Pregnancy and HIV/AIDS

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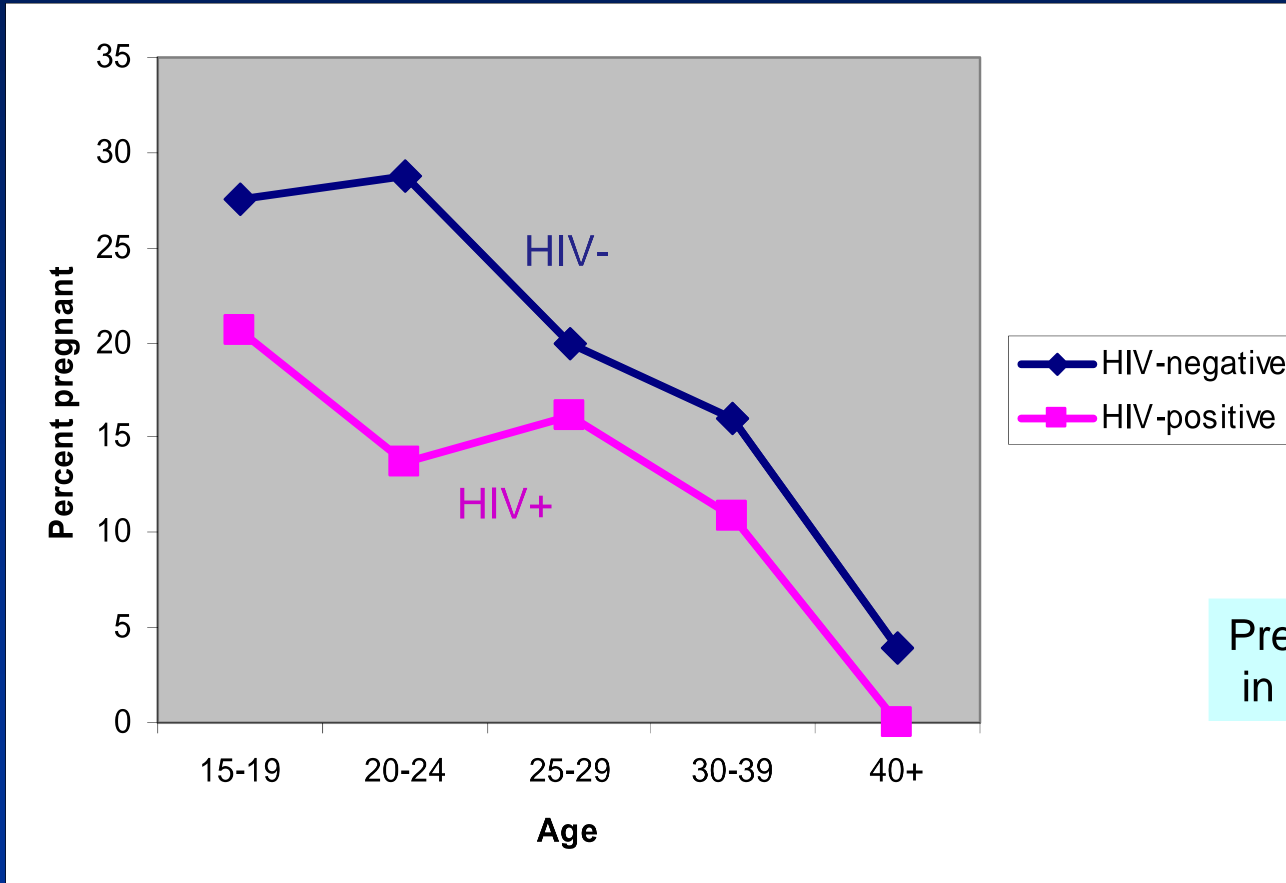
Outline

- The effects of HIV on fertility:
  - Implications for ANC surveillance and HAART
- The effects of pregnancy on HIV acquisition
  - Minimizing HIV risks during pregnancy
- The effects of pregnancy on disease progression in HIV+ women
  - Benefit of FP for HIV+ mothers
- The role of family planning in pMTCT
  - Unmet need, prevention of infant infection
- Contraception effects on
  - HIV risk in HIV-negative women
  - Contraception in HIV+ women, risks to partners

