

# Incentives conditioned on tenofovir levels to increase adherence among young women on PrEP in Cape Town

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## Background

Oral pre-exposure prophylaxis (PrEP) is a highly effective HIV prevention technology when taken daily.

African adolescent girls and young women (AGYW) are at high risk of HIV and thus a key population targeted for PrEP.

In the VOICE and FEM-PrEP placebo-controlled PrEP efficacy trials, <30% of AGYW had any detectable tenofovir in plasma or leukocytes.

Adherence to PrEP among African AGYW may be improved with feedback about their adherence based on drug levels, incentives conditioned on high tenofovir levels.

Incentives in the first few months after PrEP initiation could assist AGYW in overcoming side effects and other barriers when taking a pill a day for HIV prevention.

We conducted a randomized clinical trial to evaluate whether PrEP adherence among South African AGYW was increased with short-term incentives in addition to drug level feedback.

## Methods

Sexually active HIV-negative AGYW ages 16-25 were enrolled in the 3Ps (Perception, Partners, Pills) for Prevention Study in Masiphumelele township near Cape Town between March 2017 and May 2018.

Adherence was assessed by red cell tenofovir diphosphate (TFV-DP) concentrations in dried blood spots (DBS), a measure of average and cumulative use in the prior month.

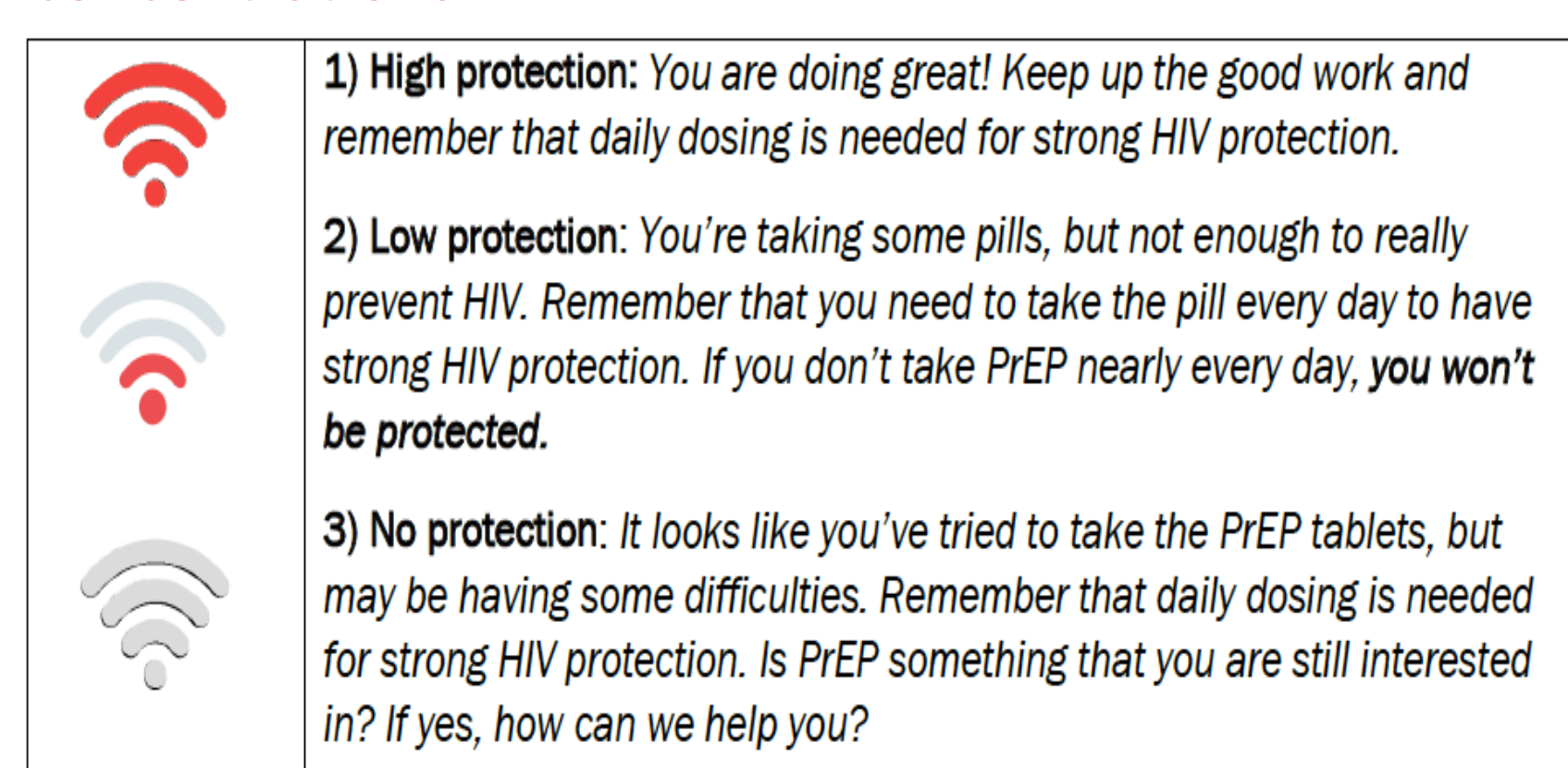
AGYW were randomized 1:1 at enrollment to the incentive arm (counseling at months 2 and 3 about the prior month's drug level with a 200 Rand, \$13, incentive conditioned on TFV-DP $\geq$ 700), or to the standard arm (counseling at months 2 and 3 about the prior month's drug level without an incentive).

