Sexual transmission of HIV: a heterogeneous event

Deutsch-Österreichischer AIDS Kongress

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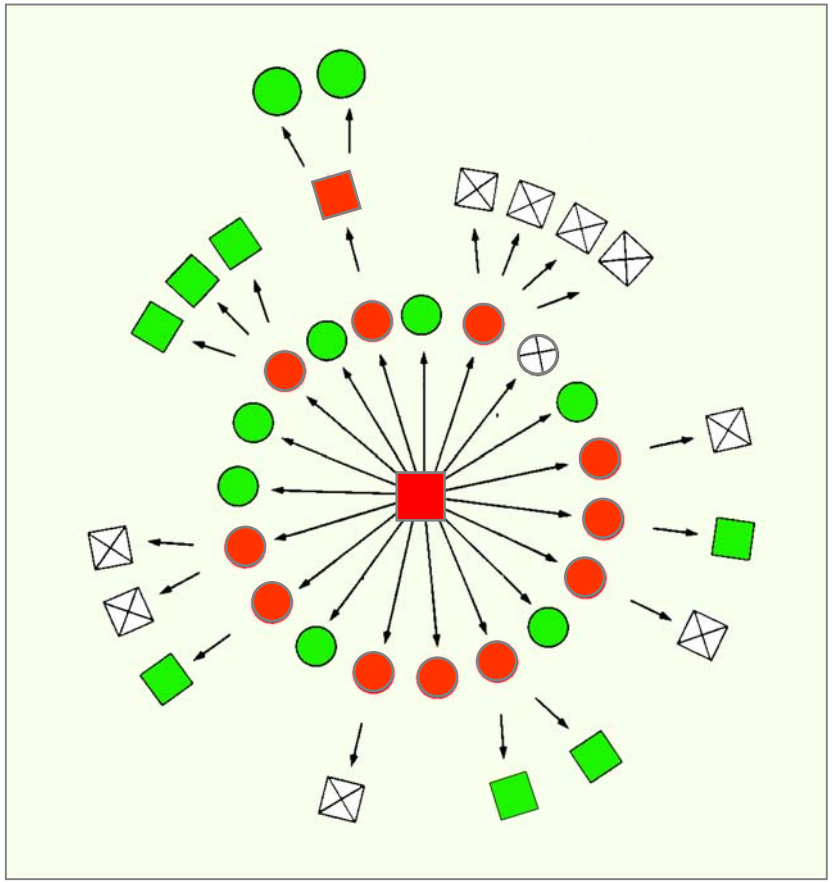
Heterosexual Transmission

