

The biology and risks of HIV transmission

Rupert Kaul
University of Toronto

HIV transmission summary

- SUSCEPTIBILITY = access to susceptible target cells at the mucosal site of exposure
 - Increased by inflammation (more cells)
 - Increased by ulcers (more access to cells)
 - Different for different mucosal surfaces
- TRANSMISSION = all about level of virus in genital secretions

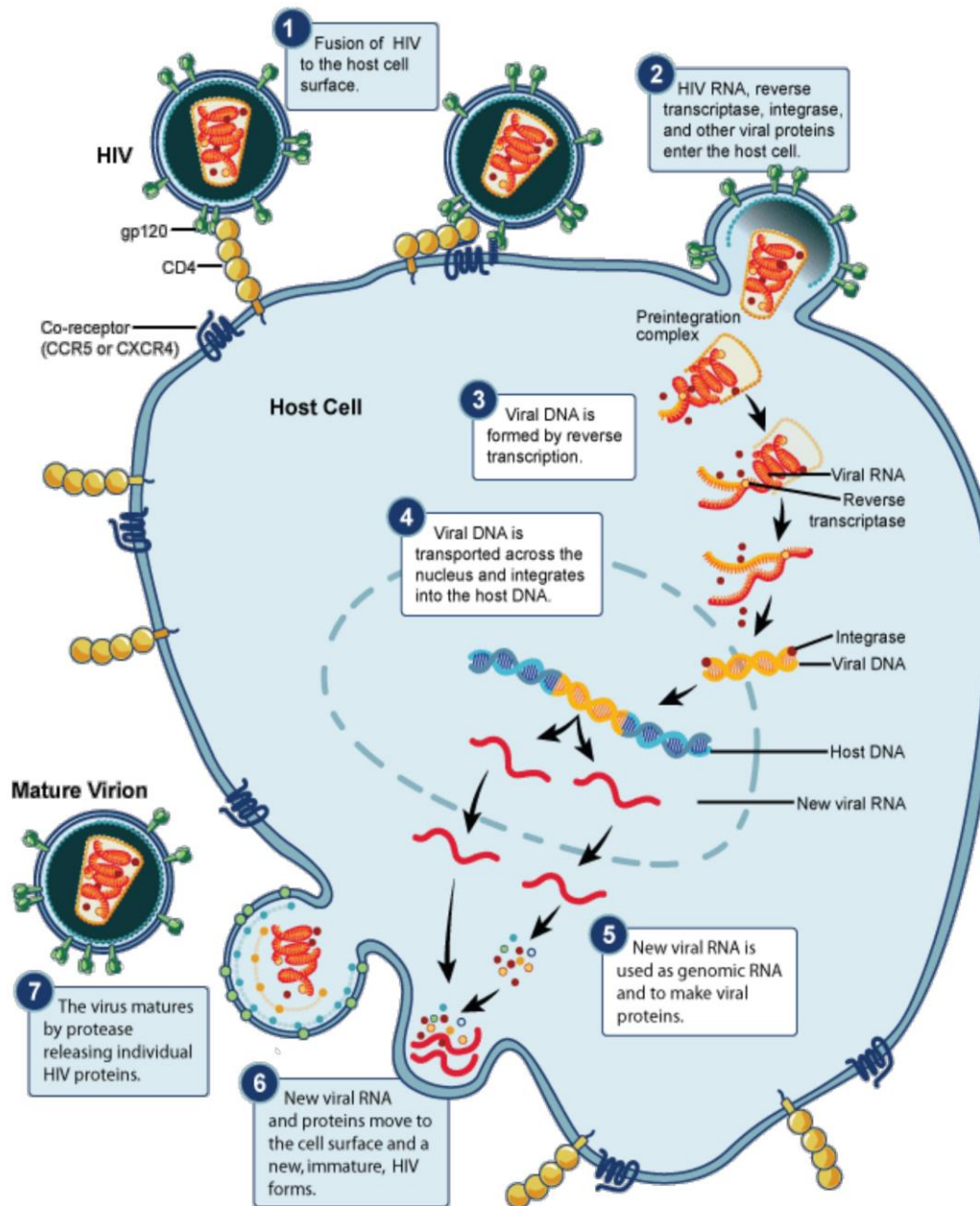
How risky is condomless sex?

Per-act HIV transmission risk estimates Patel *et al.*

Table 1. Estimated per-act probability of acquiring HIV from an infected source, by exposure route.

Exposure route	Risk per 10 000 exposures to an infected source	95% Confidence interval
Parenteral exposure		
Blood transfusion	9250	(8900–9610)
Needle-sharing injection drug use	63 ^b	(41–92)
Percutaneous needle stick	23	(0–46)
Sexual exposure ^a		
Receptive anal intercourse	138 ^c	(102–186)
Insertive anal intercourse	11 ^d	(4–28)
Receptive penile–vaginal intercourse	8 ^e	(6–11)
Insertive penile–vaginal intercourse	4 ^e	(1–14)
Receptive oral sex	Low ^f	(0–4)
Insertive oral sex	Low ^f	(0–4)
Vertical transmission		
Mother-to-child transmission	2260 ^g	(1700–2900)

