Real-World Adherence of HIV-1 Oral Pre-Exposure Prophylaxis Regimens in the USA: A Group-Based Trajectory Modeling Approach

THPEC172

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Conclusions

- This study describes real-world adherence to oral pre-exposure prophylaxis (PrEP) using prescription data and identified population characteristics that are associated with adherence trajectories in the USA
- A total of 76,212 eligible PrEP-naïve individuals initiated oral PrEP between January 2021 and December 2022
  - Individuals were categorized into four adherence-trajectory groups using group-based trajectory modeling (GBTM): early low (15%), delayed low (21%), medium (26%), and high (37%) adherence
  - Most cisgender men (CGM) aged ≥35 years using emtricitabine/tenofovir alafenamide (F/TAF) demonstrated high adherence, while most cisgender women (CGW) aged <35 years using emtricitabine/tenofovir disoproxil fumarate (F/TDF) had low adherence
- These results underscore the importance of strategies for increasing adherence in priority populations to help reach HIV-1 prevention goals as part of the 'Ending the HIV Epidemic in the US' (EHE) initiative

Plain Language Summary

- Medication taken before exposure to HIV-1 can prevent infection; however, this depends on people taking their medication consistently as instructed by their healthcare provider
- This study used prescription data from 2021–2022 to see how often people took their medication in the real world, and if this was influenced by population characteristics
- By examining prescription refills, it was found that 37% of people had high levels of adherence (took their medicine as prescribed), 26% had medium adherence, and 37% had low levels of adherence
  - The type of HIV-1 prevention medication, gender identity, age, region, and race/ethnicity all affected the level of adherence
  - Most cisgender men aged ≥35 years receiving a type of HIV-1 prevention medication called emtricitabine/tenofovir alafenamide had high levels of adherence, while most cisgender women aged <35 years using emtricitabine/tenofovir disoproxil fumarate had low levels of adherence
- These results stress the need to make sure that people can access and use their medication, and to remove any barriers that may stop or prevent its consistent use

Background

- Daily oral HIV-1 PrEP with F/TDF or F/TAF is highly effective at preventing HIV-1 acquisition when taken as prescribed[1,2]
- In a study of men who have sex with men (MSM), four doses per week of F/TDF corresponded with a 96% reduction in HIV-1 risk[3], but sub-optimal adherence to PrEP is common, which reduces its real-world effectiveness[4]
  - Managing PrEP adherence is a key strategy of the EHE initiative to reduce HIV-1 incidence toward national 2030 HIV-1 prevention goals[5]
  - Barriers to PrEP adherence are broad and include lack of knowledge and awareness, socio-economic factors, stigma, and access difficulties[6]
- Understanding the population factors affecting real-world adherence to PrEP is critical to optimizing PrEP care delivery and prioritizing resources to support effective PrEP use[7]

Objective

- To use GBTM in a retrospective observational study to describe real-world, population-level adherence to oral PrEP regimens and to assess the associated correlates of adherence using a Classification and Regression Tree (CART)

Methods

Population

- HIV-negative individuals aged ≥18 years were identified from the IQVIA Longitudinal Prescription and Diagnosis Database (LRxDx)[8,9]
  - Eligible individuals were PrEP naïve prior to January 2021 and had initiated oral F/TDF, F/TAF, or generic F/TDF (gF/TDx) between January 2021 and December 2022
- Transgender men (TGM) and women (TGW) were identified by a highly specified algorithm incorporating claims for gender dysphoria and gender-affirming surgery or hormone therapy
  - Individuals not identified as transgender were classified as CGM or CGW

Evaluation of Adherence

- Following first prescription, adherence (defined as prescription refill) was observed over seven 30-day windows; proportion of days covered (PDC) was calculated for each 30-day window
  - As new HIV-1 infections resulted in PrEP discontinuation and disrupted adherence patterns, individuals acquiring HIV-1 during adherence observation windows were excluded
- GBTM was used to identify PDC-based adherence patterns[10–12] and characteristics driving adherence trajectories were assessed using CART, a decision tree algorithm that recursively splits data to maximize homogeneity within subsets
- Adherence trajectory distributions were assessed in subgroups of participants formed from all combinations of the top drivers of adherence