Visits were at 0,1, 2, 3, 6, 9 and 12 months

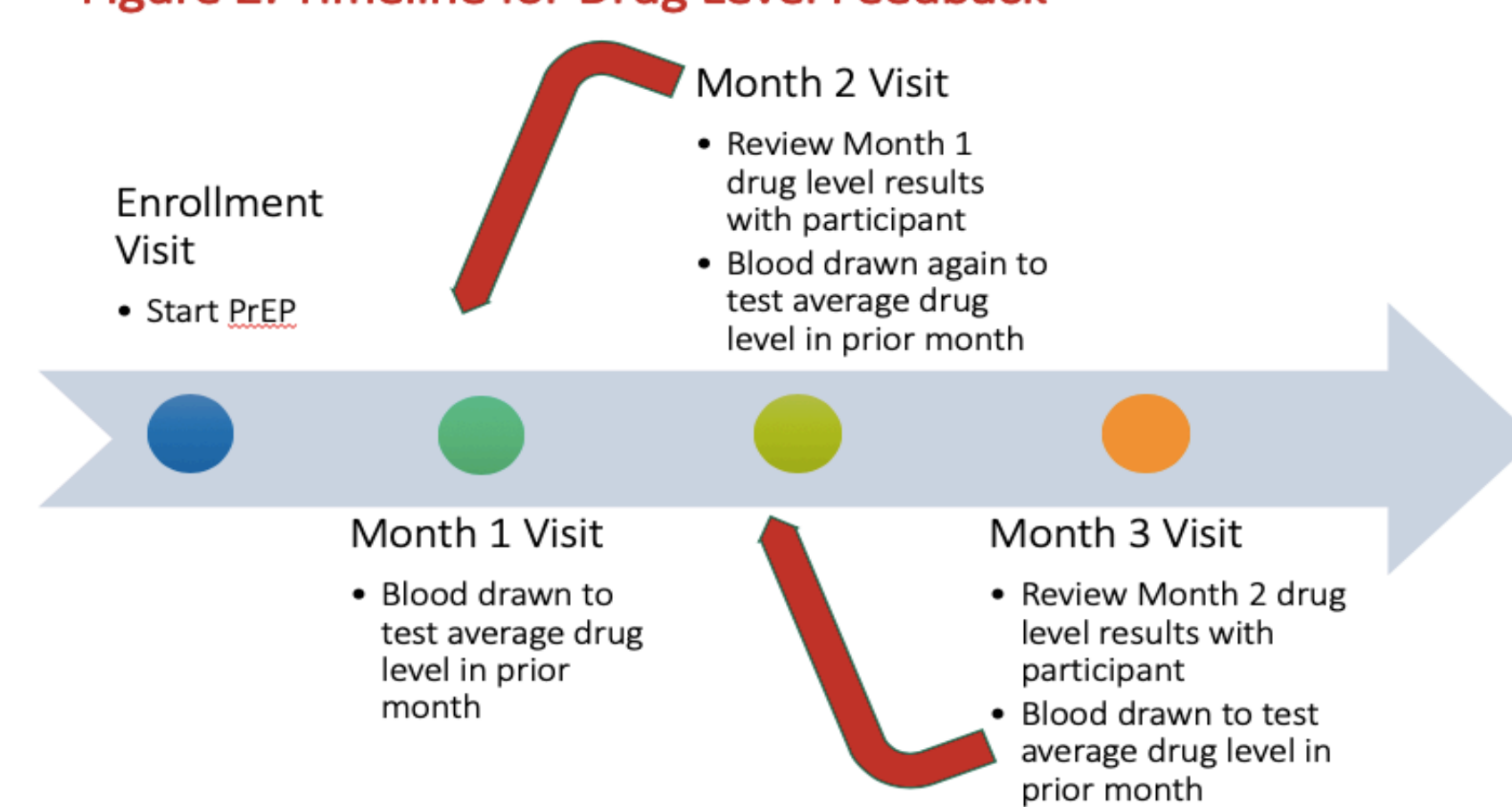
Women in both arms were provided counseling about their adherence based on semi-quantitative categories;