- **ANAL: 1/72 (bottom) and 1/909 (top)**
- **ORAL: much lower - ?1/10,000**



HIV acquisition

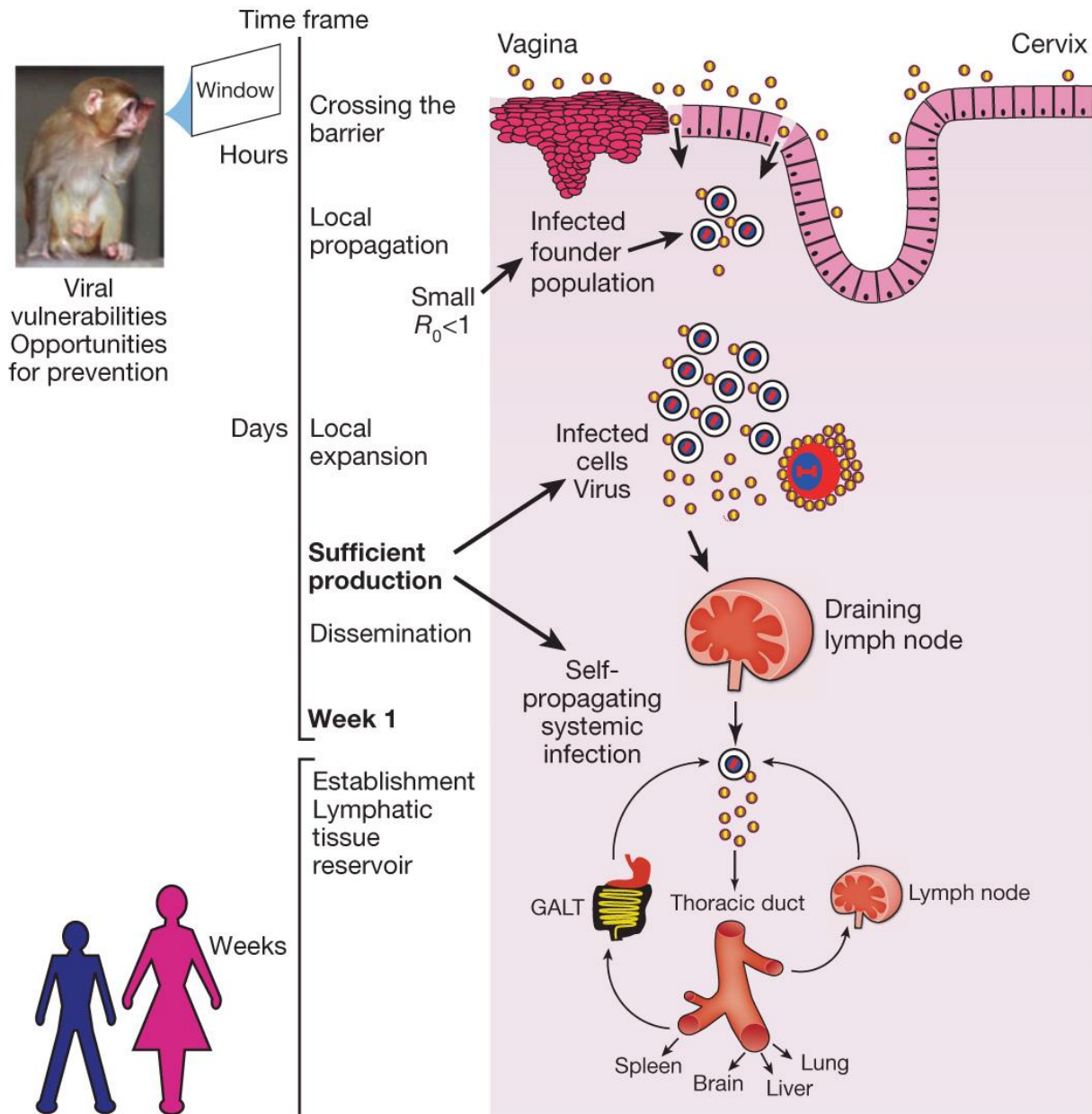


Figure 1 | Time frame, sites and major events in vaginal transmission and the fast phase of lentivirus infection.

Foreskin and HIV prevalence

- but is it causing increased HIV risk?