Results

Population

- Among 76,212 new PrEP users (median age, 33 years; range, 18–84 years), the majority were CGM (87%), non-Hispanic White (63%), resided in EHE jurisdictions (57%), and used gF/TDF only (54%) (**Table 1**)
- Individuals were classified into four adherence-trajectory groups: early low (15%), delayed low (21%), medium (26%), and high (37%) adherence (**Figure 1**)

Table 1. Population Demographics and Characteristics Stratified by Oral PrEP Adherence-Trajectory Groups

	All (N=76,212)	Early Low (n=11,710)	Delayed Low (n=16,303)	Medium (n=19,840)	High (n=28,359)
Median (range) age, years	33.0 (18.0, 84.0)	31.0 (18.0, 84.0)	31.0 (18.0, 84.0)	33.0 (18.0, 84.0)	34.0 (18.0, 84.0)
Age groups, n (%)					
18–29 years	27,764 (36.4)	5152 (44.0)	7111 (43.6)	7183 (36.2)	8318 (29.3)
30–39 years	23,110 (30.3)	3222 (27.5)	4682 (28.7)	6110 (30.8)	9096 (32.1)
40–49 years	11,665 (15.3)	1534 (13.1)	2132 (13.1)	3075 (15.5)	4924 (17.4)
≥50 years	13,673 (17.9)	1802 (15.4)	2378 (14.6)	3472 (17.5)	6021 (21.2)
Gender identity, n (%)					
CGM	66,308 (87.0)	8689 (74.2)	13,615 (83.5)	17,868 (90.1)	26,136 (92.2)
CGW	8188 (10.7)	2755 (23.5)	2292 (14.1)	1459 (7.4)	1682 (5.9)
TGW	1003 (1.3)	165 (1.4)	236 (1.5)	296 (1.5)	306 (1.1)
TGM	713 (0.9)	101 (0.9)	160 (1.0)	217 (1.1)	235 (0.8)
Race/ethnicity, n (%)					
Asian and other	3151 (4.1)	466 (4.0)	680 (4.2)	885 (4.5)	1120 (3.9)
Non-Hispanic Black	11,759 (15.4)	2352 (20.1)	2866 (17.6)	2706 (13.6)	3835 (13.5)
Hispanic	13,397 (17.6)	2169 (18.5)	3068 (18.8)	3377 (17.0)	4783 (16.9)
Non-Hispanic White	47,905 (62.9)	6723 (57.4)	9689 (59.4)	12,872 (64.9)	18,621 (65.7)
Region[a], n (%)					
Midwest	11,277 (14.8)	1638 (14.0)	2187 (13.4)	3313 (16.7)	4139 (14.6)
Northeast	15,669 (20.6)	2336 (19.9)	3135 (19.2)	4037 (20.3)	6161 (21.7)
South	32,850 (43.1)	5166 (44.1)	7445 (45.7)	7709 (38.9)	12,350 (44.2)
West	16,413 (21.5)	2570 (30.0)	3536 (21.7)	4779 (24.1)	5528 (19.5)
Regimen, n (%)					
F/TDF only	4047 (5.3)	1153 (9.9)	1378 (8.5)	657 (3.3)	859 (3.0)
F/TAF only	25,885 (34.0)	3003 (25.6)	5743 (35.2)	5272 (26.6)	11,867 (41.9)
gF/TDF only	41,217 (54.1)	7515 (64.2)	8677 (53.2)	12,155 (61.3)	12,870 (45.4)
Mixed	5063 (6.6)	39 (0.3)	505 (3.1)	1756 (8.9)	2763 (9.7)
EHE, n (%)[b]	43,684 (57.3)	6860 (58.6)	9109 (55.9)	11,205 (56.5)	16,510 (58.2)
Any diabetes, n (%)	5639 (7.4)	860 (7.3)	1090 (6.7)	1459 (7.4)	2230 (7.9)
Any high-risk factors, n (%)	34,150 (44.8)	5296 (45.2)	6778 (41.6)	9298 (46.9)	12,778 (45.1)
Any hypertension, n (%)	14,833 (19.5)	2193 (18.7)	2840 (17.4)	3703 (18.7)	6097 (21.5)
Any STD, n (%)	7967 (10.5)	1373 (11.7)	1668 (10.2)	2034 (10.3)	2892 (10.2)

[a]Region data were missing for 3 (0.004%) individuals. [b]EHE, data were missing for 556 (0.7%) individuals. Comorbidity data were collected at any point during the individual's history.
CGM, cisgender men; CGW, cisgender women; EHE, 'Ending the HIV Epidemic in the US'; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; gF/TDF, generic F/TDF; PrEP, pre-exposure prophylaxis; STD, sexually transmitted disease; TGM, transgender men; TGW, transgender women.