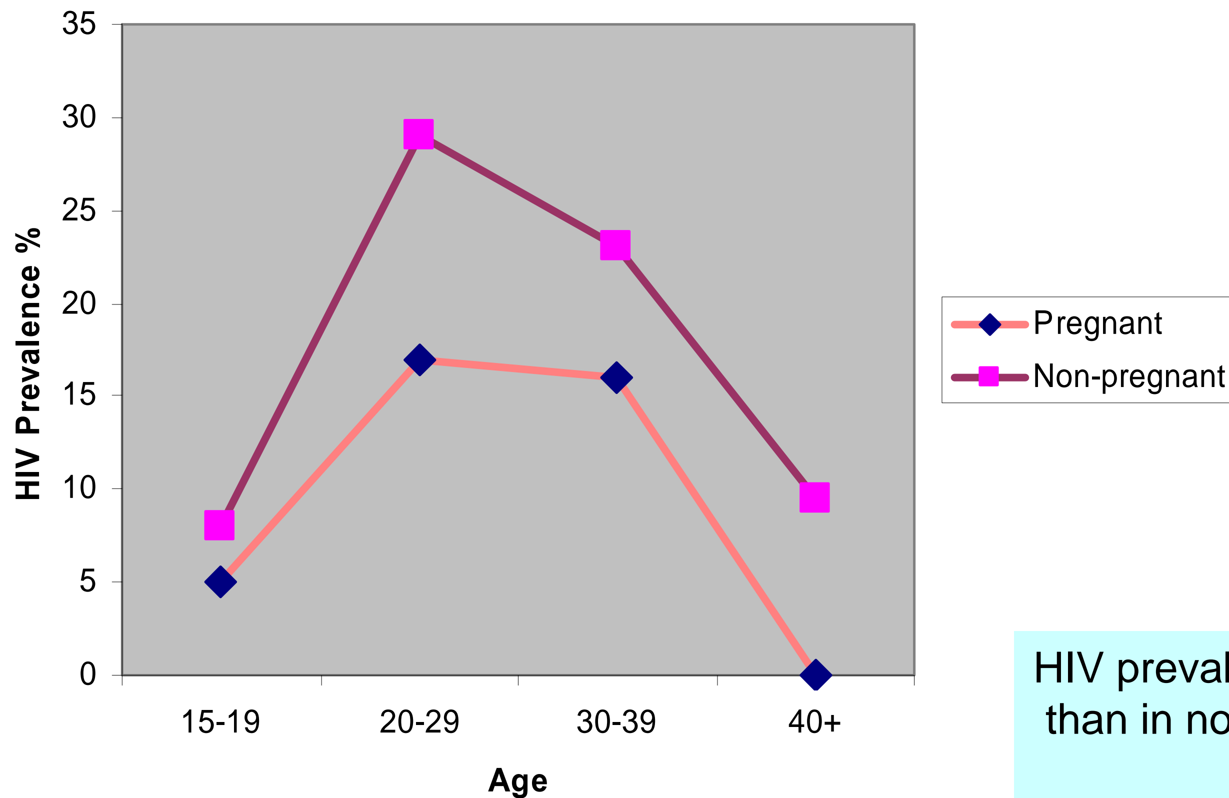
Prevalence of Pregnancy in HIV+ and HIV- women, Rakai, Uganda

(Gray et al Lancet 1998)



Pregnancy rates are lower in HIV+ than HIV- women

HIV Prevalence in Pregnant and non-Pregnant Women Rakai **(Gray et al Lancet 1998)**



HIV prevalence is lower in pregnant than in non-pregnant women

ANC surveillance underestimates population HIV prevalence by excluding Non-pregnant women

Effect of HIV on conception and pregnancy loss

- **Pregnancy rates:**
  - HIV+ 23.5/100 py
  - HIV-neg 30.1/100 py
  - RR = 0.73 (0.57-0.93)
- **Spontaneous abortion:**
  - HIV+ 18.5%
  - HIV-neg 12.2%
  - RR = 1.50 (1.01-2.27)
- HIV reduces the likelihood of pregnancy and increases rates of pregnancy loss

The effects of HIV viral load on the probability of pregnancy. Rakai (Nguyen *et al Int J STD AIDS* 2006)