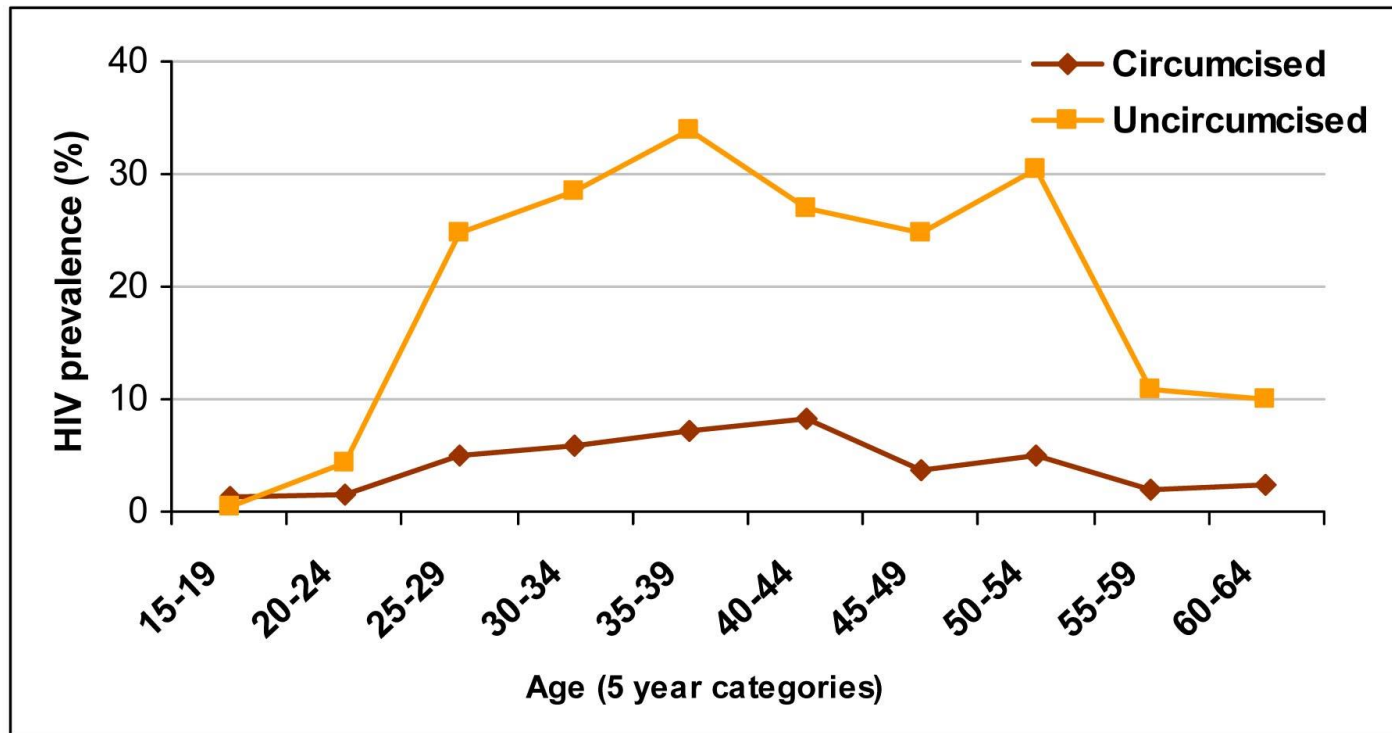


Figure 9. HIV prevalence among Kenyan men ages 15-64 who were tested by circumcision status, KAIS 2007.

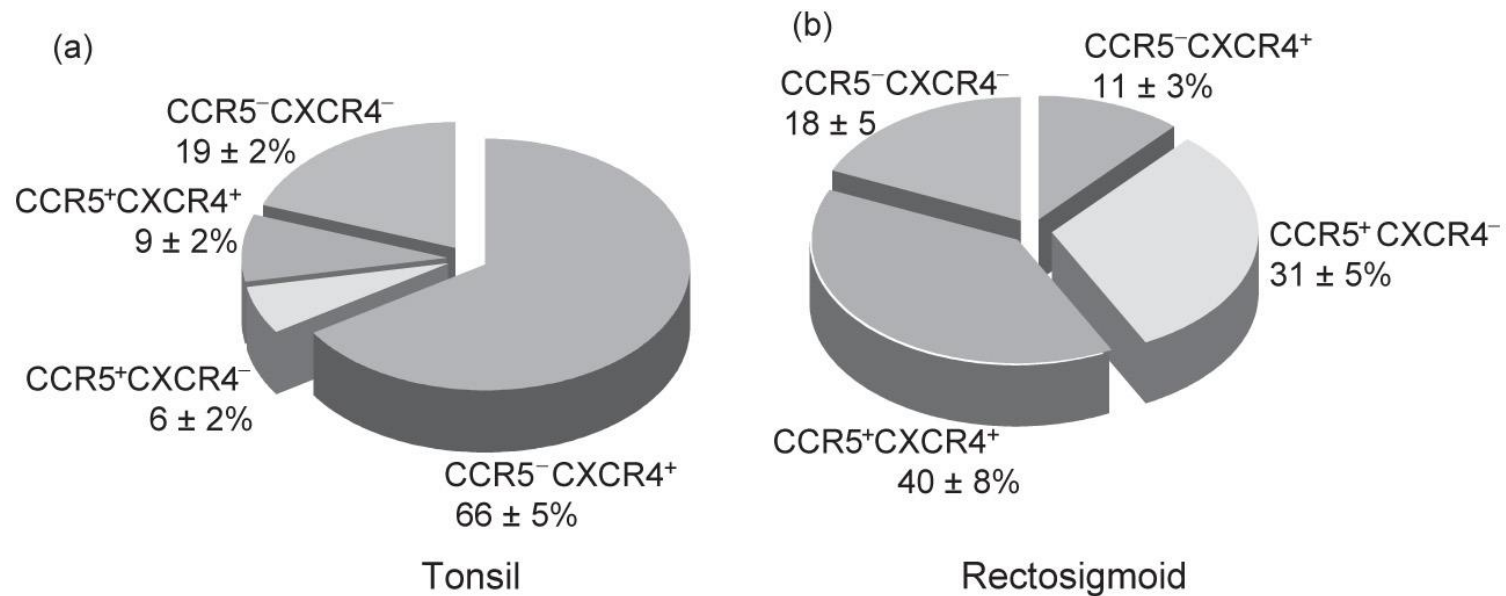
Circumcision and HIV prevention

- 3 large randomized trials of male circumcision
- Very consistent results in Uganda, Kenya, S Africa
- Reduced HIV rates by >60%
- Impact in heterosexual men with a foreskin
- Also reduced herpes, syphilis, HPV (men) and HPV, bacterial vaginosis (female partners)
- Less benefit in MSM – may benefit if top only