Results (cont.)

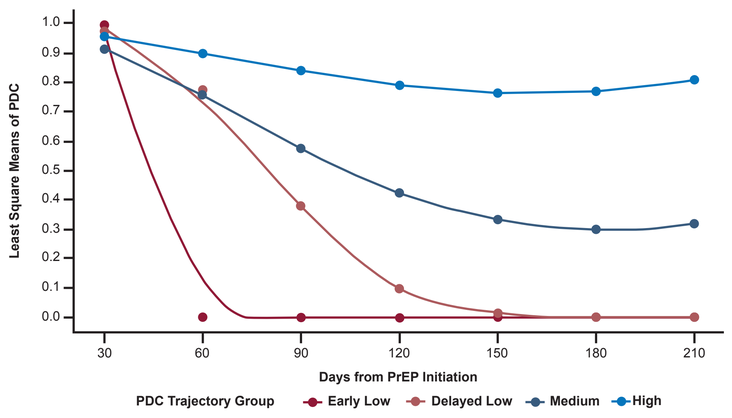
Potential Drivers of Adherence Trajectories (CART)

- PrEP regimen was the most important factor (i.e., based on explanatory power) associated with adherence trajectory (**Figure 2**)
  - Among F/TAF only users, 46% were in the high and 12% were in early-low group; among F/TDF users (brand and generic), 30% were in the high and 19% were in the early-low group
- Other factors, in order of importance, were gender identity, age, region, and race/ethnicity (**Figure 2**)

Factors Accounting for Adherence-Trajectory Categorization

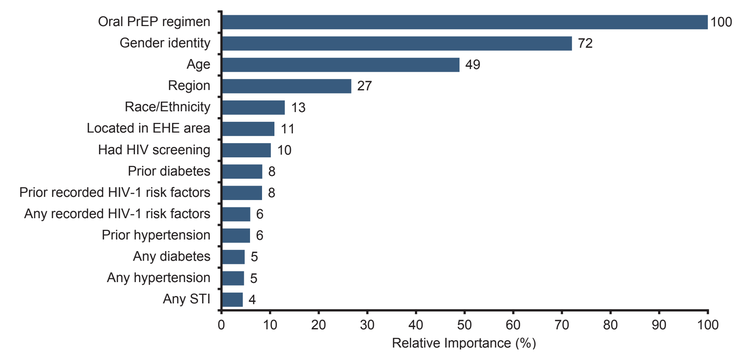
- When participants were grouped by regimen, gender identity, and race/ethnicity, CGM using F/TAF only demonstrated the highest adherence, while most CGW with any F/TDF had low adherence (**Figure 3**)
- Among all 26 subgroups defined by the five top drivers of adherence, the four subgroups with the highest adherence included CGM aged ≥35 years using F/TAF (**Figure 4**)
  - Of the subgroups with ≥40% of individuals in the high adherence trajectory, the majority were aged ≥35 years and using F/TAF only (7/10 for each)
  - CGW aged <35 years had the lowest adherence, followed CGW aged ≥35 years

Figure 1. Proportion of Days Covered for Oral PrEP Adherence-Trajectory Groups (GBTM Analysis)



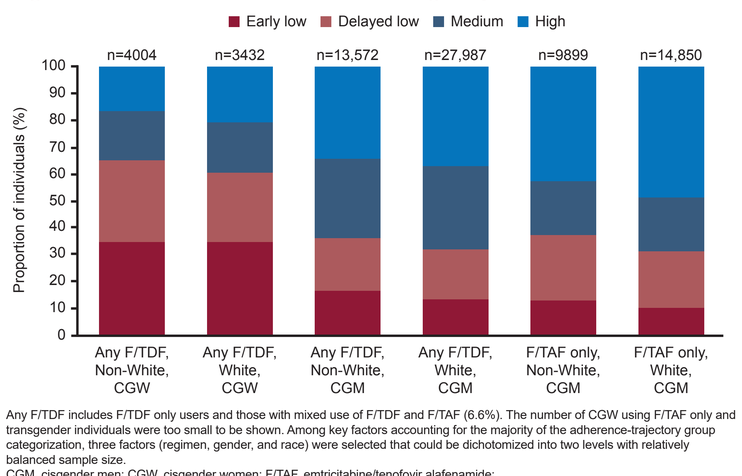
GBTM, group-based trajectory modeling; PDC, proportion of days covered; PrEP, pre-exposure prophylaxis.

