

# A Pooled Analysis of the Effect of Adherence on the Renal Safety of FTC/TDF (Truvada) for PrEP: 7 International Demonstration Projects

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## Background

- Clinical trials have reported that use of once daily oral FTC/TDF (emtricitabine/tenofovir disoproxil fumarate) for HIV pre-exposure prophylaxis (PrEP) substantially reduces HIV-1 acquisition for individuals at high sexual risk, particularly in the population of men who have sex with men (MSM).<sup>1,2</sup>
- The efficacy of FTC/TDF for PrEP greatly depends on adherence, however, adverse events (AEs) may impact PrEP use and adherence. Renal AEs or elevations of serum creatinine were reported in 1-4% participants taking PrEP in clinical trials.<sup>1,2</sup>
- Dried blood spot (DBS) analyses of tenofovir-diphosphate (TFV-DP, in femtomoles per punch) in red blood cells measure chronic TDF drug use, which provide an integrated, objective evaluation of adherence for individuals taking FTC/TDF for PrEP.

## Objective

- To evaluate the association between PrEP adherence, objectively measured by TFV-DP concentration in DBS, with the rate of renal AEs and lab abnormalities in a large, globally diverse pool of PrEP demonstration projects.

## Methods

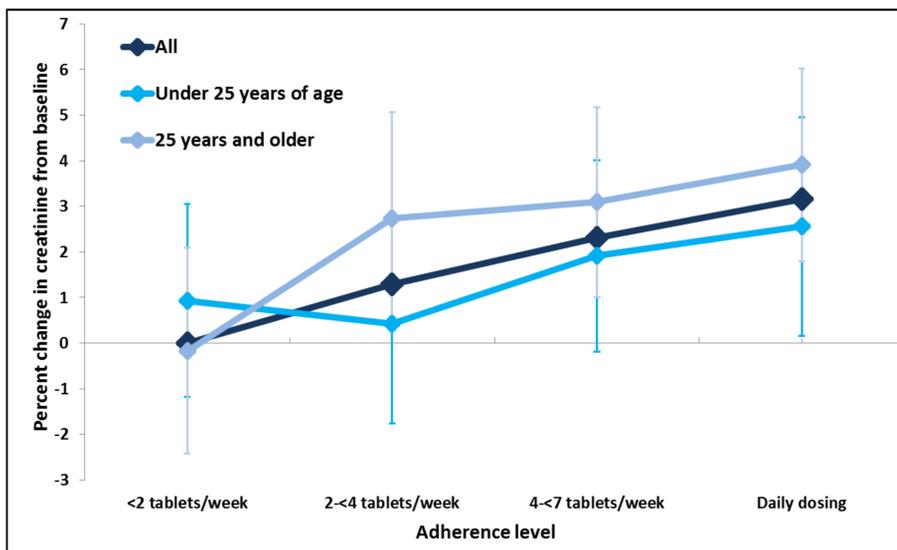
- Data were pooled from 7 open-label HIV prevention studies or demonstration projects. The mean TFV-DP concentration was determined for each participant based on DBS from all follow up visits of the participant. Categories of the mean TFV-DP DBS are used to define FTC/TDF for PrEP dosage equivalent.
- Demographics, on-treatment renal AE, and creatinine lab tests were collected at baseline and during follow-up visits for up to 1-year.
- Poisson regression was used to calculate incidence rates of renal AEs and lab abnormalities. Mixed linear regression was used to calculate the percent change and probability of creatinine over the threshold of 1.3mg/dl during the study period.

## Results

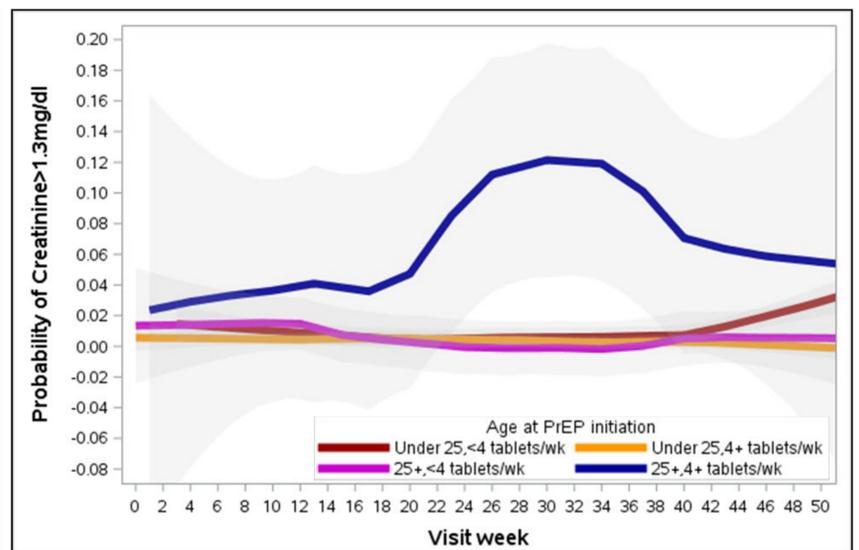
**Table 1. Incidence rate of renal adverse events for participants by DBS-measured PrEP adherence and age at PrEP initiation**

