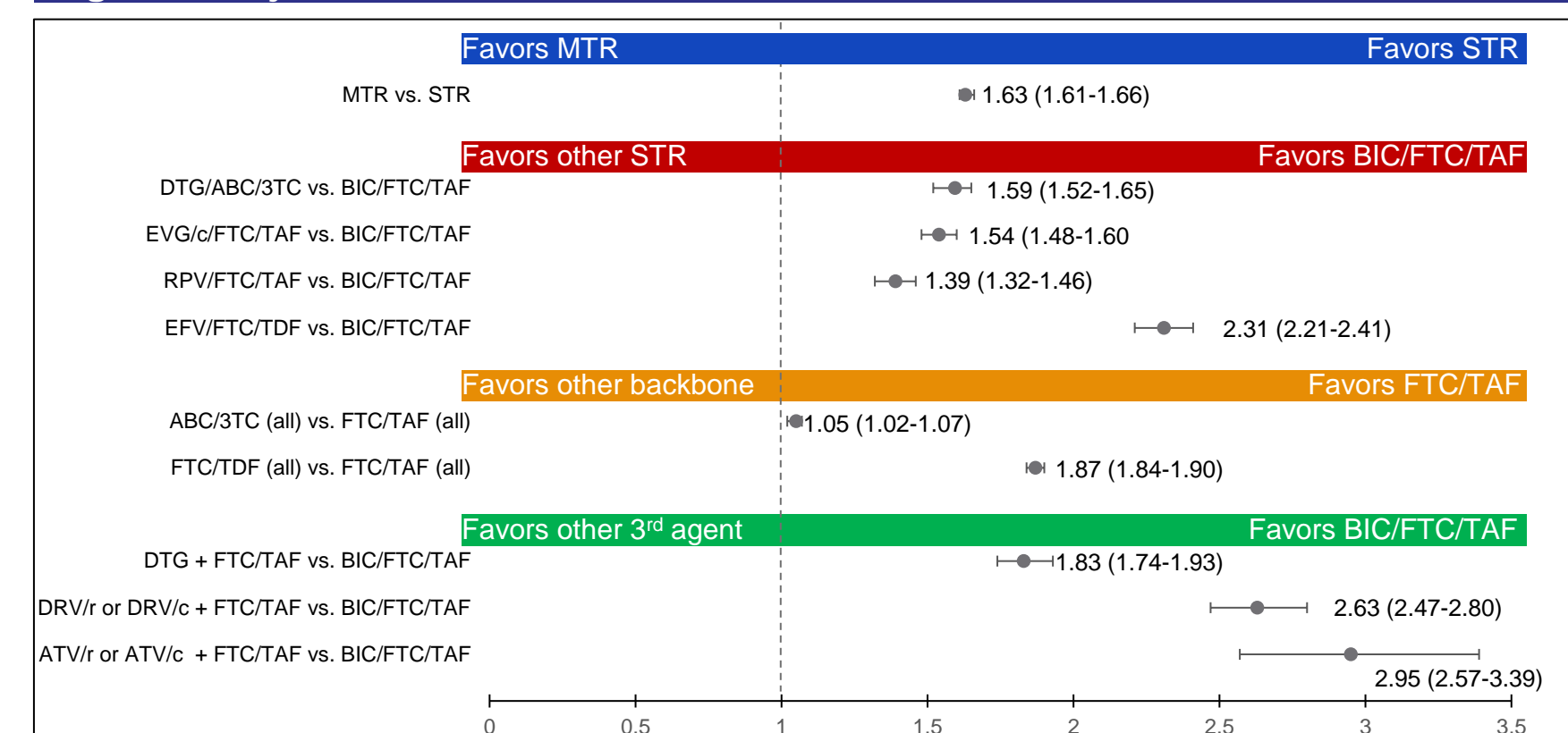### Figure 2. Treatment Persistence: STRs vs. MTRs

Figure 3. Treatment Persistence among Regimens

♦ After controlling for baseline characteristics, adjusted results show (**Figure 4**):
  ♦ MTRs were associated with 1.63 greater risk of treatment discontinuation compared to STRs (p<0.001)
  ♦ Among STRs, compared to BIC/FTC/TAF, risk of discontinuation was:
    – 1.39 times higher for RPV/FTC/TAF
    – 1.54 times higher for EVG/c/FTC/TAF
    – 1.59 times higher for DTG/ABC/3TC
    – 2.31 times higher for EFV/FTC/TDF (all p<0.001)
  ♦ In comparing backbones, compared to FTC/TAF-based regimens, risk of discontinuation was:
    – 1.05 times higher with ABC/3TC-based regimens
    – 1.87 times higher with FTC/TDF-based regimens (both p<0.001)
  ♦ In comparing third agents combined with the FTC/TAF backbone, compared to BIC, risk of discontinuation was:
    – 1.83 times higher with DTG + FTC/TAF
    – 2.63 times higher with DRV/r or DRV/c + FTC/TAF
    – 2.95 times higher with ATV/r or ATV/c + FTC/TAF (all p<0.001)

Figure 4. Adjusted* Hazard Ratios for Treatment Discontinuation

Favors MTR	Favors STR
MTR vs. STR	1.63 (1.61-1.66)
Favors other STR	Favors BIC/FTC/TAF
DTG/ABC/3TC vs. BIC/FTC/TAF	1.59 (1.52-1.65)
EVG/c/FTC/TAF vs. BIC/FTC/TAF	1.54 (1.48-1.60)
RPV/FTC/TAF vs. BIC/FTC/TAF	1.39 (1.32-1.46)
EFV/FTC/TDF vs. BIC/FTC/TAF	2.31 (2.21-2.41)
Favors other backbone	Favors FTC/TAF
ABC/3TC (all) vs. FTC/TAF (all)	1.05 (1.02-1.07)
FTC/TDF (all) vs. FTC/TAF (all)	1.87 (1.84-1.90)
Favors other 3rd agent	Favors BIC/FTC/TAF
DTG + FTC/TAF vs. BIC/FTC/TAF	1.83 (1.74-1.93)
DRV/r or DRV/c + FTC/TAF vs. BIC/FTC/TAF	2.63 (2.47-2.80)
ATV/r or ATV/c + FTC/TAF vs. BIC/FTC/TAF	2.95 (2.57-3.39)

*Covariates include age group, gender, geographic region, insurance type, index year, pre-index medications, and number of unique prescriptions on index date

Limitations

♦ Patients were primarily covered by commercial insurance, and results may differ for Medicaid and Medicare populations
♦ The geographic spread of patients is skewed towards the South.
♦ Since newer regimens are less likely to be displaced by new entrants, availability of new regimens could have biased older regimens towards having shorter persistence

Conclusions

♦ Among US adult PLWH, STRs used as first-line therapy were associated with longer persistence on first-line therapy compared to MTRs
♦ The proportion of patients remaining on therapy at 6 or 12 months was highest for BIC/FTC/TAF, and BIC/FTC/TAF was associated with a lower risk of discontinuation compared to other regimens
♦ Among the NRTI backbones, FTC/TAF-based regimens had greater persistence than ABC/3TC or FTC/TDF-based regimens

References

1. NaykuM, Beer L, Shu F. Non-persistence to antiretroviral therapy among adults receiving HIV medical care in the United States. AIDS Care. 2019;31(5):599-608.
2. Department of Health and Human Services. What is HIV/AIDS? https://www.aids.gov/hiv-aids-basics/hiv-aids-101/what-is-hiv-aids/. Accessed Sep 17, 2020