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Background

- Men who have sex with men (MSM) bear the greatest burden of HIV-1 acquisition among individuals at risk, representing 66% of all new HIV infections in 2017.¹
- Since 2010, 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.^{2,3}
- The efficacy of FTC/TDF for PrEP greatly depends on adherence, estimated at 76% reduction in HIV infection if the individual takes 2 tablets per week, and over 90% for 4 tablets per week among MSM.^{2,3}
- Dried blood spot (DBS) analyses of tenofovir-diphosphate (TFV-DP, in femtomols 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 assess the pattern of FTC/TDF for PrEP use in a globally diverse MSM population;
- To evaluate the association between PrEP adherence, objectively measured by TFV-DP concentration in DBS, with the rate of new HIV infections in the pooled population.

Methods

- Data were pooled from 8 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 as <2 (less than 350 fmol/punch of TFV-DP), 2-3 (350-699 fmol/punch), 4-6 (700-1,249 fmol/punch), and ≥7 (≥1,250 fmol/punch) tablets of FTC/TDF PrEP per week.
- Demographics, HIV-1 infection status, and DBS measures of TFV-DP were collected at baseline and during follow-up visits.
- Logistic regression was used to estimate odds ratios for adherence, and Poisson regression to calculate incidence rates and incidence rate ratios of new HIV cases.

Results

- A total of 3,058 participants were given FTC/TDF PrEP and had at least one measurement of TFV-DP in DBS during follow-up visits up to 3.4 years.
- Of the 3,058 participants, 99% were men who have sex with men (MSM), 68% were in the U.S., 29% in South America, 2% in Asia, and 1% in Africa.
- In the pooled population, the median age at PrEP initiation was 30 years (interquartile range, IQR, 25-38), and the median PrEP exposure was 0.96 years (IQR, 0.90-1.39).

Results (Cont.)

Table 1. Number of participants by level of TFV-DP in DBS and odds ratios with corresponding 95% confidence interval of adherence by age at PrEP initiation

	<350 fmol/punch (<2 tablets/wk)		350-<700 fmol/punch (2-3 tablets/wk)		700-<1250 fmol/punch (4-6 tablets/wk)		1250+ fmol/punch (7+ tablets/wk)		Odds ratios (95% CI) for adherence (≥700 fmol/punch versus <700 fmol/ml as reference)
	N	%	N	%	N	%	N	%	
All Participants	780	26%	413	14%	1039	34%	826	27%	
Age at PrEP Initiation (Years) (Median, Q1-Q3)	26 (23-32)		29 (23-36)		32 (26-39)		34 (28-45)		
<25	292	40%	133	18%	192	26%	114	16%	0.30 (0.23-0.38)
25-29	205	29%	91	13%	240	34%	163	23%	0.73 (0.57-0.92)
30-39	192	21%	120	13%	344	38%	260	28%	Reference
≥40	81	12%	67	10%	258	37%	288	42%	1.53 (1.18-2.00)
Missing	10	56%	2	11%	5	28%	1	6%	N/A

Table 2. Incidence rate per 100 person-year and incidence rate ratio with corresponding 95% confidence intervals of new HIV infections by DBS measured adherence

Mean TFV-DP (fmol/punch) in DBS	Non-HIV Infected		HIV Infected		Incidence Rate Per 100 Person-Year (95% CI)	Incidence Rate Ratio (95% CI)
	N	%	N	%		
<350 (<2 tablets/week)	749	24.8%	31	75.6%	3.41 (2.37-4.90)	24.56 (7.48-80.63)
350-<700 (2-3 tablets/week)	406	13.5%	7	17.1%	1.59 (0.76-3.33)	11.44 (2.96-44.23)
700+ (4+ tablets/week)	1862	61.7%	3*	7.3%	0.14 (0.04-0.43)	Reference

‡: All 3 participants were MSM who had sustained a mean TFV-DP over 1000 fmol/punch for the first 6 months, but dropped to ~200 fmol/punch after and remained at low concentration for at least 3 months prior to the detection of HIV infection.