	Reported Renal Adverse Events			Creatinine > 1.3 mg/dl		
	Total N	N	Incidence Rate per 100 PYR (95% CI)	Total N	N	Incidence Rate per 100 PYR (95% CI)
<b>Adherence Level Measured in DBS (fmol/punch)</b>	2823	157		2157	72	
<350 (<2 tablets/week)	738	9	0.63 (0.27-1.48)	597	5	0.30 (0.09-0.95)
350-<700 (2-<4 tablets/week)	408	11	1.67 (0.80-3.51)	307	9	1.08 (0.42-2.79)
700-<1250 (4-<7 tablets/week)	1002	67	3.71 (2.13-6.47)	719	30	1.21 (0.51-2.88)
Daily dosing	675	70	4.77 (2.59-8.79)	534	28	1.36 (0.52-3.56)
<b>Age at PrEP initiation</b>						
<25	755	9	2.07 (1.07-3.97)	588	3	0.80 (0.26-2.47)
25-29	648	26	8.21 (5.59-12.06)	460	14	5.57 (3.30-9.41)
30-39	800	57	14.55 (11.22-18.86)	585	22	6.54 (4.30-9.93)
40+	602	63	19.00 (14.84-24.32)	508	31	10.32 (7.25-14.67)

**Figure 1. Least square means of percent creatinine change from baseline by level of adherence measured by TFV-DP in DBS**



**Figure 2. Probability (95% CI) of creatinine > 1.3 mg/dl during the study period by level of adherence measured by TFV-DP in DBS**



## Findings and Conclusions

- Among the 2,823 participants received FTC/TDF PrEP, 99% were men who have sex with men (MSM), with 50% in USA, 47% in South America, 2% in Asia, and 1% in Africa. The median age at PrEP initiation was 29 years (interquartile range, IQR, 24–38), and the median PrEP exposure was 8.4 months (IQR, 2.9–11.0).
- A total of 157 (5.6%) participants reported renal AEs within 1 year of PrEP initiation, with an incidence rate/100 person-years (IR, 95% confidence interval, CI) of 0.63 (0.27-1.48), 1.67 (0.80-3.51), 3.71 (2.13-6.47), and 4.77 (2.59-8.79), respectively, for participants taking <2, 2–3, 4–6, or 7+ tablets/week of PrEP.
- Of 2,157 participants with >1 creatinine test during follow-up, 72 (3.3%) had at least one test over 1.3 mg/dl, of whom 81%, 13%, and 7% were taking ≥4, 2–3, and <2 tablets/week of PrEP. Percent change of creatinine from baseline increased with higher level of adherence.
- Incidence of renal AE and creatinine over 1.3mg/dl increased with older age. The effect of FTC/TDF on creatinine increase was more marked for older than that for younger participants. Individuals who were 25 years and older and adhere at ≥4 tablets/week were more likely to have elevated creatinine, compared with younger or non-adherent individuals.
- These findings underscore the importance of assessing and monitoring renal function for individuals using FTC/TDF for PrEP.

## Acknowledgments

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## References

- Grant RM, Lama JR, Anderson PL, et al. Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men. *N Engl J Med*. 2010;363(27):2587-2599.
- Baeten J, Mugo N, Ndase P, Mujugira A, Donnell D, et al. The Partners PrEP Study: Enrollment of HIV-1 serodiscordant couples into a phase III, randomized trial of antiretroviral pre-exposure prophylaxis for HIV-1 prevention [Poster]. Paper presented at: 18th Biennial International AIDS Conference; July, 2010; Vienna, Austria.