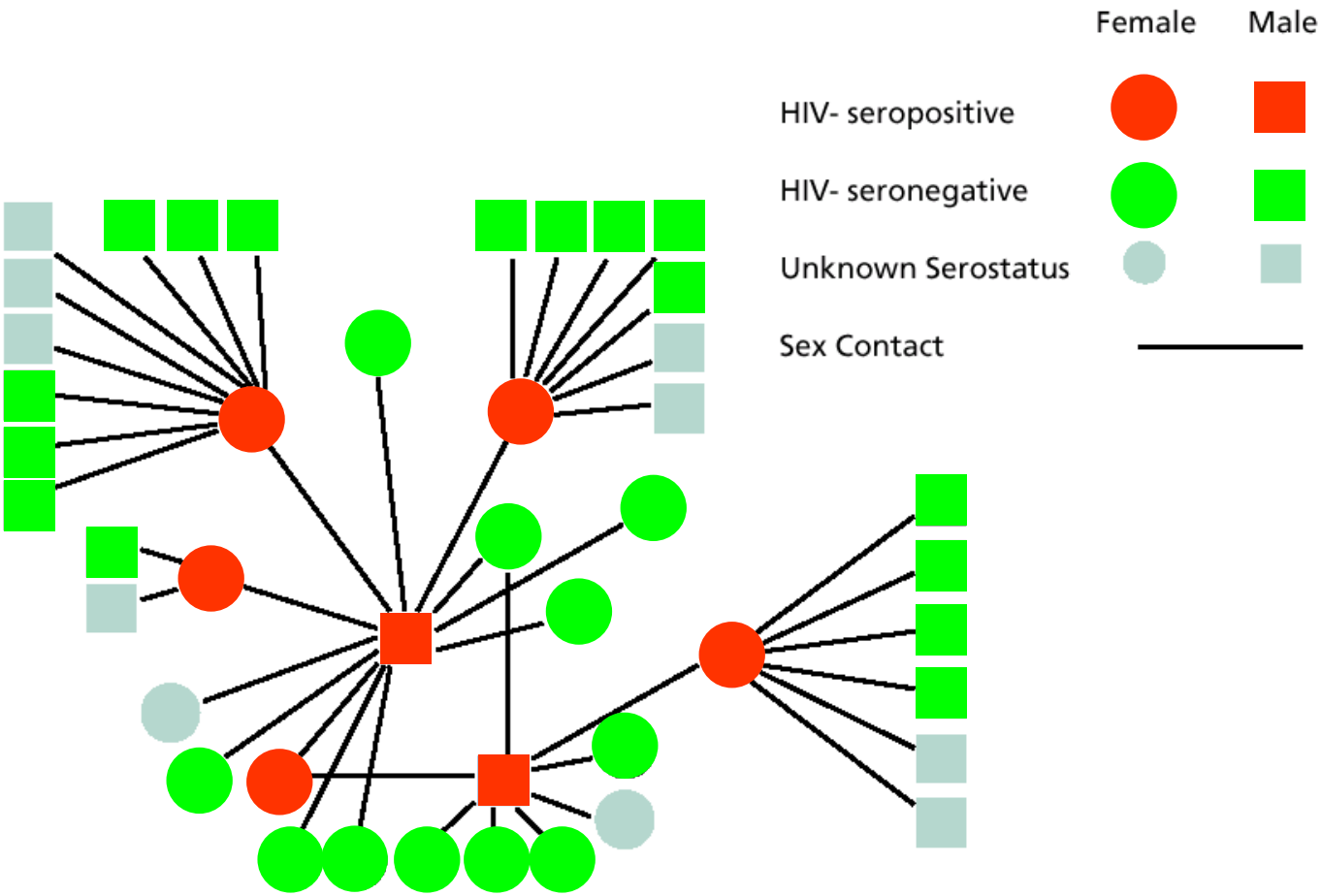


♀ HIV-pos.

♂ HIV-neg.

Clumeck N, et al, NEJM, 1989;321:1460

Sexual network and HIV



MMWR, 2000;49:861-864

Transmission risk per sex contact

	Partner studies	Anonymous contact
♀ → ♂	1- 9% partner pos. <0.3% per contact	3.1% - 8.2%
♂ → ♀	9-18% partner pos 0.3% per contact	

Padian, JAMA 1987
De Vincenzi, NEJM 1994
Nicolosi, Epidemilogy 1994

Mastro, AIDS 1994
Cameron, Lancet 1989

Risk after single sexual exposure

- 422 customers of Kenyan prostitutes
- 293 HIV-neg, prospectively followed
- 12% s/c rate in 12 wk period
  - Non circumcision: OR 8.2 (3-23)
  - GUD OR 4.7 (1.3-17)
- 73 men: only one single contact
  - 8.2% s/c rate (6/73), 43% of uncircumcised