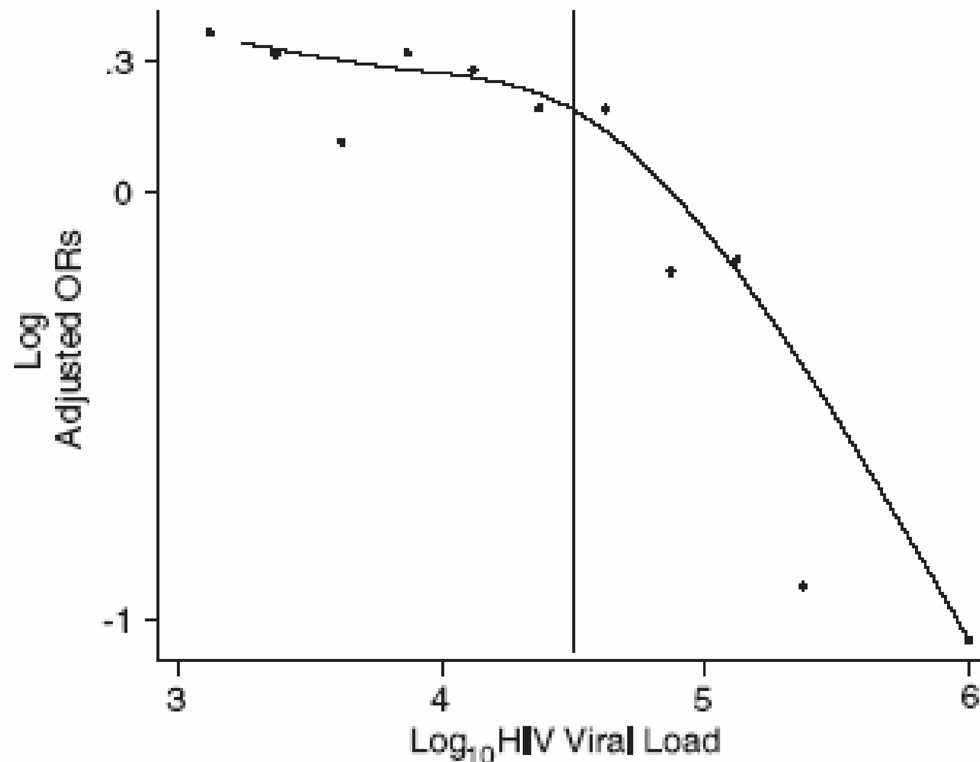


Figure 2 Plot of the log-transformed adjusted ORs ($n=11$) by log viral load with smoothing spline (bandwidth 5). The vertical line at 4.5 $\log_{10}$ HIV viral load indicates the location of the spline knot from the segmented linear regression model

Probability of pregnancy declines rapidly with Viral loads >4.5 log (~31,600 cps/mL)

Implications for HAART

- HAART reduces viral load and is likely to increase fertility
- Desire to become pregnant may increase with improved health and treatment optimism
- Risks of MTCT are reduced by HAART
- Need to offer FP to women on HAART if they desire to limit childbearing

Drug interactions between hormonal contraceptives and HAART

(JAIDS 2005;38, Suppl 1)

- NNRTI and PIs induce changes in liver cytochrome P450 enzymes which also metabolize estradiol and progestins.
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- HAART regimens can reduce blood estradiol levels and may impair contraceptive efficacy
- CDC recommends
  - Use of non-hormonal contraceptives (e.g., barriers) in HIV+ women on HAART
  - Avoidance of low dose pills to prevent contraceptive failure

Pregnancy and the risks of maternal HIV acquisition

- Malawi (Taha *AIDS 1991*) HIV incidence
  - During pregnancy 7.9/100 py
  - Postpartum 3.6/100 py
- Uganda (Gray *AmJ ObGyn 2000*) HIV Incidence
  - Pregnancy 3.2/100 py
  - Postpartum 1.6/100 py
- Rwanda (Leroy, *AIDS* 1994) HIV Incidence
  - 0-6 months postpartum 7.6/100 py
  - 3 years postpartum 2.5/100 py

