

# Association Between Use of Tenofovir Alafenamide for HIV Pre-Exposure Prophylaxis and Statin Initiation in Adults in an Integrated Health System in California

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## Background

- Two oral daily pre-exposure prophylaxis (PrEP) approved by the US FDA
  - Emtricitabine/Tenofovir Disoproxil Fumarate (TDF) – 2012
  - Emtricitabine/Tenofovir Alafenamide Fumarate (TAF) – 2019
- Switching from TDF to TAF can worsen the lipid profile in people with HIV.
- In DISCOVER PrEP trial, decrease in total & low-density lipoprotein cholesterol levels from baseline was smaller in TAF user (vs TDF users).
- There is a paucity of data regarding a possible association of TAF use and statin initiation among people on PrEP.

## Objective and Hypothesis

- Objective:** To compare the difference in statin initiation among adults initiating PrEP with TAF vs with TDF.
- Hypothesis:** Adults who initiated PrEP with TAF are more likely to start a new statin compared with adults initiating PrEP with TDF.

## Study Design, Setting and Population

- Design:** Retrospective cohort study
- Study Setting:** Kaiser Permanente Southern California, an integrated health care delivery system
- Study Population:** Adult ( $\geq 18$  years) members who initiated PrEP during Oct. 2019 - May 2022 without statin use at the time of PrEP initiation. Persons with documented HIV infection, chronic kidney disease, or abnormal labs at baseline or had  $< 30$  days follow-up were excluded.

## Methods

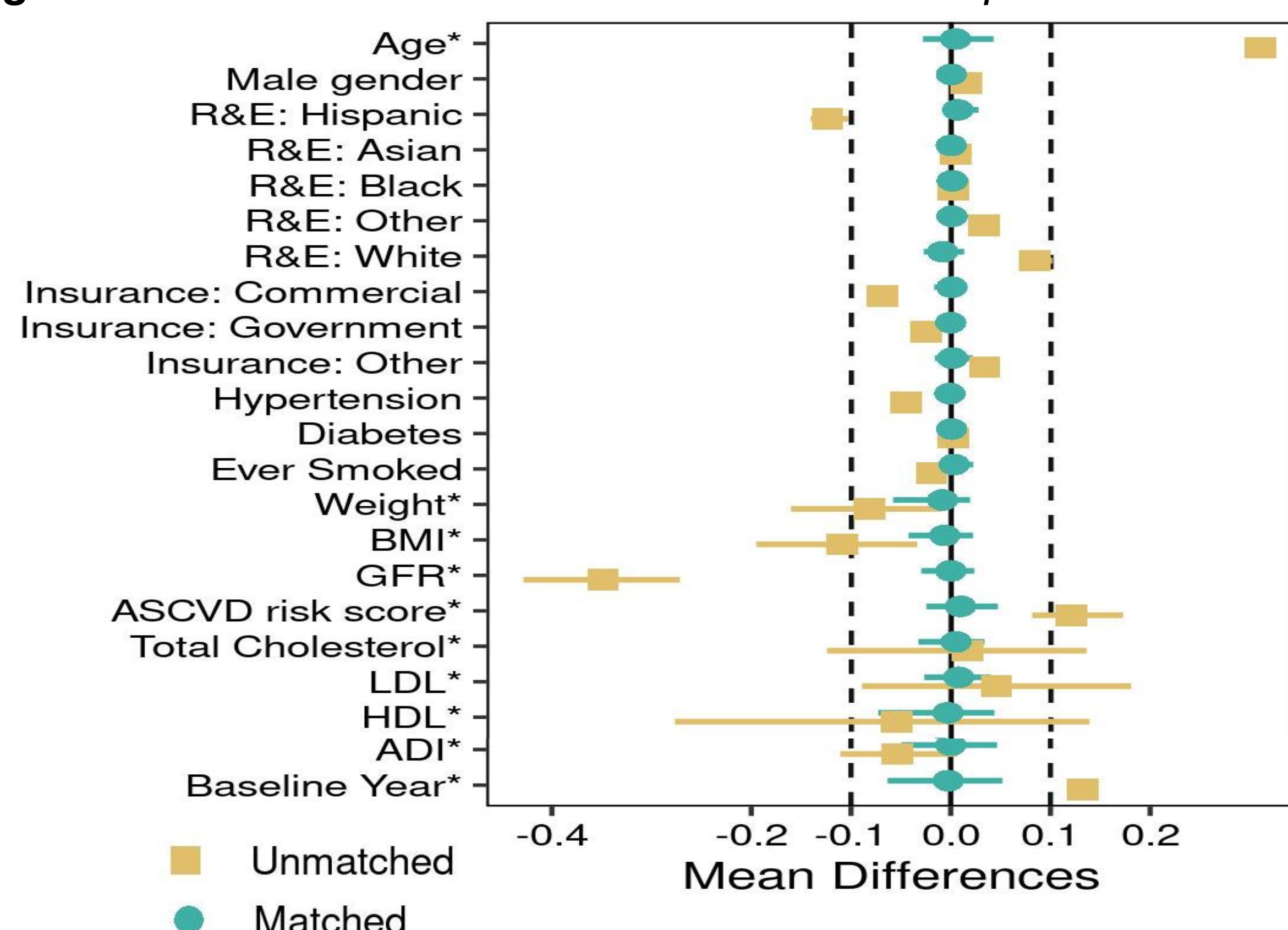
- Exposure:** PrEP initiation with TAF or TDF (control)
- Index date:** PrEP initiation during the study period
- Matching:** Individuals initiating TAF were 1:4 matched to those initiating TDF using a propensity score at index date
- Propensity score:** Structured based on baseline demographics (age at PrEP initiation, sex, race & ethnicity), insurance type, medical center, neighborhood deprivation index, calendar year at PrEP initiation; baseline body mass index, lipids, atherosclerotic cardiovascular disease (ASCVD) risk score; smoking history, diabetes, dyslipidemia, and hypertension.
- Outcome:** Statin initiation ascertained through on pharmacy (sold) data.
- Follow-up:** Since PrEP initiation, for a maximum of 2 years or until June 30, 2022 (end of study period)
- Risk estimate:**
  - odds ratio (OR) and risk difference (RD), estimated using logistic regression with g-computation
  - hazard ratio (HR), estimated using Cox proportional hazards regression
- Subgroup analysis:** Among people aged 40 years or older at index date
- Informed consent:** waived by the institutional review committee
- Software:** R 4.3.0/RStudio
- Packages:** mice, marginaleffects, MatchIt