Cameron et al, 1989, Lancet ii:403-7

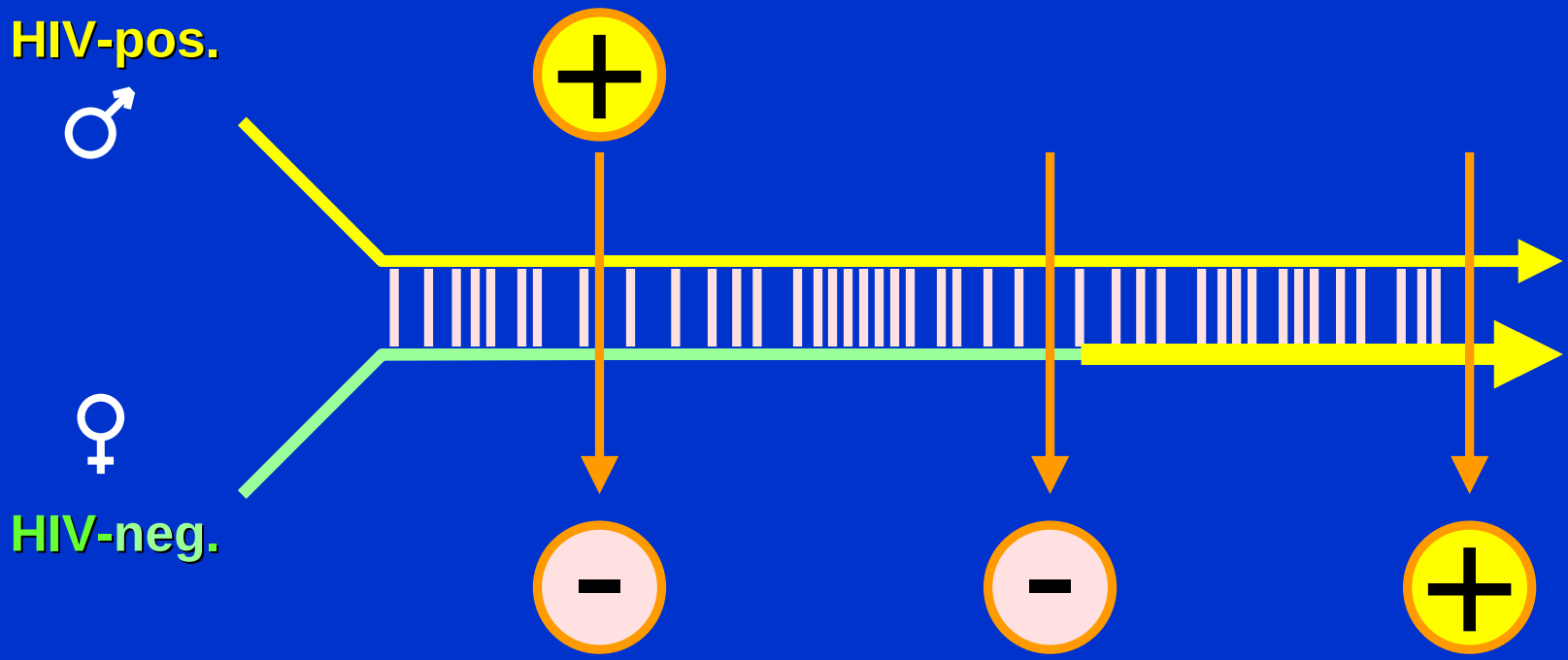
Mastro study, Thailand

- 1115 military conscripts (21y)
  - 6.9% HIV-pos (n=77)
- Sex with female prostitutes
- mathematical modelling:
  - risk after single contact: 3.1% (2.5-4.0)
  - adjusted for random error in self reported frequency of contact: 5.6% (4.1-7.5%)
- Risk signif. higher in men reporting Hx of STD

