CROI 2015 1122

Procreation in HIV-Serodiscordant Couples: TasP, PrEP, or Assisted Reproduction?

ANRS 12008

Guillaume Mabileau[1,2], Michaël Schwarzinger[1,2], Juan Flores[1], Catherine Patrat[2,3], Dominique Luton[2,4], Sylvie Epelboin[4], Laurent Mandelbrot[2,5], Sophie Matheron[1,2,6], Yazdan Yazdanpanah[1,2,6]

1 Inserm, IAME UMR 1137, Paris, France; 2 Université Paris Diderot, Sorbonne Paris Cité, Paris, France; 3 AP-HP, Bichat-Claude Bernard Hospital, Reproductive Biology Department, Paris, France; 4 AP-HP, Bichat-Claude Bernard Hospital, Gynecology Obstetrics Department, Paris, France; 5 AP-HP, Louis Mourier Hospital, Gynecology Obstetrics Department, Colombes, France; 6 AP-HP, Bichat-Claude Bernard Hospital, Infectious Diseases Department, Paris, France

ABSTRACT

BACKGROUND: In the U.S., 2014 CDC guidelines based on expert recommendations have for the first time recommended PrEP as one of several options for fertile HIV-uninfected female/HIV-1-infected male couples on combination antiretroviral therapy (cART) with plasma HIV RNA <50 copies/mL desiring a child. However, in France, medically assisted procreation (MAP) is still the highest recommended strategy. The aim of this study was to assess residual risk of HIV transmission, cost, and cost-effectiveness (CE) of various strategies that can help fertile HIV serodiscordant couples to have a child: (i) unprotected sexual intercourse (TasP); (ii) TasP limited to fertile days (FertilD); (iii) TasP with pre-exposure prophylaxis (PrEP) (tenofovir/emtricitabine); (iv) strategy (ii) + PrEP limited to fertile days; (v) medically assisted procreation (MAP).

METHODOLOGY: We used a decision model. Input variables were from the international literature: 85% probability of live births in different strategies, 0.0083%/month HIV-transmission risk (β) with unprotected vaginal intercourse, 1% HIV mother-to-child transmission rate, and 4.4% birth defect risk related to cART when mother infected at conception. FertilD and PrEP were estimated to decrease β by 80% and 67%, respectively, and by 93.4% for PrEP+FertilD (1-(1-0.80)*(1-0.67)). Tenofovir/emtricitabine monthly cost was at €540. The CE analysis was performed from the French societal perspective (2013 euros), with a 4% annual discount rate.

RESULTS: The probability of transmission to the female partner was highest with unprotected sexual intercourse strategy and lowest for MAP, followed by PrEP during fertile period. FertilD was associated with the lowest costs and dominated PrEP, which was less effective with the highest costs. PrEP+FertilD cost-effectiveness ratio was €1,130,000/life year saved (LYS) when compared with FertilD; €3,600,000/LYS for MAP when compared with PrEP+FertilD. Results were robust to multiple sensitivity analyses.

CONCLUSIONS: In fertile HIV-uninfected female/HIV-1-infected male couples, targeting fertile days lead to a low risk of HIV transmission. Unlike 2014 CDC and French guidelines recommendations, considering PrEP during fertile period or MAP decrease the risk but these strategies are associated with unfavorable CE ratio.

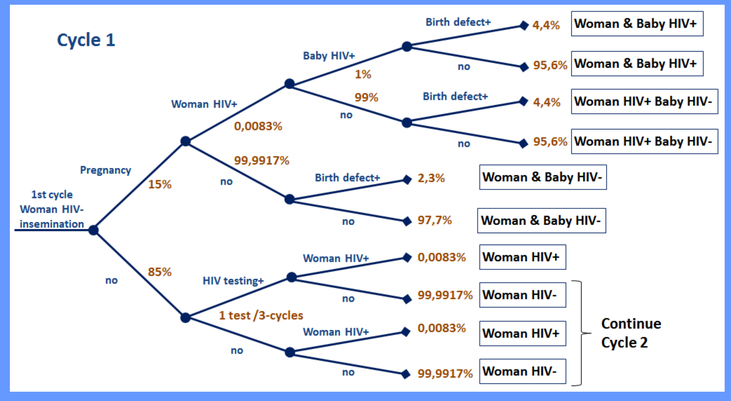
FIVE STRATEGIES TESTED (Table 1)

TasP:	Unprotected sexual intercourse (“Treatment as Prevention” strategy)
FertilD:	TasP limited to fertile days determined by urine ovulation testing
PrEP:	Continious pre-exposure prophylaxis (tenofovir/emtricitabine) for the woman
PrEP+FertilD:	PrEP limited to fertile days (protected sexual intercourse otherwise)
MAP:	Six intrauterine insemination attempts at most per couple with sperm washing

DATA (Table 2)

