

Effectiveness of Contraception for HIV-Infected Women using Antiretroviral Therapy

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Background: Ensuring safe, effective contraception for women with HIV is a public health imperative. Some data has suggested that antiretroviral therapy (ART) may diminish contraceptive effectiveness, particularly for the combination of implants and NNRTIs, such as nevirapine (NVP) and efavirenz (EFV). In this study, we determined the effectiveness of different hormonal contraceptives by women's ART use, determined by the clinical endpoint of pregnancy.

Methods: Data from 5,153 HIV-infected women participating in three longitudinal studies (Partners in Prevention HSV/HIV Transmission Study, Couples Observation Study, and Partners PrEP Study) from seven countries in Africa between 2004-2012 were used for this analysis. All women were in seroliscordant couples and were not using ART at enrollment. Study visits were conducted quarterly; hormonal contraception and condoms were provided. Visits when women were using non-hormonal methods (diaphragms, IUDs, tubal ligations, or hysterectomics) or were >=50 years old were excluded. Women were consored during each pregnancy and returned to the risk set at the first visit they were not pregnant. Multivariable Cox regression models were used, with pregnancy as a repeated outcome, to test the interaction between each contraceptive method (implant, injectable, oral contraception (OC), or none) and any ART use. Age, CD4 count, site, and study were included a priori; sexual frequency and any condomiess sex were added as significant covariates. The analysis was then repeated, restricting ART use to NP and EFV separately.

	% (n) or mediar
AT BASELINE (n=5,153 women)	(IQR)
Age, years	29 (24-34)
17-24	26.1 (1344)
25-29	27.8 (1430)
30-34	23.8 (1224)
35-39	13.8 (713)
40-44	5.8 (297)
45-49	2.8 (144)
Education >8vrs	32.3 (1664)
Any monthly income	41.4 (2131)
Married	88 1 (4542)
Years living with study partner	4.5 (1.8-9.2)
Number of children with study partner	1 (0-2)
Pregnant	3.5 (170)
Number of sou acts in last month	4 (2, 9)
Number of condemises sey acts in last	4 (2, 0)
month	0 (0 1)
Anno and and an an and a la la share with	0 (0-1)
Any condomiess sex acts in last month	28.7 (1477)
Other sexual partner	1.2 (61)
Any gonorrhea, chlamydia or	
trichomonas	14.0 (723)
Any gonorrhea, chlamydia or	
trichomonas among male study	
partner	7.3 (377)
CD4 count, cells/mm ³	
<200	0.7 (34)
200-349	19.8 (1019)
350-499	28.4 (1464)
<u>></u> 500	51.2 (2636)
HIV viral load (log ₁₀), copies/ml	3.85 (3.14-4.45)
Hormonal Contraceptive use	
Implant	2.3 (118)
Injectable	17.4 (896)
Oral	4.3 (221)
None	75.7 (3900)
On ART	0 (0)
Study	
Partners PrEP Study	54.1 (2790)
Partners in Prevention HSV/HIV	
Transmission Study	41.3 (2129)
Couples Observation Study	4.5 (234)
DURING FOLLOW-UP VISITS	% (n)
Ever became pregnant	24.1 (1240)
Contraceptive use	()
Ever used implant	9.0 (466)
Ever used injectable	39.6 (2039)
Ever used oral contracention	14.2 (732)
Ever on ART	31.0 (1596)
Ever on NVD	22.1 (1101)
Ever on NVP	23.1 (1191)
Ever on EFV	4.8 (247)

Table 1. Characteristics of Study Population

Results: 5,153 women contributed 9,266 person-years (median 1.8 years). Participants were young (54% under 30) and healthy (51% CO4 counts ≥500 cells/mm3) at enrollment. During follow-up 24% of women became pregnant and 31% initiated ART. Pregnancy incidence was 14.8 per 100 person-years overall.

Use of implants reduced the risk of pregnancy by more than 90%, both among women on ART and not on ART. Injectables reduced pregnancy risk by ~80% and OCs reduced pregnancy by ~65%, with no statistical difference between women on ART versus women not on ART.

There were approximately 1000 person-years of follow-up on NVP and 200 person-years on EFV. There was no evidence of significant effect modification when limiting the analysis to NVP or EFV. However, the estimated effectiveness of all methods was somewhat attenuated among EFV users.



Table 2: Contraceptive Effectiveness, by ART & Contraception Use

Hormonal Contraception Use	ART	Pregnancies/Person-Years (Pregnancy Incidence per 100 person-years)	aHR* (95% CI)	p-value for interaction term**
	None	1067/4733.6		
None		(22.5)	ref	
		7/507.5	0.05	
Implant		(1.4)	(0.02-0.11)	ref
		111/2100.5	0.20	
Injectable		(5.3)	(0.16-0.24)	ref
		63/573.1	0.36	
Oral Pills		(11.0)	(0.28-0.47)	ref
	A ADT	111/843.5		
None		(13.2)	ref	
		1/94.1	0.06	
Implant		(1.1)	(0.01-0.45)	0.73
	ANY ART	11/332.8	0.18	
Injectable		(3.3)	(0.10-0.35)	0.79
		5/81.2		
Oral Pills		(6.2)	0.37 (0.15-0.91)	0.97
	NVP	86/624.7		
None		(13.8)	ref	
		0/67.7		
Implant‡		(0)		
		8/245.6	0.18	
Injectable		(3.3)	(0.09-0.38)	0.80
		4/62.4	0.35	
Oral Pills		(6.4)	(0.13-0.97)	0.95
	EFV	16/127.5		
None		(12.6)	ref	
		1/16.7	0.43	
Implant		(6.0)	(0.07-2.50)	0.12
		2/52.2	0.29	
Injectable		(3.8)	(0.07-1.22)	0.63
		1/7.7	0.86	
Oral Pills		(12.9)	(0.11-6.76)	0.46

*Adjusted for site, study, age (categorical), any condomless sex, total sex, CD4 (categorical). Any ART, NVP, a ** p-values for interactions are from IR tests. • Due to small sample size, estimates are not included from the Cox model.

Conclusions: In this large evaluation of three prospective studies, modern contraceptive methods remained highly effective in reducing pregnancy risk in HIV-infected women, including those concurrently using ART. While limited evidence from other studies suggests that some ART agents could diminish the effectiveness of contraceptive implants, these data emphasize that implantable contraception is highly effective compared to no contraception and more so than shorter-acting methods such as injectables and oral pills. Follow-up time on EFV was limited and all hormonal methods showed reduced effectiveness among EFV users, though these differences were not statistically significant. These results of real-world hormonal contraception effectiveness are important considerations in determining family planning guidelines for women with HIV.

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