Pregnancy and the risks of maternal HIV acquisition

Study	Pregnancy status	HIV incidence/ 100 py
Malawi (Taha *AIDS 1991*)	Pregnant Postpartum	7.9 3.6
Uganda (Gray *AmJ ObGyn 2000*)	Pregnant Postpartum	3.2 1.6
Rwanda (Leroy, *AIDS* 1994)	0-6 mths postpartum 3 years postpartum	7.6 2.5

No study adjusted for risk behaviors

HIV incidence during pregnancy, Rakai

(Gray et al Lancet 2005)

	Pregnant	Lactating	Neither preg/lact
Incident cases/ women years (wy)	23/997	40/3043	275/24,161
Incidence/100 wy	2.3	1.3	1.1
Adjusted IRR (95%CI)	2.0 (1.3-3.1)	1.2 (0.8-1.6)	1.0

HIV incidence during pregnancy was also significantly higher than during lactation Adj IRR = 1.76 (1.05-2.94)

Male sexual behaviors in married couples during pregnancy

	Pregnant	Lactating	Neither preg/lact
Number of couples	1,240	1,378	8,338
Males with 2+ sex partners (%)	36.0* ↓	39.8	39.2
Mean number of sex partners reported by the male	1.48** ↓	1.57	1.57

Husbands of pregnant women report fewer partners

Female HIV incidence in married couples

	Pregnant N=1240	Lactating N= 1378	Neither preg/lact N=8338
Female HIV: incidence/ 100 wy	1.4	1.1	1.1
Male HIV+ ie:M+F- discordant couples (%)	8.9	8.9	9.6
Incidence in discordant couples/100 wy	15.0	9.6	8.3
Male HIV viral load in discordant couples (log cps/mL)	4.11^{ns}	4.18	4.20

Implications

- If pregnant women are at increased risk of HIV due to pregnancy, there is a case for promoting condom use in pregnant women to prevent:
  - HIV
  - STIs which may adversely affect the fetus/infant

Pregnancy and HIV disease progression in Developed countries

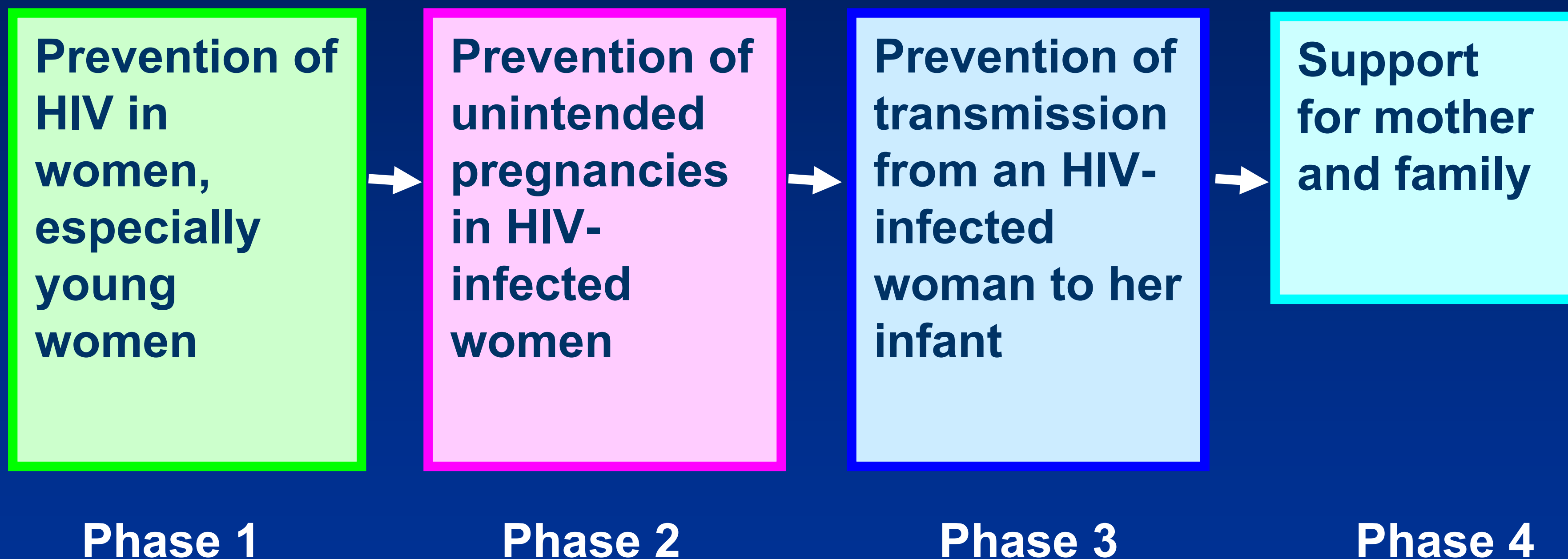
- Pregnancy reduces CD4 counts, mainly a hemodilution effect, recovers after delivery
- No evidence that pregnancy accelerates HIV disease progression (Weiser *et al JAIDS* 1998, Minkoff *et al Am J Obstet Gynecol* 2003, Saada *et al AIDS* 2000,Martin *et al JAIDS* 2006)
- HIV increases infectious complications of pregnancy (e.g., PID, post-CS). European HIV in Obstetrics Group, *AIDS* 2004,