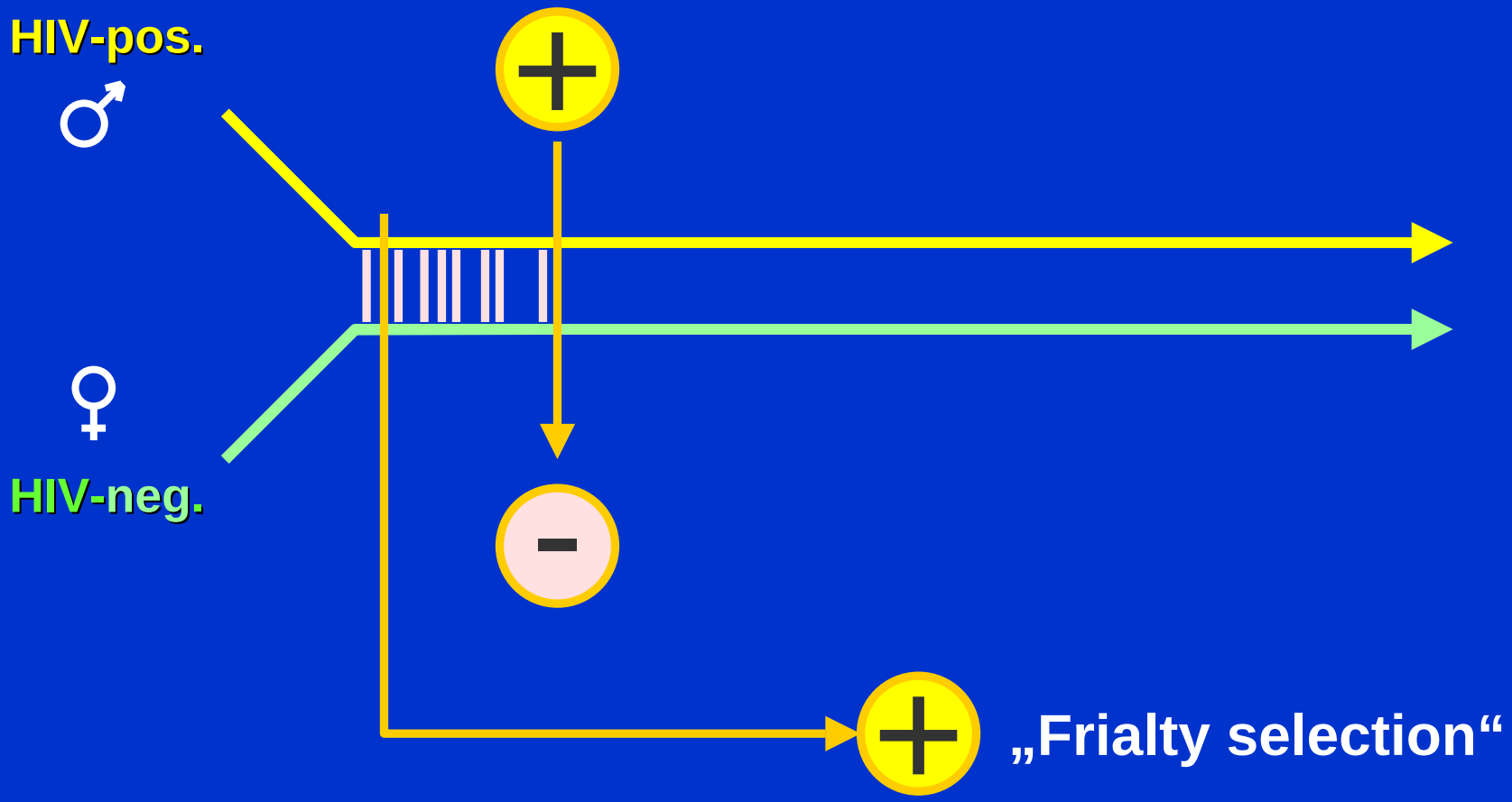
Mastro et al, 1994, Lancet 343:204-7

Calculating Transmission Risk in HIV Discordant Couples

Frequently cited: De Vincenzi et al, NEJM, 1994;331:341-6



Selection of Non-Transmittors



Results from Math Modelling

- Transmission risk within partnership highest during early period of sexual relationship
- Transmission best perscribed per partnership, not per contact

- Wiley et al, Heterogeneity in the probability of HIV transmission per sexual contact: the case of male- to- female transmission in penile-vaginal intercourse. Stat Med 1989: 8:93