Foreskin surface area and HIV acquisition in Rakai, Uganda (size matters)

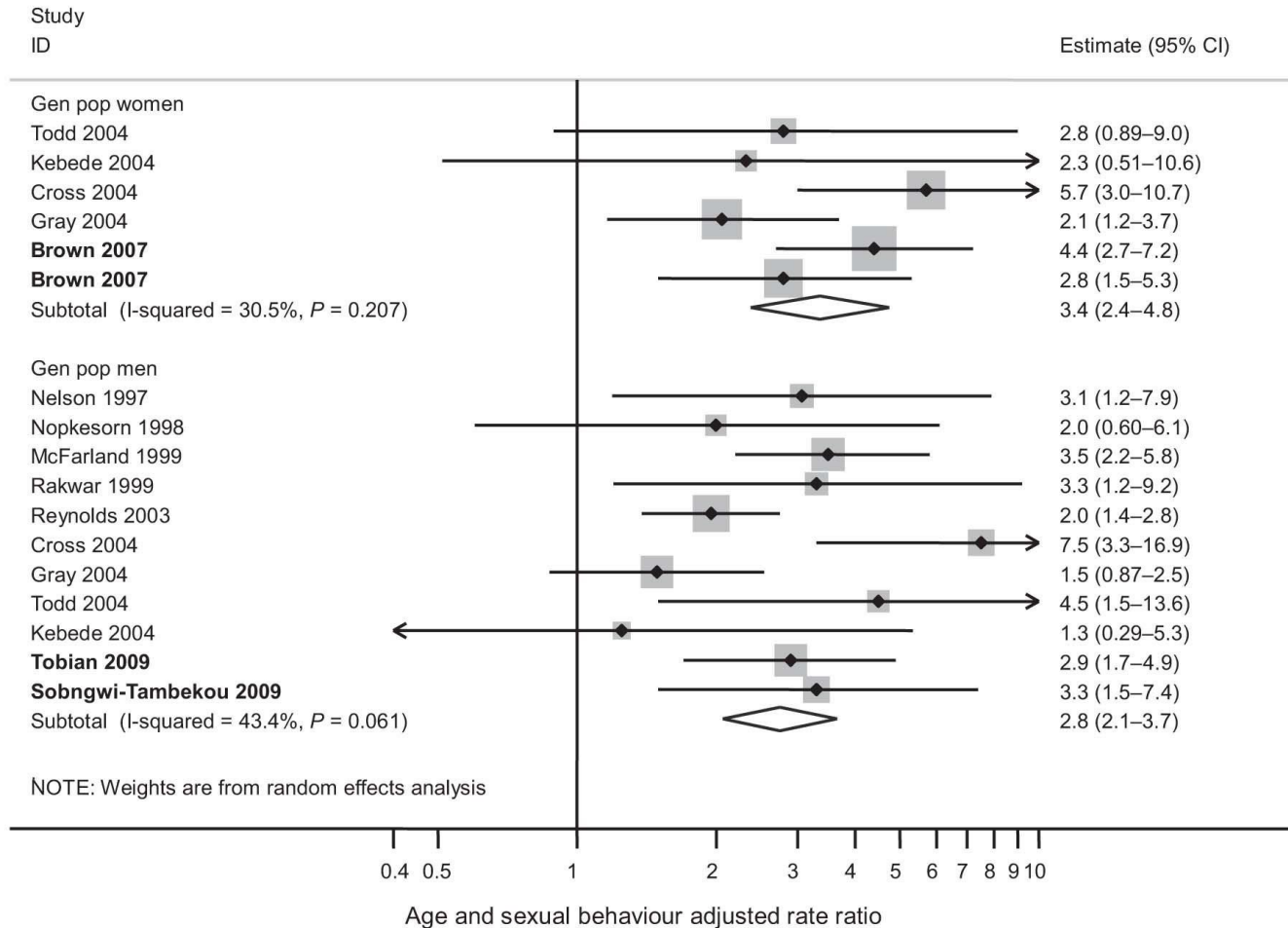
Conclusion: The risk of male HIV acquisition is increased among men with larger foreskin surface areas. © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins

The type of mucosa is important



Expression of HIV-1 co-receptors on CD4 T cells in tonsillar and rectosigmoid tissues.

