PRE-EXPOSURE PROPHYLAXIS ADHERENCE TRAJECTORIES AND HIV AND SEXUALLY TRANSMITTED INFECTIONS RISK

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BACKGROUND

- Preexposure prophylaxis (PrEP) is effective in preventing HIV transmission. However, non-adherence limits its efficacy.
- Group-based trajectory modeling (GBTM) can be used to identify meaningful subgroups of PrEP use adherence trajectories with potentially different HIV risk Profiles.
- **Objective:** To examine the association between adherence trajectories of PrEP use and the risk of HIV and sexually transmitted infection (STI) acquisition among PrEP users.

METHODS

- **Design:** **Retrospective cohort study**
- **Source:** 2012-2021 MarketScan Commercial Insurance Research Database
- **Cohort:** Patients 12-64 years of age prescribed (≥30 days) tenofovir-disoproxil-fumurate and tenofovir-alafenamide with emtricitabine for PrEP using an algorithm developed by the CDC
  - We required individuals to have no HIV outcome and continuous enrollment for 180 days after index date
  - Exclusion criteria: Individuals with diagnosis codes (using International Classification of Diseases, Ninth [ICD-9] and Tenth [ICD-10] Revisions) or prescriptions for HIV, hepatitis B virus, or HIV postexposure prophylaxis within the year before PrEP initiation and 30 days after initiation.
- **Index Date:** Day 31 after PrEP initiation
- **Data Analysis:**
- GBTM: Longitudinal assessment of 15-day PDC over 720 days after index date
- IPTW Cox proportional hazards regression to compare risk of HIV between identified PrEP trajectory groups
  - Follow-up from 180 days after index until HIV outcome
  - HIV outcome: 1 inpatient or 2 outpatient or 2 backbone medications
- IPTW-weighted Poisson regression models to compare STI diagnosis rates between groups

RESULTS

- Of 23,258 new PrEP users, 4 unique trajectories identified: minimal use (10.5%), rapidly-declining (25.4%), gradually-declining (24.3%), and consistently high (39.8%) groups **(Table 1 and Figure 1)**.
- Compared to the PrEP minimal use group, the consistently high adherence (adjusted hazard ratio [aHR]: 0.50 [0.30-0.84]) and gradually declining (aHR: 0.53 [0.31-0.90]) groups were associated with lower risk of HIV (**Table 2**).
- Compared with the PrEP minimal use group, the consistently high (adjusted incidence rate ratio [aIRR]: 2.06 [1.64–2.58]), gradually declining (aIRR: 1.73 [1.38–2.18]) and rapidly declining (aIRR: 1.35 [1.07–1.72]) adherence groups were associated with higher risk of STI (**Table 3**).

Table 1: Demographic characteristics of PrEP users by trajectory group, using 2012-2021 MarketScan database (N=23,258)

	Consistently High (39.8%)	Gradually Declining (24.3%)	Rapidly Declining (25.4%)	Minimal Use (10.5%)	Max SMD* after IPTW
N	9246	5658	5918	2436	
Male	9113 (98.6%)	5529 (97.7%)	5616 (94.9%)	1975 (81.1%)	0.06
Age Group					
12-24	866 (9.4%)	1239 (21.9%)	1762 (29.8%)	834 (34.2%)	0.05
25-34	2869 (31.0%)	2042 (36.1%)	2007 (33.9%)	699 (28.7%)	0.04
35-44	2443 (26.4%)	1200 (21.2%)	1072 (18.1%)	425 (17.4%)	0.06
>=45	3068 (33.2%)	1177 (20.8%)	1077 (18.2%)	478 (19.6%)	0.04
AUD	161 (1.7)	128 (2.3)	159 (2.7)	61 (2.5%)	0.03
SUD	361 (3.9)	318 (5.6)	388 (6.6)	186 (7.6)	0.06
SMI	1169 (12.6)	863 (15.3)	1045 (17.7)	432 (17.7)	0.04
Previous STI	6375 (68.9)	3781 (66.8)	3896 (65.8)	1364 (56.0)	0.03

SMI: Serious Mental illness (bipolar disorder, panic disorder, PTSD, OCD, borderline personality disorder; STI: Sexually Transmitted Infection (Gonorrhea, chlamydia, syphilis); AUD: Alcohol Use Disorder; SUD: Substance Use Disorder
* SMD >0.10 was considered a non-negligible difference.