- High adherence:  $\geq$ 700 fmol/punch (correlates with  $\geq$ 4 doses/week in the prior month and associated with high efficacy in MSM).
- Medium adherence: >16 fmol/punch-699 fmol/punch (1-3 doses per week in the prior month)
- No protection (below limits of detection)

**Figure 1: Drug level feedback based on semiquantitative measures of intracellular tenofovir diphosphate (TFV-DP) concentrations**



**Figure 2: Timeline for Drug Level Feedback**

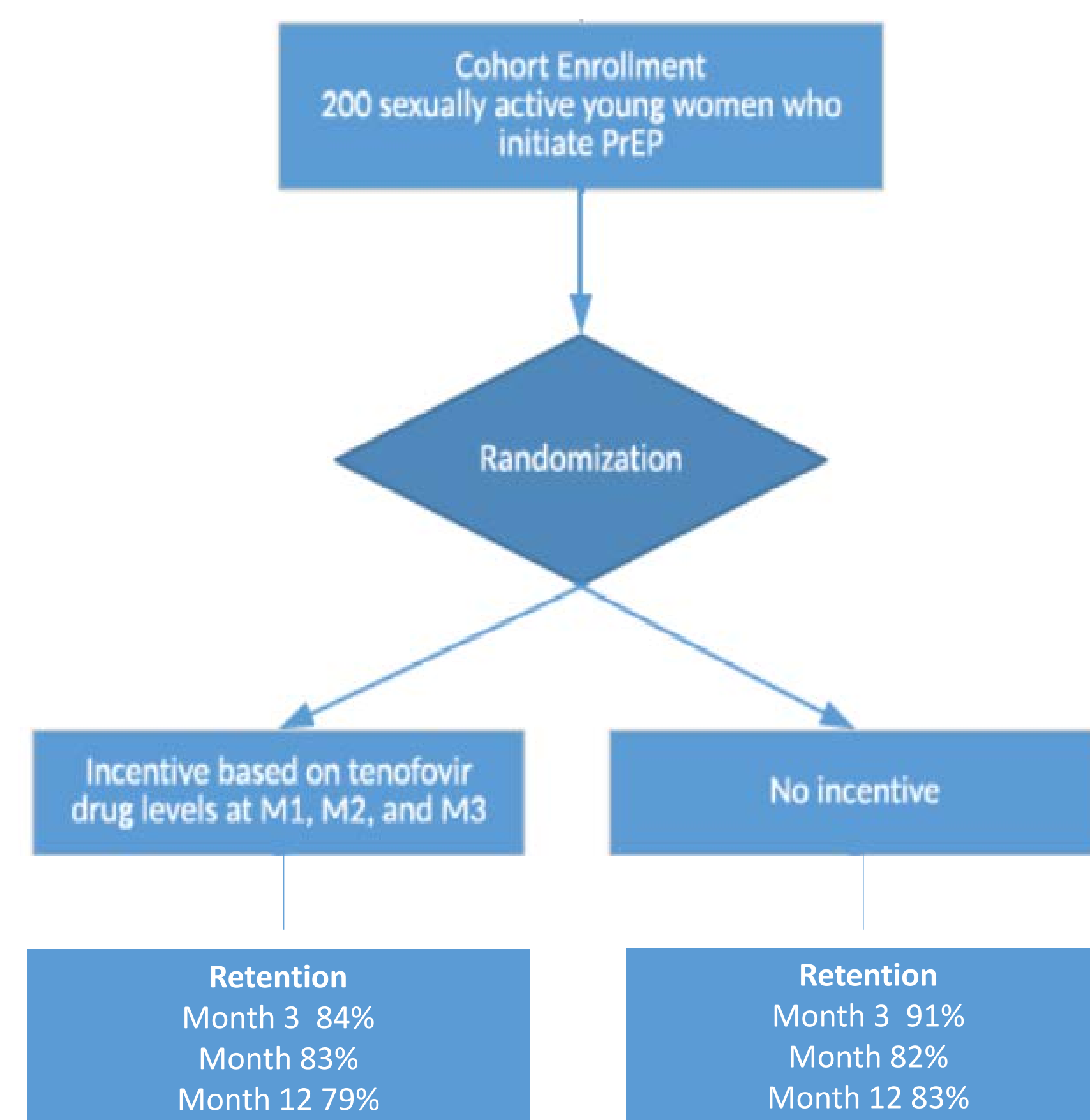


The primary outcome was high adherence at 3 months ( $\geq$ 700 fmol/punch).

Month 3 levels were compared by study arm for the primary outcome and by intention to treat (ITT) analysis, which assumed women without a visit and missing a test were not highly adherent.



## Results



### Demographics (N= 200 women)

- Median age was 19 (IQR 17-21)
- 78% had secondary education or higher

### Behavioral Characteristics at baseline

- 86% had a primary partner; median relationship duration of 12 months
- 17% said their primary partner had other partners and 55% were not sure
- Condom use was low: 32% always or often used a condom; 22% never used a condom