Genital infections and HIV risk



HIV meds in HIV negative people

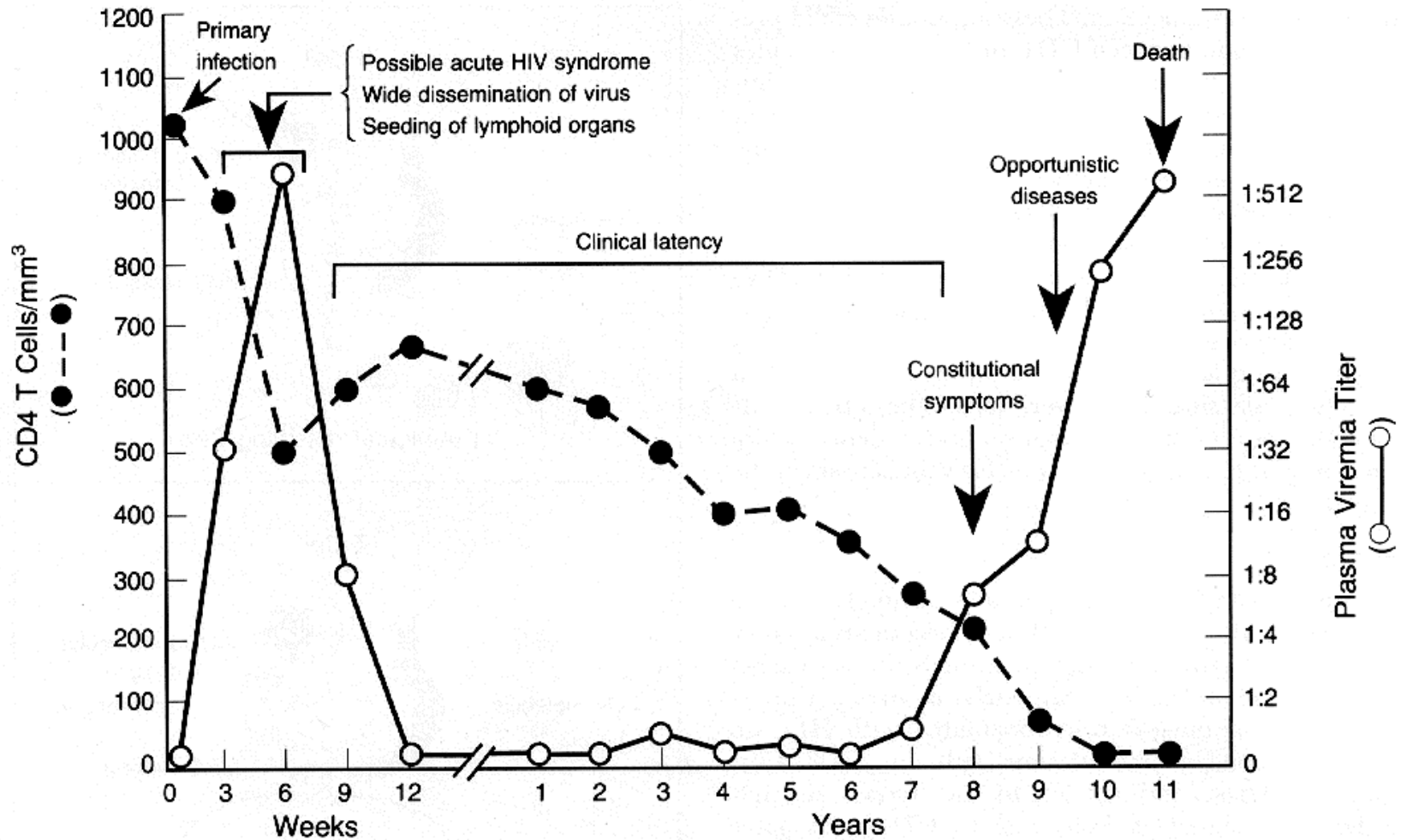
- 2500 men “at high risk for acquisition of HIV infection” in USA, SA, Thailand
- Intervention: Truvada once daily PrEP
- Result: 44% reduction in HIV incidence
- Estimated risk reduction:
 - 76% for two doses per week
 - 96% for four doses per week
 - 99% for seven doses per week

Newer PrEP studies at CROI 2015

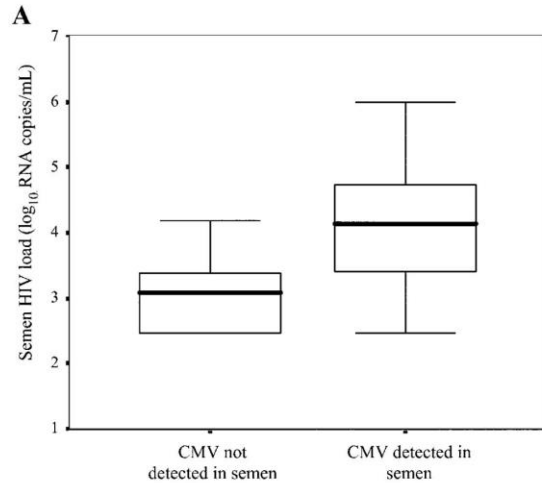
- IPERGAY study – randomized, double blinded
 - “On demand” truvada vs. placebo in French MSM
 - 86% reduction in HIV incidence: stopped early
 - Increase in mild GI side effects
- PROUD study – randomized, open label
 - Daily truvada vs. placebo in UK MSM
 - 86% reduction in HIV incidence: stopped early
 - No difference in STIs