Pregnancy and mortality in HIV+ women in developing countries

	HIV+ Maternal mortality x 10^5	HIV- Maternal mortality x 10^5
South Africa (Khan et al AIDS 2001)	323	149
TB mortality	122	38.5
Uganda (Gray et al Am J Obst Gyn 2001)	532	357

Trends of increasing maternal mortality in Malawi and Zimbabwe associated with increasing HIV prevalence (Bicego *et al AIDS* 2002)

WHO Four-phase Strategy for Perinatal HIV Prevention



FP for prevention of MTCT

- Simulation models suggest that FP for HIV+ mothers can prevent MTCT:
  - 8 SSA countries; ~6-35% decrease pregnancies to HIV+ women is equivalent to NVP. (Sweat et al AIDS 2004)
  - 14 SSA countries; FP added to pMTCT averts 71,000 infections compared to 39,000 for PMTC alone (Stover USAID 2004)
  - Current FP levels in SSA avert ~ 22% of pediatric infections (Reynolds STI 2005)

Family Planning and HIV status in Uganda

- Uganda DHS 2004-5
  - 15.6% of women use modern FP
  - 7.5% of women are HIV+
- Rakai Modern FP use (Lutalo *et al SFP* 2000)
  - HIV-neg 7.7%
  - HIV+ 10.3%
  - 89.7% of HIV+ infected women are at risk of pregnancy

Postpartum FP use by HIV+ women in Cote d'Ivoire

(Desgrees-Du-Lou et al Int J STD AIDS 2002)

- 149 HIV+ women,
  - 60% use no postpartum FP
  - 97% did not want another pregnancy
  - Repeat pregnancy 16.5/100 py
  - 50% or repeat pregnancies unwanted
  - 33% aborted
- Joseph Matovu 69% HIV+ women do not want to become pregnant again

Overwhelming need for FP in HIV+ women

UNAIDS/WHO guidelines on prevention of breast milk MTCT

- Guidelines recommend HIV+ either do not breastfeed, or wean early (4-6 months)
- This could increase fertility by reducing postpartum amenorrhea
- Need for postpartum contraception

Hormonal contraception and risks of HIV acquisition

- Do hormonal contraceptives increase the risk of HIV acquisition in HIV-negative women?
- Do hormonal contraceptives increase HIV shedding in HIV+ women?