- 19% reported interpersonal violence in the past year
- 13% reported weekly alcohol use

### Curable STIs at baseline

- 32% had a curable STI : 25% with chlamydia and 11% with gonorrhea

**Table 1: PrEP adherence, as assessed by TFV-DP levels at 3 months by study arm**

Tenofovir diphosphate in DBS at month 3	Total	Incentive Arm	Control Arm
Concentration in fmol/punch			
Median (IQR)	694.5 (397.5, 1020.5)	758.0 (446.0, 1140.0)	608.0 (288.0, 969.0)
N Undetectable (BLQ)	4	1	3
N Detectable	160	80	80

- All but one sample had detectable TFV-DP at 3 months.
- At 3 months, half had high adherence ( $\geq$ 700 fmol/punch)
- 80% had medium or greater adherence at 2 and 3 months.

**Table 2: PrEP acceptance by visit month**

	Incentive Arm	Control Arm
Enrollment	101 (100%)	99 (100%)
Month 1	87 (97.8%)	86 (100%)
Month 2	80 (96.4%)	73 (98.6%)
Month 3	77 (91.4%)	82 (95.3%)
Month 6	65 (79.3%)	68 (89.5%)
Month 9	54 (75.0%)	48 (72.7%)



Young woman from 3P PrEP demand creation campaign, McCann Global Health

## Results (continued)

**Table 3: High PrEP adherence (TFV-DP  $\geq$ 700 fmol/punch) at 3 months by study arm; primary and intent to treat analysis**