HIV transmission

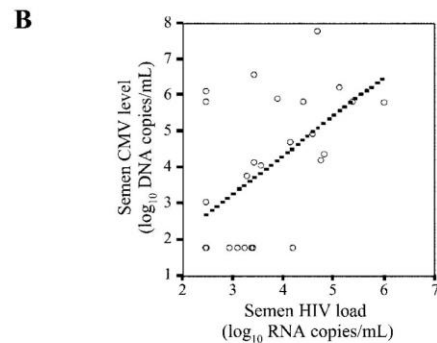
HIV: clinical course



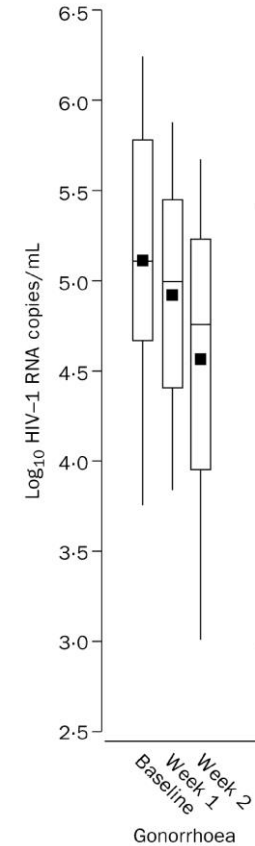
Genital infections



- Semen viral load is increased by co-infections
 - Asymptomatic
 - Symptomatic



- sVL may increase ~10 fold in both cases



Sheth P.

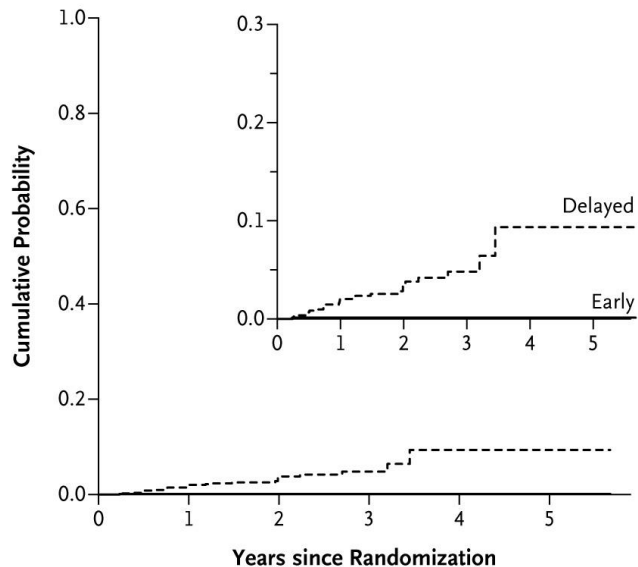
J Infect Dis, 2006.

Cohen M.

Lancet. 1997.

ART and transmission: HPTN 052

A Linked HIV Transmission



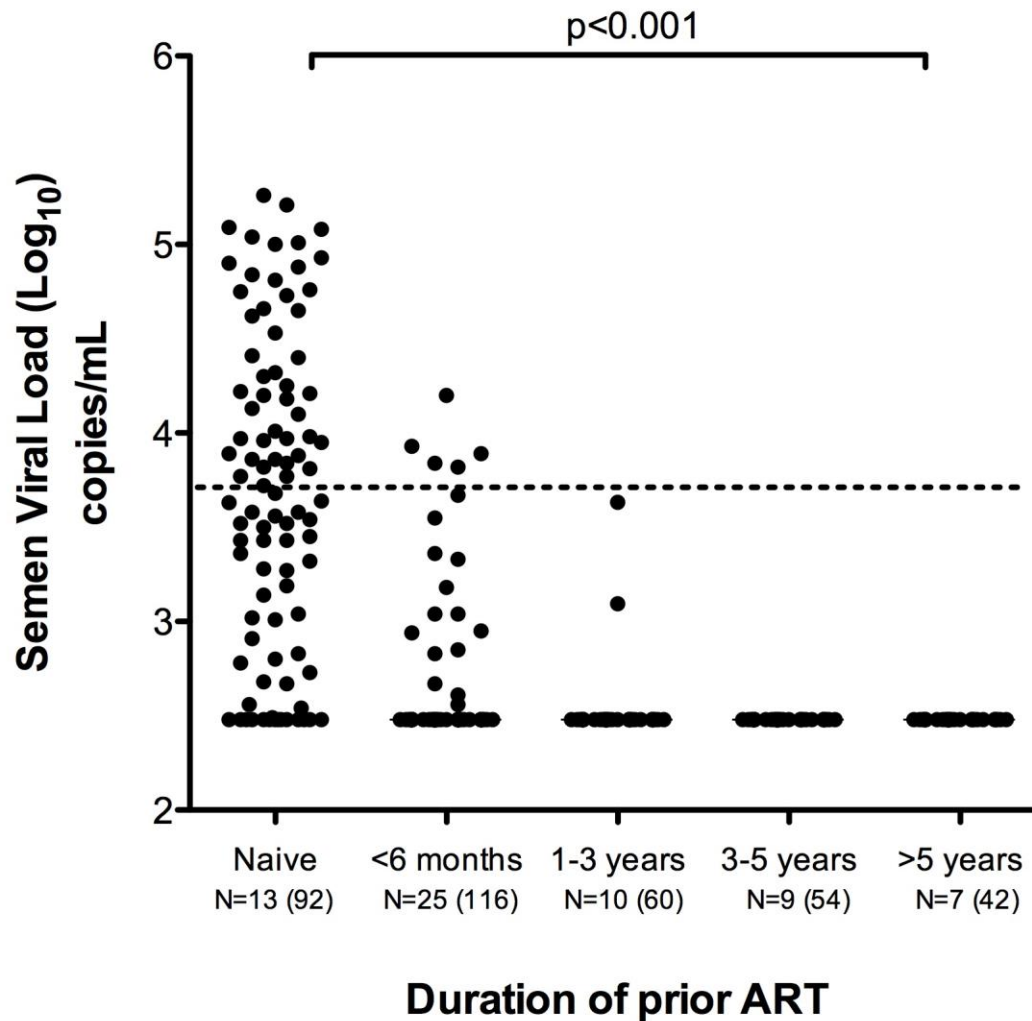
No. at Risk

Early	893	658	298	79	31	24
Delayed	882	655	297	80	26	22

- 1,763 het. couples
- 29 “linked” transmissions
- Only 1 in ART arm: 96% reduction
- Also reduced AIDS, esp. TB

Cohen M. NEJM. 2011;365:493-505.