Meta-analysis of studies of HIV acquisition and hormonal contraceptive use

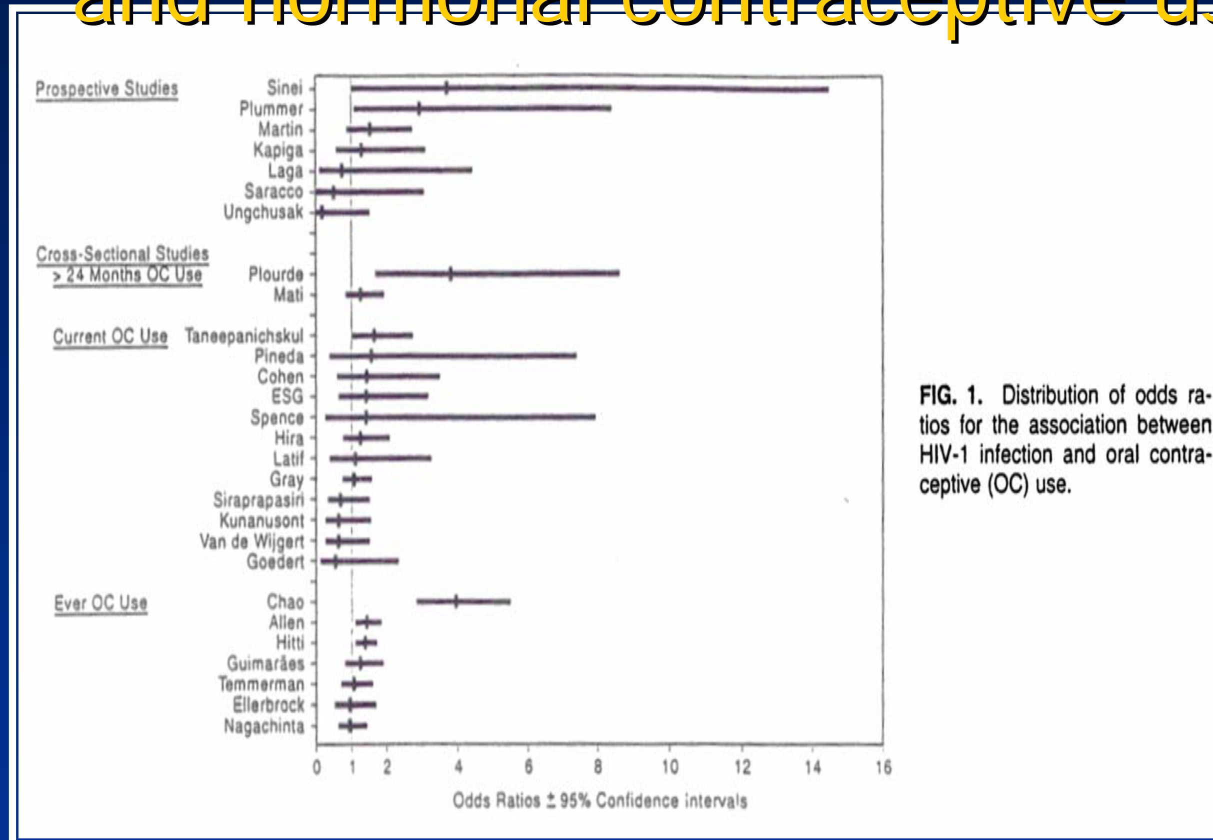


FIG. 1. Distribution of odds ratios for the association between HIV-1 infection and oral contraceptive (OC) use.

No consistent evidence that hormonal contraceptive increase HIV Susceptibility. Problems of confounding by risk behaviors

Hormonal Contraception and HIV Acquisition, Rakai, Uganda

Kiddugavu *et al AIDS* 2003;17:233

	Hormonal contraception HIV Incid/100 py	No hormonal cont HIV Incid/ 100 py	Adjusted RR (95% CI)
All	2.3	1.5	0.94 (0.5-1.6)
Pills	2.5	1.5	1.12 (0.5-2.6)
Injection	2.3	1.5	0.84 (0.4-1.7)

Hormonal contraceptive users have higher risk behaviors and HIV incidence (self-selection), after adjustment there is no increased risk of HIV acquisition

Hormonal contraception and HIV progression (Baeten et al JAIDS 2005)

- Hormonal contraception at time of HIV acquisition is associated with increased HIV viral load set point and more rapid declines in CD4 counts

Hormonal Contraception and HIV Shedding in HIV+ women

Wang et al AIDS 2004;18:205

- 101 HIV+ Kenyan women observed before and after start of oral contraception (OC) or depot Provera
- Measured cervical HIV shedding
- Hormonal contraception, increased HIV shedding from 42% to 52% (minor effect)
- No change in genital tract viral load (i.e., intensity of shedding)
- Use of hormonal contraception in HIV+ women is probably not a risk to their partners

Summary

- HIV suppresses fertility, HAART may increase fertility and affect hormonal contraceptive efficacy
- Pregnancy increases the rate of HIV acquisition, need barrier contraception during pregnancy
- Pregnancy may increase disease progression in HIV+ women in SSA
- Prevention of unintended pregnancies to HIV+ mothers could prevent many pediatric infections
- Hormonal contraceptive probably do not increase HIV susceptibility or infectivity