	Incentive Arm		Control Arm		Statistical Comparison	
	N	TFV $\geq$ 700 N(%)	N	TFV $\geq$ 700 N(%)	RR (95% CI)	p-value
Primary analysis (M3)	81	45 (55.6%)	85	35 (41.2%)	1.35 (0.98, 1.86)	0.0667
Secondary analysis (ITT)						
M3	97	45 (46.4%)	97	35 (36.1%)	1.29 (0.92, 1.81)	0.1480
Duration of Effect (ITT)						
M6	96	13 (13.5%)	94	7 (7.5%)	1.82 (0.76, 4.36)	0.1798
M12	94	5 (5.3%)	87	3 (3.5%)	1.54 (0.38, 6.26)	0.5444

- We observed a non-significant higher proportion of AGYW with TFV-DP  $\geq$ 700 fmol/punch at month 3 in the conditional incentive arm (56%) than the standard arm (41%), RR=1.4 (95% CI 1.0, 1.9, p=0.07). ITT analysis showed lower proportions adhering but similar difference between arms
- There was no significant difference by age ( $\leq$ 19) in the effect of conditional incentives on adherence at three months, and no effect modification (p=0.8)
- The proportions with high adherence decreased from months 3 to months 6 and 12 and there was no significant difference by arm.

**Table 4: Effect of conditional incentive on 3 month TFV-DP concentration a continuous outcomes**

	Incentive Arm		Control Arm		Difference Mean (95% CI)	p-value*
	N	Mean (SD)	N	Mean (SD)		
Month 3 tenofovir concentration by arm	81	822.0 (522.0)	85	689.1 (546.3)	132.8 (-30.8, 296.5)	0.1111

- There was a nonsignificant trend of higher mean TFV-DP levels at 3 months in the conditional incentive arm

**Table 5: Baseline predictors of high adherence: (TFV-DP  $\geq$ 700 fmol/punch) at 3 months**

Baseline factors	TFV -DP Concentration at M3		Univariate Model		Multivariate Model	
	< 700 fmol/punch N(%)	$\geq$ 700 fmol/punch N(%)	Odds Ratio (95% CI)	p-value	Adj. OR (95% CI)	p-value
Partner HIV Status						
HIV Negative	52 (58.4%)	37 (41.6%)	reference		reference	
HIV Positive or Unknown HIV status	34 (44.2%)	43 (55.8%)	1.8 (1.0, 3.3)	0.07	1.7 (0.9, 3.3)	0.12
Sexually active, past 30 days						
Yes	72 (56.7%)	55 (43.3%)	reference		reference	
No	14 (35.9%)	25 (64.1%)	2.34(1.1, 5.0)	0.02	2.0 (0.9, 4.5)	0.07
Disclosed plans to take PrEP						
Yes	75 (49.3%)	77 (50.7%)	3.8 (1.1, 17.1)	0.03	4.1 (1.2, 19.2)	0.03
No	11 (78.6%)	3 (21.4%)	reference		reference	

## Conclusions

- Early PrEP adherence was high among African AGYW in an open label PrEP demonstration project in a Cape Town township
  - TFV-DP levels indicate that by 3 months, half of AGYW were taking an average of four or more doses per week in the prior month.
- Receiving a modest cash incentive conditioned on high adherence (TFV-DP  $\geq$ 700 fmol/punch) at months 1, 2, and 3 was associated with a non-statistically significant trend towards higher adherence at 3 months among AGYW.
- The effect of the conditional incentive did not persist at 6 or 12 months after PrEP initiation.
- Being not sexually active in the prior month and disclosure about their PrEP use were associated with higher adherence at 3 months.
- PrEP use declined over the 12 months in both the conditional incentive and non-incentive arms.
- Further understanding of factors associated with PrEP discontinuation and interventions to support PrEP persistence with this population are needed.

### Acknowledgments

US NIH and South African Medical Research Council for grant R01MH107251; Gilead for study drug donation; 3P team and study participants for their contributions