Findings and Conclusions

- In this multi-national pooled analysis of FTC/TDF PrEP use in a geographically diverse MSM population receiving PrEP, 26%, 14%, 34%, and 27% of all participants were taking <2, 2-3, 4-6, and ≥7 tablets of FTC/TDF PrEP per week, respectively.
- Participants under 30 years of age were less likely to remain adherent at ≥4 tablets/week, which is the established protective dosage of FTC/TDF PrEP. Participants 40 years of age and older were significantly associated with increased adherence.
- A total of 41 out of the 3,058 individuals tested HIV positive (IR=1.13/100 person-years exposure, 95% confidence interval, CI, 0.82-1.54), and 38 of the 41 cases (93%) had TFV-DP consistent with taking less than 4 FTC/TDF tablets/week.
- Individuals taking ≥4 tablets/week were protected from HIV infection at a low incidence rate of 0.14/100 person-years, compared with 3.41 and 1.59 for individuals who took <2 and 2-3 tablets/week.

References

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Figure 1. Number of participants and incidence rates (95% confidence interval) of new HIV infection in the pooled analyses by level of TFV-DP in DBS

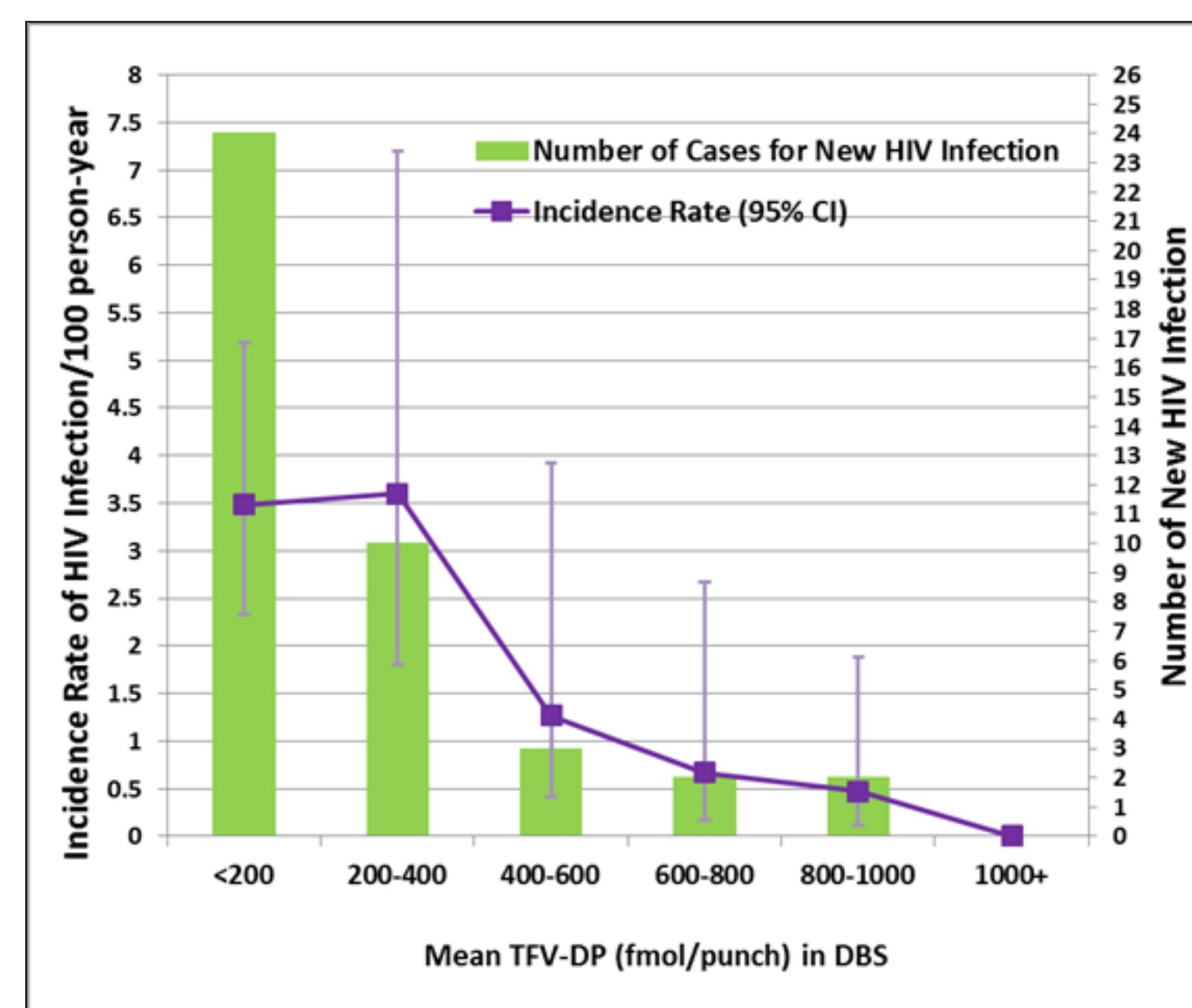
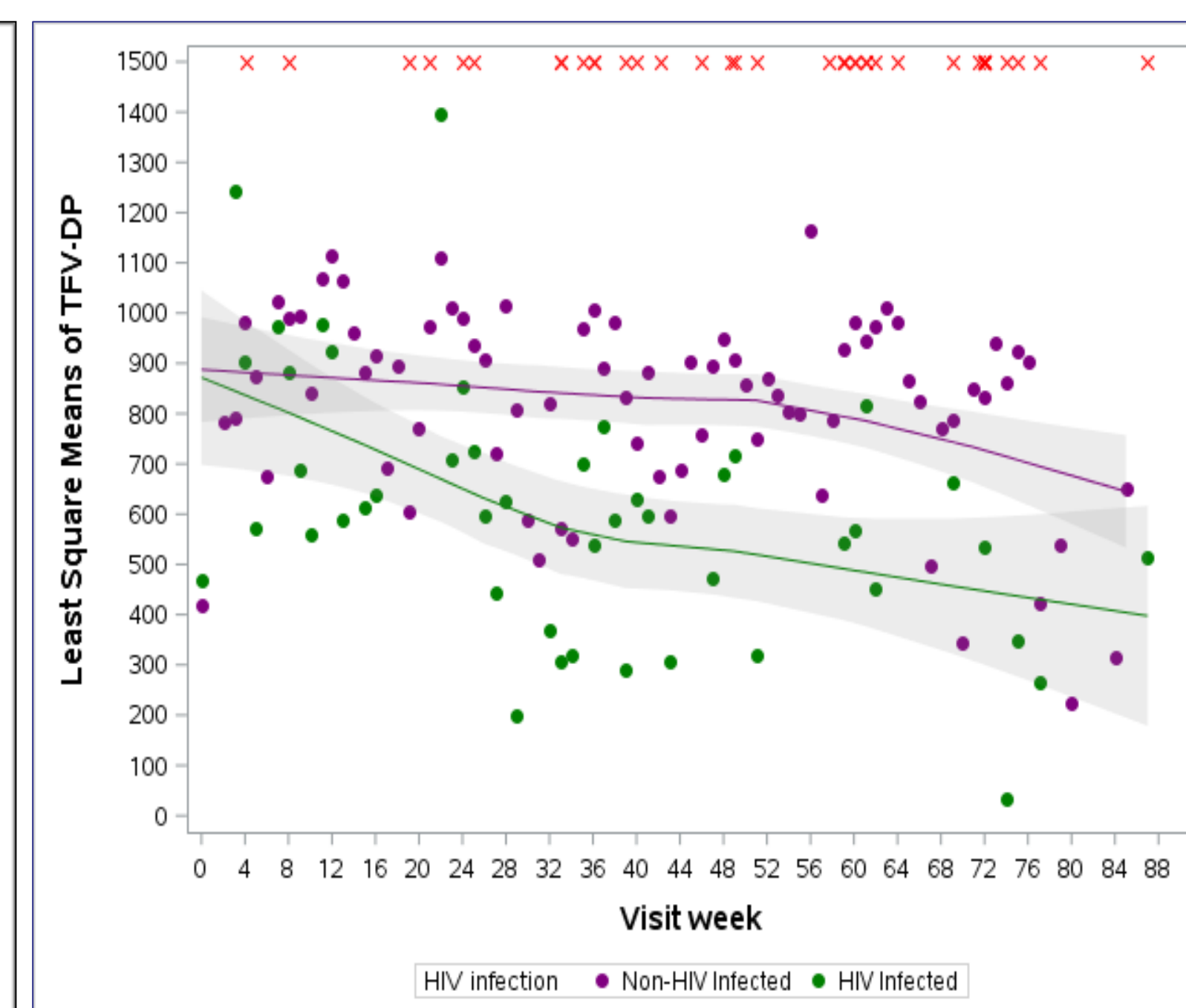


Figure 2. Least Square Means of TFV-DP concentration measured in DBS by visit week



Notes: Generalized linear mixed model was adjusted for age at PrEP initiation, random effect by individual study. 'x' on the figure represents visit week when a new HIV infection was detected