Figure 1: Adherence trajectories of PrEP use over 720 days after index date (N=23,258)

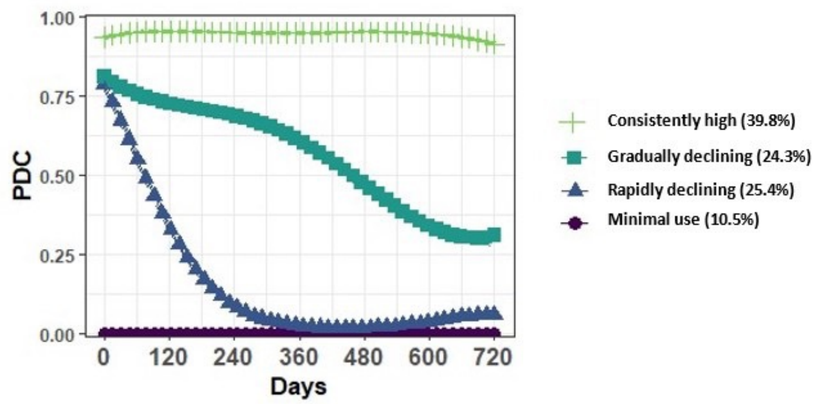

Table 2: Risk of HIV among PrEP users by trajectory group (N=23,258)

PrEP Trajectories	Consistently high (n=9246)	Gradually declining (n=5658)	Rapidly Declining (n=5918)	Minimal use (n=2436)
Crude Incidence per 10,000 person-years	71.41	59.90	70.93	87.88
Mean Follow-up, days (SD)	392.51 (189.55)	409.27 (173.89)	365.23 (183.42)	358.04 (189.33)
Adjusted HR (95% C.I.)[a]	0.50 (0.30-0.84)	0.53 (0.31-0.90)	0.71 (0.43-1.18)	Reference

HR: Hazard Ratio; PrEP, preexposure prophylaxis; CI: Confidence Interval; SD: Standard Deviation
[a]HIV testing was controlled as a time-varying covariate (adjusted HR, 1.22; 95% CI, 1.07-1.40).

Table 3: Risk of STIs among PrEP users by trajectory group (N=23,258)

PrEP Trajectories	Consistently high (n=9246)	Gradually declining (n=5658)	Rapidly Declining (n=5918)	Minimal use (n=2436)
Crude Incidence per 10,000 person-years	170.09	128.85	80.67	50.37
Mean Follow-up, days	572.51 (189.55)	589.27 (173.89)	545.23 (183.42)	538.04 (189.33)
Adjusted IRR (95% C.I.)[a]	2.06 (1.64-2.58)	1.73 (1.38-2.18)	1.35 (1.07-1.72)	Reference

IRR: incidence rate ratio; PrEP, preexposure prophylaxis; CI: Confidence Interval; SD: Standard Deviation
[a]STI testing was controlled as a time-varying covariate (adjusted incident rate ratio, 1.26; 95% CI, 1.24-1.28).

Discussion

- <40% of PrEP users were consistently adherent in the first 2 years of initiation.
- Compared with the minimal PrEP use group, consistently high PrEP adherence and gradually declining PrEP adherence were associated with significantly decreased risk of HIV acquisition. However, those groups also had higher rates of STI.
- Limitations: The database did not have race data and is only generalizable to commercially insured PrEP users.
- Strength: This is the first study applying GBTM to a large commercial claims database to measure PrEP adherence.

Conclusions

In this retrospective cohort study of 23,258 examining adherence trajectories of PrEP use, individuals in the consistently high and gradually declining adherence trajectories were associated with lower HIV risk but with higher STI risk compared to the minimal PrEP use group.

Public health efforts centered on adherence are needed to ensure PrEP users are protected from HIV and to achieve the long-term goal of HIV eradication.