INPUT PARAMETERS	VALUES	RANGES	SOURCES
SUCCESS RATE OF PREGNANCY (OVERALL)	0.85	--	Gnoth et al. 2013; fixed
BASELINE TRANSMISSION RISKS IN HIV SERODISCORDANT COUPLES DESIRING A CHILD			
Transmission risk from male to female partner, per month	0.000083	0.0--0.001	Cohen et al. 2011 Patel et al. 2014
Mother-to-child transmission, overall risk	0.01	0.005--0.03	Boer et al. 2010 Giaquinto et al. 2005
STRATEGIES TO REDUCE HETEROSEXUAL TRANSMISSION			
Intrauterine insemination with sperm washing and negative HIV testing of the washed sample			
Maximum number of cycles	6	--	NABM
Residual risk of transmission per cycle	0.000001	0.0--0.01	Gilling-Smith et al. 2006 Dulioust et al. 2010
Relative risk of transmission with PrEP (tenofovir/emtricitabine in uninfected woman)	0.33	0.1--0.33	Baeten et al. 2012 Day et al. 2013
Relative risk of transmission with FertilD determined by urine ovulation testing vs. no FertilD	0.2	0.1—1	Lampe et al. 2011; discussed
Relative risk of transmission with FertilD associated with PrEP	0.066	0.01--0.33	calculated
BIRTH DEFECTS			
HAART regimens initiated in the first trimester of pregnancy if the woman is HIV+	0.044	0.025--0.07	Sibiude et al. CROI 2013
Birth defects in the general population	0.023		EUROCAT
LIFE EXPECTANCY			
Age of woman in HIV-serodiscordant couple desiring a child	33.0	25.0--35.0	Vitorino et al. 2011
Life expectancy of women 33 [25-35] years old in the French general population	52.0	50.0--60.0	INSEE 2010 [French gen. pop.]
Life expectancy at birth (50% male, 50% female)	81	78--84 [boy-girl]	INSEE 2010 [French gen. pop.]
Reduction in life expectancy for HIV+ patients with early presentation (mean CD4 count 510 cells/mL) as compared with general population	0.64	0.6--1.0	Sloan et al. 2012 [French HIV pop.]
COSTS (€2013)			
COSTS RELATED TO INSEMINATION STRATEGIES			
Intrauterine insemination			
Initial fixed costs (preconception counseling, transportation, semen collection & sperm washing)	405.30	205.30--810.60	
Procedure costs per cycle (intrauterine insemination, transportation)	561.57	387.29--646.91	
Urine pregnancy test, unit costs	8.10		NABM
HIV testing of the couple, unit costs	18.90		
tenofovir/emtricitabine (PrEP), drug costs per month	536.40	457.50--536.40	
Urine ovulation tests, costs per month	17.00	12.00--50.00	
Consultation with a physician	23.00	--	ameli.fr
COSTS RELATED TO HIV TRANSMISSION			
Lifetime (undiscounted) costs for HIV care if woman infected at conception	641,000	350,000	Sloan et al. 2012
Lifetime (undiscounted) costs for HIV care if baby born infected	1,000,000	500,000	
DISCOUNT RATE	0.04	0.0--0.04	

MARKOV MODEL (Figure 1)



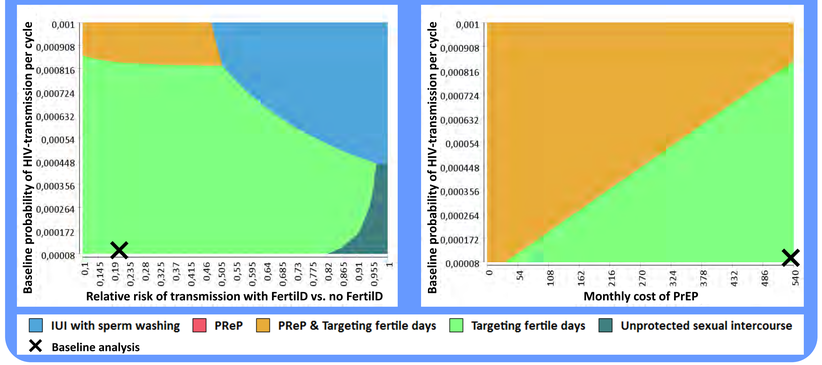
Probabilities illustrated in the decisional tree (Figue 1) were for the baseline strategy (« Treatment as Prevention »); 1 cycle=1 month

RESULTS (Table 3)

Reproductive strategy	HIV-infected women/10,000 pregnancies	HIV-infected babies/10,000 pregnancies	Life expectancy* (undiscounted)	Life expectancy* (4% discount rate)	Costs (4% discount rate)	ICER* (€/LYS)
FertilD	0.9	0.002	113.046	40.408	€ 786	--
TasP (baseline)	5.4	0.014	113.030	40.404	€ 787	**Dominated**
PrEP+FertilD	0.3	0.001	113.049	40.409	€ 1,324	**1,128,000**
MAP	0.0	0.000	113.050	40.409	€ 3,208	**3,595,000**
PrEP	1.8	0.005	113.043	40.408	€ 3,836	**Dominated**

*Incremental cost-effectiveness ratios (ICERs) are rounded off to the nearest €1,000/life year saved; 1€=1.32 USD. The comparator strategy is always the next smallest, not dominated, alternative. When dominated, the strategy is less effective and more costly than some alternative strategies.

Table 2 presents results of the baseline analysis regarding the residual risk of HIV transmission, cost, and cost-effectiveness of different strategies. The probability of transmission to the female partner was highest with the TasP strategy and lowest for MAP. FertilD was associated with the lowest costs and dominated PrEP. PrEP+FertilD cost-effectiveness ratio was €1,130,000/life year saved (LYS) when compared with FertilD; €3,600,000/LYS for MAP when compared with PrEP+FertilD. In two-way sensitivity analysis (figures below), FertilD remained the most cost-effective strategy (ICER < 3*French GDP = 90,000€) considering plausible ranges of values for uncertain parameters having the most impact on the results.



CONCLUSIONS

In fertile HIV- female/HIV+ male couples with plasma HIV RNA <50 copies/mL, targeting fertile days lead to a low risk of HIV transmission and not significantly different from MAP or PrEP during fertile period that are both associated with unfavorable CE ratio. PrEP during fertile period could however be very cost-effective if the cost of PrEP decreases in particular with the advent of generic drugs.