PrEP Does Not Diminish the Pregnancy Prevention Effectiveness of Hormonal Contraception

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Background

- For women at risk of HIV-1, effective contraception and effective methods of HIV-1 prevention are public health imperatives.
- Antiretroviral pre-exposure prophylaxis (PrEP) is a promising new strategy for prevention of HIV-1, and joint use of hormonal contraception and PrEP could offer dual protection.
- In FEM-PrEP, more pregnancies were observed among women randomized to daily oral emtricitabine/tenofovir disoproxil fumarate PrEP compared to placebo, raising a concern that PrEP potentially reduces the pregnancy-prevention effectiveness of hormonal contraception.
- We assessed the impact of tenofovir-based PrEP on hormonal contraceptive effectiveness in a large clinical trial of PrEP for HIV-1 prevention.

Methods

Data were from the Partners PrEP Study: 4758 HIV-1 serodiscordant couples enrolled July 2008 - November 2010 at 9 sites in Kenya & Uganda

- HIV-1 uninfected partners were randomized 1:1:1 to daily oral:
  - tenofovir (TDF),
  - emtricitabine/TDF
  - or placebo
- Followed up to 36 months

Inclusion criteria for this analysis:

- Uninfected partner was female
- Not later determined to be infected at enrollment

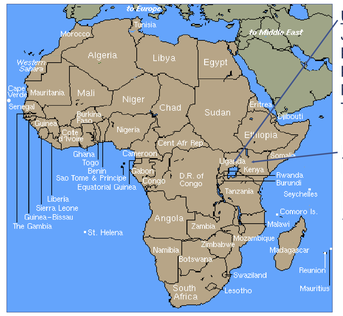
Follow-up data

HIV-1 uninfected women

- Monthly visits
- 2 rapid antibody tests for HIV-1
- Pregnancy urine test
- Self-reported
  - contraception
  - sexual behavior

HIV-1 infected male partners

- Quarterly visits
- Self-reported ART use



Statistical methods

- Andersen-Gill extension of Cox proportional hazards to account for repeated events
- Incident pregnancy: defined by LMP prior to first positive test
- Predictors:
  - PrEP (both TDF containing arms combined) vs. placebo
  - Contraceptive method
  - Their interaction
  - Potential confounders

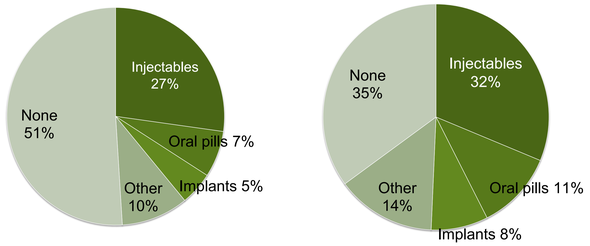
Results

1785 HIV-1 uninfected women are included in this analysis.

Table 1. Enrollment characteristics

	PrEP (N=1164)	Placebo (N=621)
Age, years	33 (28, 38)	33 (28, 39)
Number of children with study partner	3 (1, 5)	3 (1, 5)
No children with study partner	169 (15%)	93 (15%)
Partnership duration, years	12 (6, 19)	12 (6, 18)
Number of sex acts with study partner in prior month	4 (2, 7)	4 (2, 8)
Any unprotected sex with study partner in prior month	262 (23%)	144 (23%)
Any sex with additional partner in prior month	4 (0%)	4 (1%)
Infection with Neisseria gonorrhoeae, Chlamydia trachomatis, or Trichomonas vaginalis	94 (8%)	76 (12%)

Distribution of contraceptive use



At enrollment
among all 1785 women

Throughout follow-up
% of all non-pregnant follow-up time

Table 2. Pregnancy prevention effectiveness of hormonal contraception: contraceptive methods compared to no contraception, by PrEP vs. placebo.

Contraceptive method	PrEP or placebo	# pregnancies*	Person-years	Incidence rate	Contraceptive method vs. no contraception: adjusted HR^	p-value for difference in effect, PrEP vs. placebo
No contraception	PrEP	100	687.2	14.6		
	Placebo	53	303.8	17.4		
Oral pills	PrEP	37	209.3	17.7	0.96 (0.58-1.58) p=0.87	0.24
	Placebo	11	108.7	10.1	0.55 (0.26-1.19) p=0.13	
Injectables	PrEP	29	564.3	5.1	0.26 (0.16-0.41) p<0.001	0.47
	Placebo	17	319.7	5.3	0.19 (0.10-0.37) p<0.001	
Implants	PrEP	1	150.6	0.7	unable to model^^	
	Placebo	0	79.7	0.0		

HR=hazard ratio

* 25 additional pregnancies occurred in the PrEP arms and 15 in the placebo arm when contraception method was reported as IUD, diaphragm, other, or was not reported.

^ HRs are reported with 95% confidence intervals.. The Cox model was adjusted for, at enrollment: age, number of children, partnership duration, and sexually transmitted infections, and, during follow-up: any unprotected sex and sexual frequency with the study partner, any sex with additional partners, and ART initiation by the HIV-1 infected partner.

^^ For implantable contraception, too few pregnancies occurred for the Cox model to reliably estimate hazard ratios and confidence intervals. The unadjusted incidence rate ratio (IRR) for implants among women on PrEP was 0.05 (95% CI: 0.00-0.26, p<0.001) and on placebo was 0.00 (95% CI: 0.00-0.27, p<0.001). Exact confidence intervals were estimated in Stata 12 assuming a poisson probability distribution of pregnancy events.

Conclusions

- We found no evidence that PrEP reduced the effectiveness of hormonal contraception for pregnancy prevention.
- As seen previously in similar populations, women reporting contraceptive pill use had little protection from pregnancy, possibly due to poor adherence.
- Injectable or implantable hormonal contraception plus PrEP provides effective prevention for pregnancy and HIV-1.

Partners PrEP Study Team
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