- Downs et al, Probability of heterosexual transmission of HIV: Relationship to the number of unprotected sexual contacts. JAIDS, 1996, 11:388
- Shiboski & Padian: Epidemiologic evidence for time variatlon in HIV infectivity. JAIDS 1998, 19:527.

Reasons for Frialty Selection

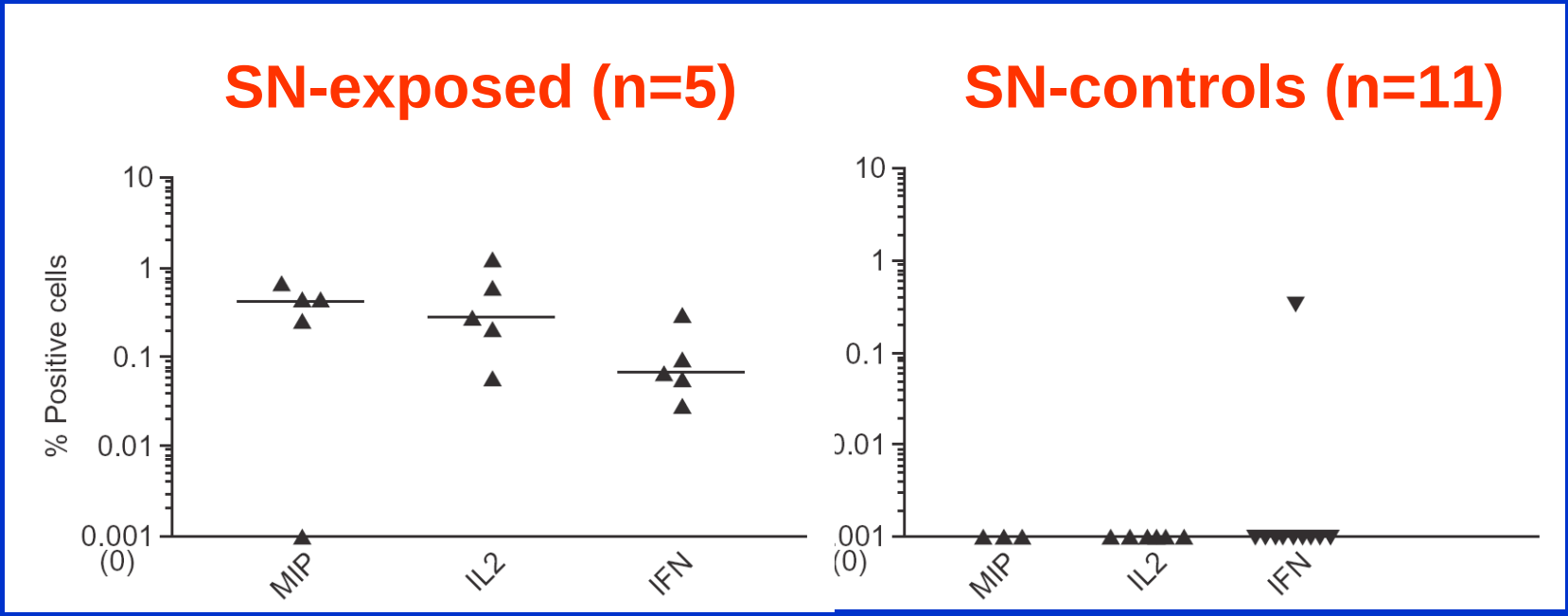
- **Genetic predisposition**
  - CCR5 Δ32-delection variant
  - other chemokine polymorphisms
  - HLA phenotype
- **Acquired immunity**
  - cell mediated immune response
  - humoral immune response