Antiretroviral therapy and the semen VL



Osborne B.
J Infect Dis, 2013

ART and transmission

- Rodger A and PARTNER study (European)

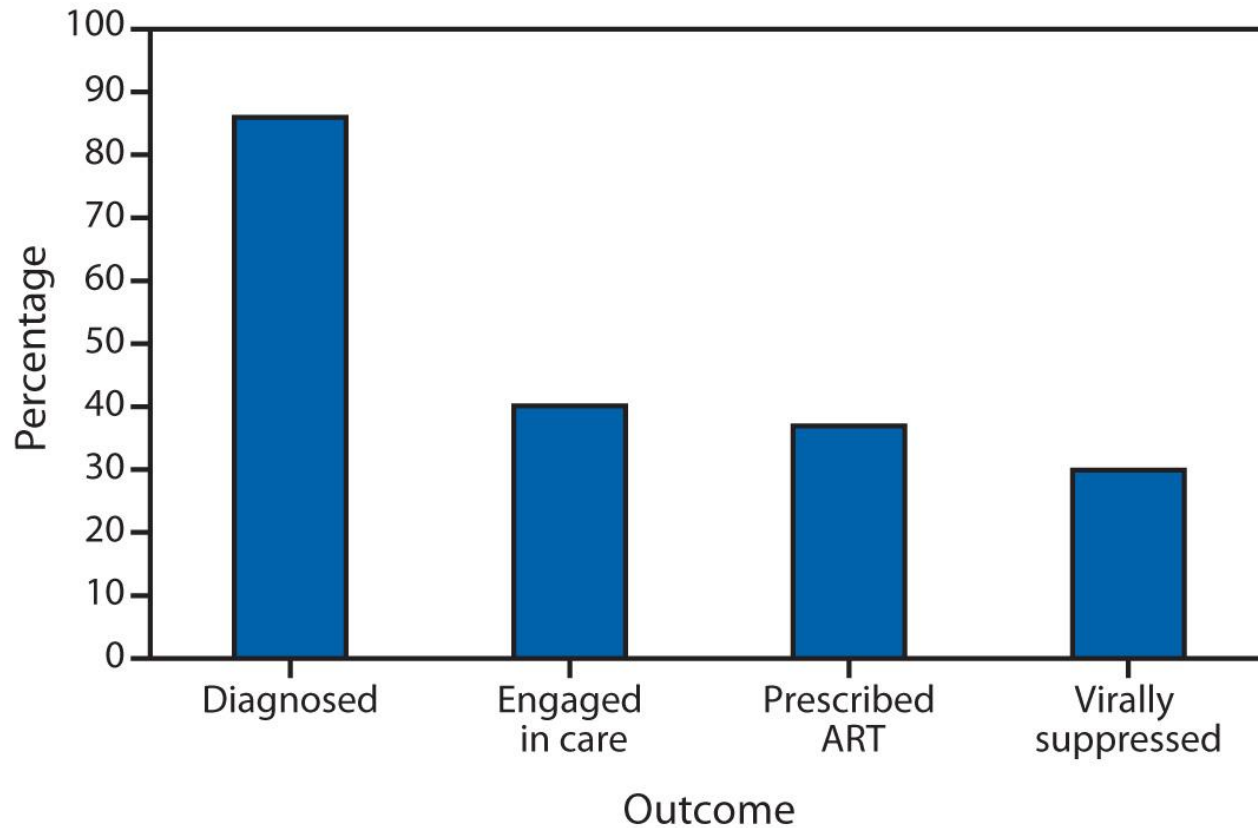
#153LB stable ART: what is transmission risk?
894 years follow up: 586 HT, 308 MSM
median duration on ART 4.9 years
condomless sex for 2 years at baseline
-then 45 times /year
no phylogenetically linked transmissions
HIV transmission = 0 (95% CI: 0-0.40/100)