## Results

### Overview of the Unmatched and Matched Cohort

- Unmatched cohort: 6,149 eligible individuals
  - Majority were on TDF (TDF: 5,767, TAF: 382)
  - Mostly male (97%) with mean age 34 years (SD: 10)
  - Mostly non-Hispanic White (35%) or Hispanic (42%)
- Balance of covariates between TAF and TDF users was generally achieved across 50 imputations (Figure 1).
- Matched cohort: 382 adults initiating TAF (mean age of 36 years, 99% male, 31% Hispanic, 42% non-Hispanic white, 7% non-Hispanic Black) and 1,528 matched adults initiating TDF.

Figure 1. Love Plot for Covariate Balance Across Imputations



### Main analysis results:

- Statin initiation was higher in TAF users than in matched TDF users.
- TAF use was associated with an increased likelihood of statin initiation compared with TDF use based on estimated RD and OR (Table 1).
- In the time-to-event analysis, the association between TAF and statin initiation was not statistically significant.

### Subgroup analysis results (among those aged $\geq 40$ years at index date):

- A total of 92 persons initiated TAF and 368 matched persons initiated TDF.
- The difference in the likelihood of statin initiation associated with TAF (vs. TDF) was greater among those who initiated PrEP at age of 40 or older than that observed in the main analysis of individuals from all age groups.
- In the time-to-event analysis, the association between TAF and statin initiation was not statistically significant.

Table 1. Differences in Risk of Statin Initiation between TAF users and Matched TDF users

Population	Incidence per 1,000 person-years		Measures of Difference (95% CI)		
	TAF	Matched TDF	RD	OR	HR
main cohort (n <sub>TAF</sub> = 382)	0.05	0.03 (0.02, 0.04)	0.9% (0.4, 1.3)	2.3 (1.4, 3.9)	2.3 (0.8, 6.7)
subgroup (individuals aged $\geq 40$ at index date (n <sub>TAF</sub> = 92))	0.18	0.1 (0.06, 0.15)	4.2% (1.8, 6.7)	3.1 (1.6, 5.7)	2.7 (0.9, 8.5)

## Discussion and Conclusions

- Initiating PrEP with TAF compared to TDF was associated with a greater likelihood of statin initiation in this well-matched cohort study.
- The observed increase in the likelihood of statin initiation associated with TAF use was more prominent among those who initiated PrEP at age 40 or older.
- The adherence to PrEP was not measured, therefore the potential cumulative effect is not accounted for in the analysis.
- Close monitoring of lipid levels and other risk factors for cardiovascular disease may be beneficial for people initiating TAF, especially those aged 40 or older.
- Studies in large diverse populations with longer follow-up are needed to confirm our findings and to evaluate the effects of PrEP on cardiovascular outcomes.