Figure 2. Relative Importance of Drivers of Adherence Trajectories in CART Analysis



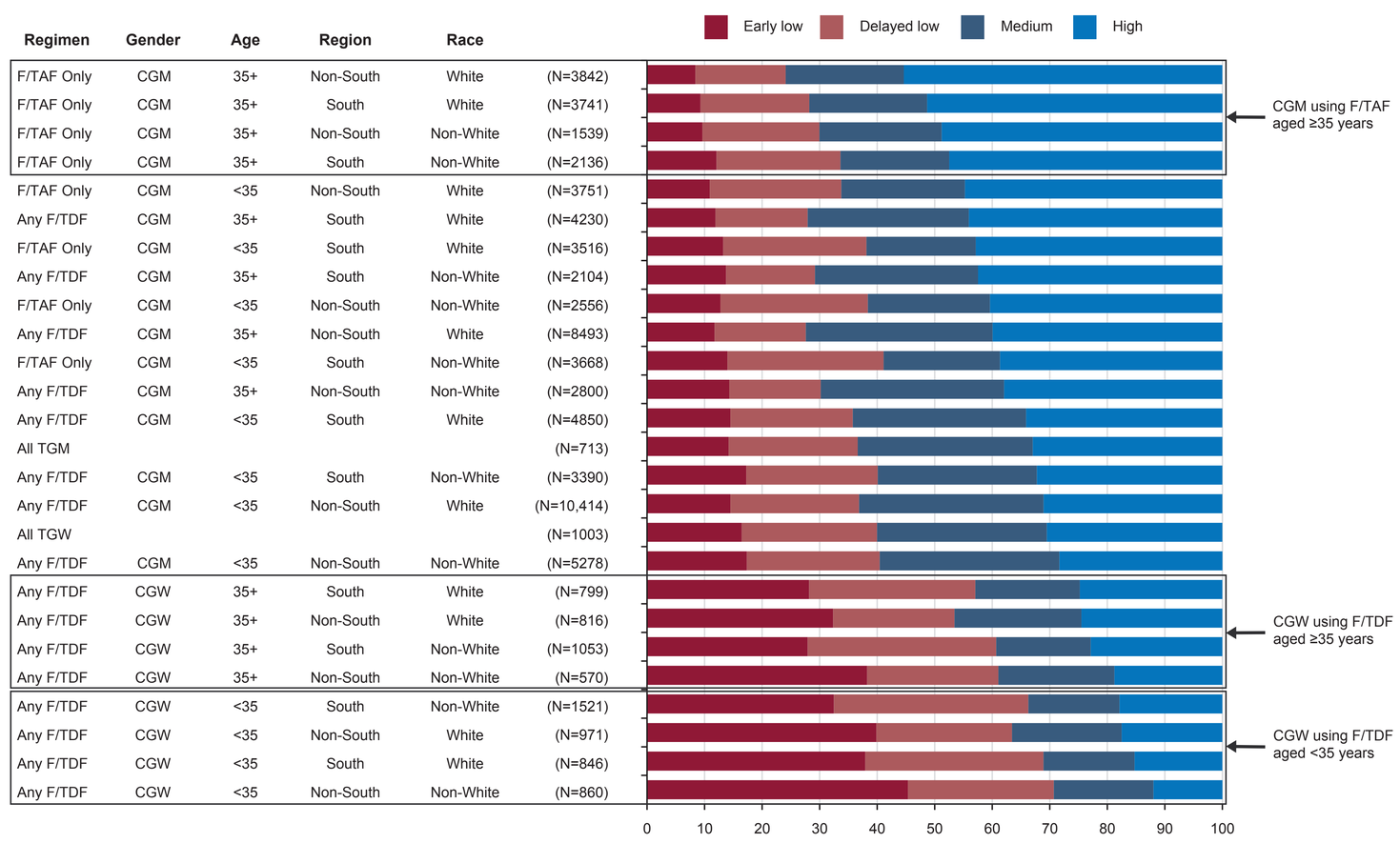
Comorbidities were identified in each medical record at any time and at a time prior to initiating PrEP. HIV–1 risk factors on record in the claims dataset were identified using a group of ICD-10 and CPT codes that were highly recommended for PrEP use by providers and included any diagnoses of an STI (A50–64), contact with, and exposure to, communicable diseases (Z20.6, Z20.2, Z20.828, Z20.9), high-risk sexual behavior (Z72.51-Z72.53), other hazardous exposures (Z77.21, Z77.9), contact with hypodermic needle (W46.0, W46.1), long-term prophylaxis (Z79.899), HIV prevention counseling (99401-99404), and HIV screening procedures (86689, 86701-86703, 87389, 87534-87538, G0432-G0435).
CART, Classification and Regression Tree; CPT, Current Procedural Terminology; EHE, 'Ending the HIV Epidemic in the US'; ICD, International Classification of Diseases; PrEP, pre-exposure prophylaxis; STI, sexually transmitted infection.