Risk Behaviour Reported by the HIV Negative Partner and Rates of Transmission							
HIV status and sexual orientation of couples	Risk behaviour reported by HIV -ve partner	Number of events (linked HIV transmissions)	Couple-years of follow up (CYFU)	Estimated number of sex acts	Transmission risk per condomless sexual contact (95% CI)	Rate of within couple HIV transmission (per 100 CYFU) (95% CI)	10 year risk of within couple HIV transmission (95% CI)
Overall	Condomless sex	0	894	44,439	0 (0 - 0.00008)	0 (0-0.40)	0 (0 - 3.9%)
	Condomless sex VL<50	0	836	41,479	0 (0 - 0.00009)	0 (0-0.43)	0 (0 - 4.2%)
	Condomless anal sex	0	374	21,032	0 (0 - 0.00017)	0 (0-0.96)	0 (0 - 9.2%)
HT m+/f-partners	Condomless sex	0	288	13,728	0 (0 - 0.00028)	0 (0-1.25)	0 (0 - 11.7%)
	Condomless vaginal sex with ejaculation	0	191	8,915	0 (0 - 0.00043)	0 (0-1.88)	0 (0 - 17.1%)
	Condomless vaginal sex without ejaculation	0	174	6,377	0 (0 - 0.00060)	0 (0-2.07)	0 (0 - 18.7%)
HT m-/f+ partners	Condomless sex	0	298	14,295	0 (0 - 0.00027)	0 (0-1.21)	0 (0 - 11.4%)
	Condomless vaginal sex	0	272	14,149	0 (0 - 0.00027)	0 (0-1.32)	0 (0 - 12.4%)
MSM	Condomless anal sex	0	308	16,416	0 (0 - 0.00023)	0 (0-1.17)	0 (0 - 11.0%)
	Condomless receptive anal sex (with or without ejaculation)	0	182	7,738	0 (0 - 0.00050)	0 (0-1.97)	0 (0 - 17.9%)
	Condomless insertive anal sex	0	262	11,749	0 (0 - 0.00033)	0 (0-1.37)	0 (0 - 12.8%)

Problems with treatment as prevention

- HIV+ partner needs to know that they are infected, be willing to take ART carefully
 - Minority of HIV+ people in USA are on treatment and undetectable
- HIV- partner needs to know who partner will be, and their HIV/treatment status

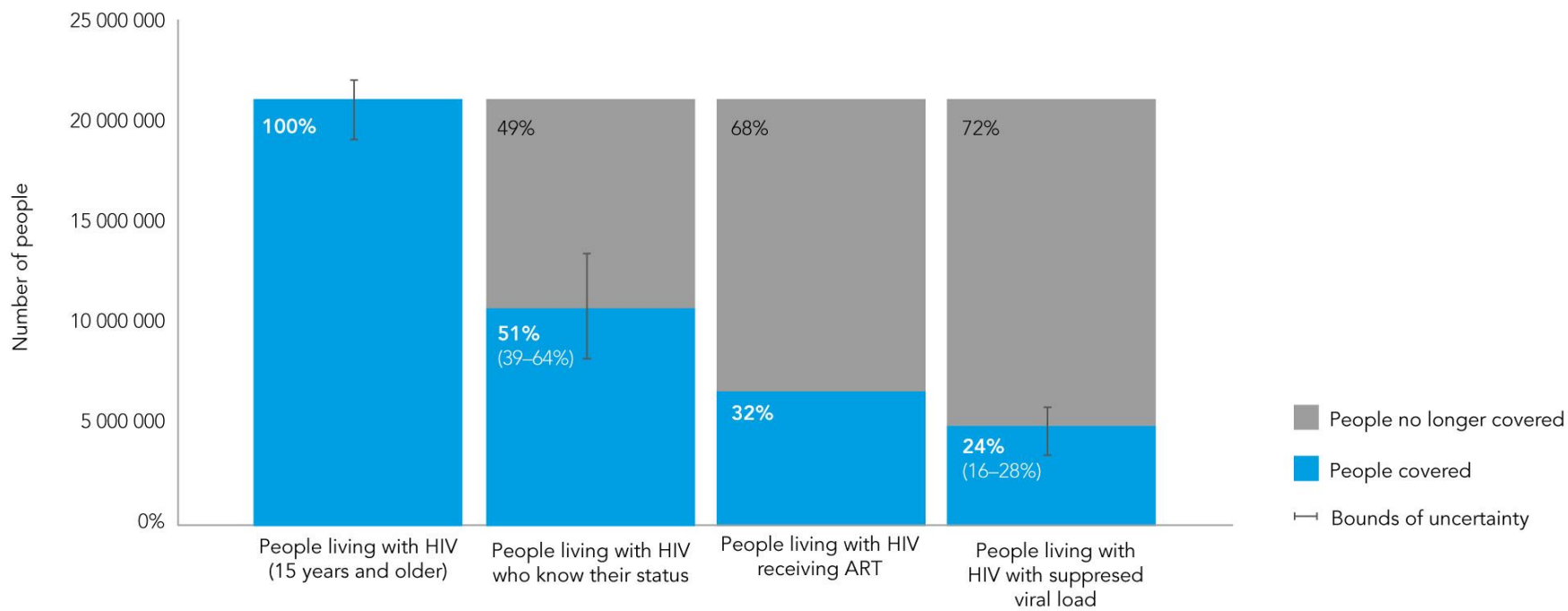
FIGURE 1. Estimated percentage of persons living with HIV infection,* by outcome along the HIV care continuum — United States, 2011



Abbreviations: HIV = human immunodeficiency virus; ART = antiretroviral therapy.

* N = 1,201,100.

FIGURE 4.3
Abbreviated HIV treatment cascade for sub-Saharan Africa, 2012



Summary

- Prevention in HIV negative men:
 - Condoms and “choose wisely” still important
 - PrEP effective, but need implementation research
 - Male circumcision has limited role in Canada
- Prevention in HIV+ men:
 - Antivirals likely to trump everything
 - STIs can have important local effects
 - Cure would be effective prevention...