Figure 3. Adherence in Selected Subgroup



Any F/TDF includes F/TDF only users and those with mixed use of F/TDF and F/TAF (6.6%). The number of CGW using F/TAF only and transgender individuals were too small to be shown. Among key factors accounting for the majority of the adherence-trajectory group categorization, three factors (regimen, gender, and race) were selected that could be dichotomized into two levels with relatively balanced sample size.
CGM, cisgender men; CGW, cisgender women; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate.

Figure 4. Adherence Across All Subgroups



Characteristic combinations were ordered from highest proportion of individuals in the high adherence-trajectory group to lowest. Any F/TDF includes F/TDF users only and those with mixed use of F/TDF and F/TAF (6.6%).
CGM, cisgender men; CGW, cisgender women; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; TGM, transgender men; TGW, transgender women.

Limitations

- Data collection based on pharmacy claims may lead to the omission of clinically-relevant data in real-world settings
- Dispensing of a PrEP prescription was used as an indirect measure of adherence; no objective measurement or validation of adherence was available
- The algorithm used for gender categorization may underreport gender identities
- Individual behavioral-level factors affecting adherence were not accessible/identifiable in the database
- In the GBTM, adherence was observed in a 210-day window after PrEP initiation to avoid survivor bias and the impact on new HIV diagnosis; therefore, long-term adherence was not measured
- The study only assessed daily oral PrEP; therefore, injectable PrEP was not considered

References: 1. Centers for Disease Control and Prevention. PrEP Medication Guide: Reduce Your Risk of Getting HIV. Available at: https://www.cdc.gov/stophivtogether/library/topics/prevention/brochures/cdc-lsht-prevention-brochure-prep-medication-guide-patient.pdf (Accessed June 2024). **2.** Centers for Disease Control and Prevention. Pre-Exposure Prophylaxis (PrEP). Available at: https://www.cdc.gov/hiv/risk/prep/ (Accessed June 2024). **3.** Anderson PL, et al. *Sci Transl Med.* 2012;4(151):151ra125. **4.** Zhang J, et al. *Lancet HIV*. 2022; 9(4):e254–68. **5.** Centers for Disease Control and Prevention. About the Ending the HIV Epidemic in the U.S. Pillars. Available at: https://www.cdc.gov/endhiv/about-ehe/pillars.html (Accessed June 2024). **6.** Sidebottom D, et al. *BMC Infect Dis*. 2018;18(1):581. **7.** Reed JB, et al. *J Int AIDS Soc.* 2021;24:e25827. **8.** IQVIA. Available IQVIA data. Available at: https://www.iqvia.com/insights/the-iqvia-institute/available-iqvia-data (Accessed June 2024). **9.** IQVIA. IQVIA Longitudinal Prescription Data (LRx) Fact Sheet. Available at: https://www.iqvia.com/-/media/iqvia/pdfs/uk/fact-sheets/iqvia-longitudinal-prescription-data.pdf (Accessed June 2024). **10.** Nagin DS. *Ann Nutr Metab.* 2014;65(2-3):205–10. **11.** Stoner MCD, et al. *AIDS Behav.* 2021;25(7):2046–53. **12.** Cooney EE, et al. *Ann Epidemiol.* 2022;70:23–31.

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