Immune response in highly exposed seronegative partners

- 12 HIV- partners of HIV-positive
- Frequent uprotected sexual exposure
- Last exposure < 6 months
- No CCR5-deletion mutant
- In vitro p24 stimulation of PBMC
  - Cytokine expression
  - Compared with non-exposed controls

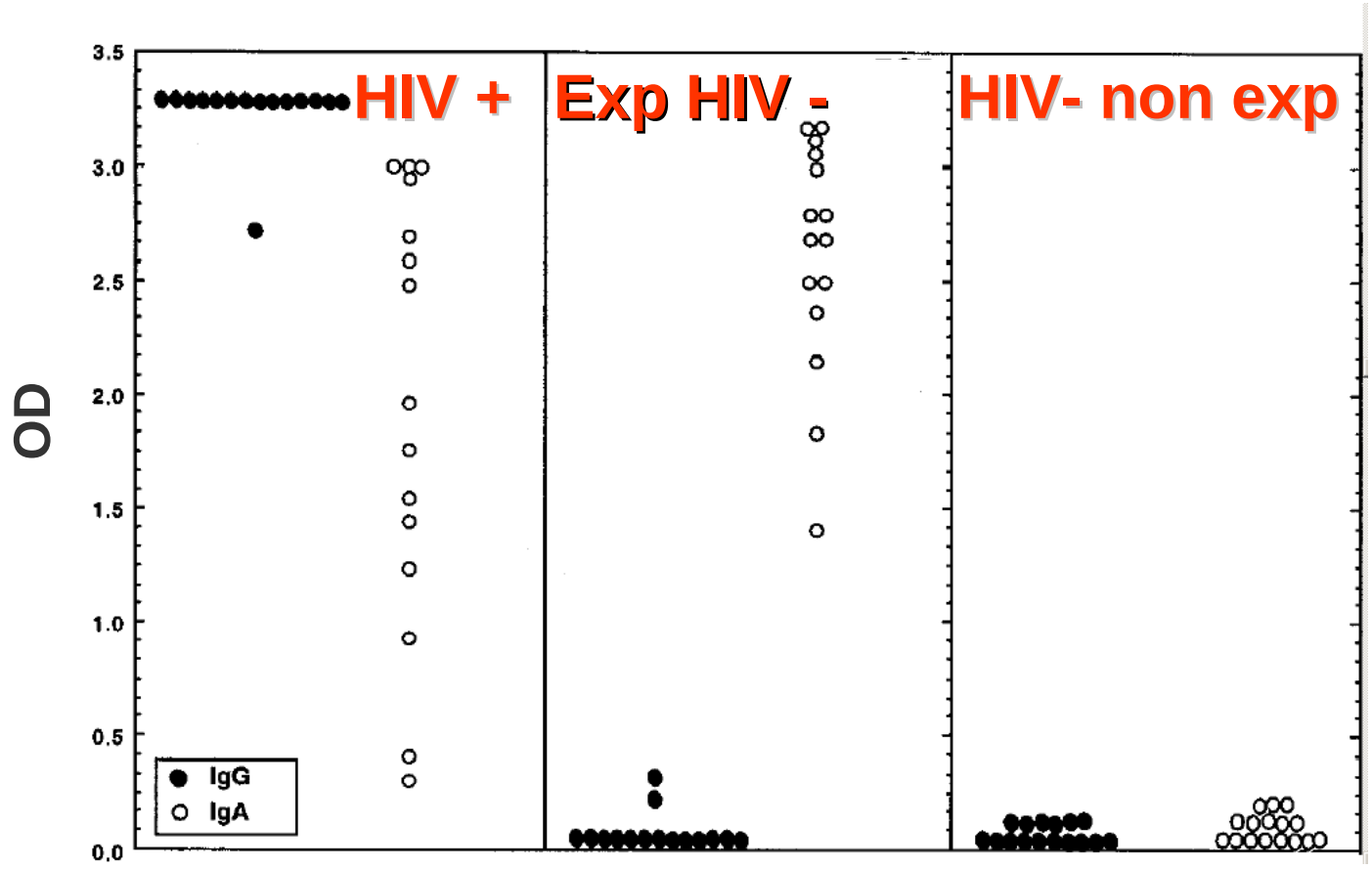
Eyson et al, AIDS 2003, 17:2299–2311

p24 response in SN-exposed



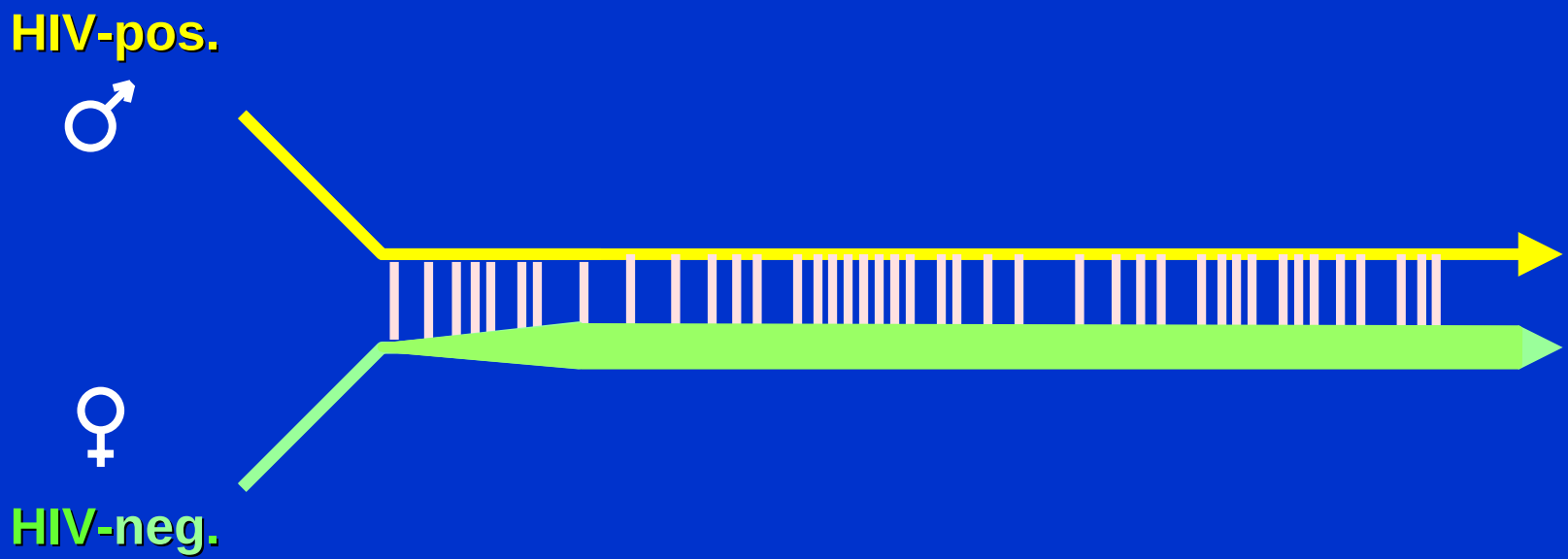
Eyson et al, AIDS 2003, 17:2299–2311

IgA in Exposed Seronegative

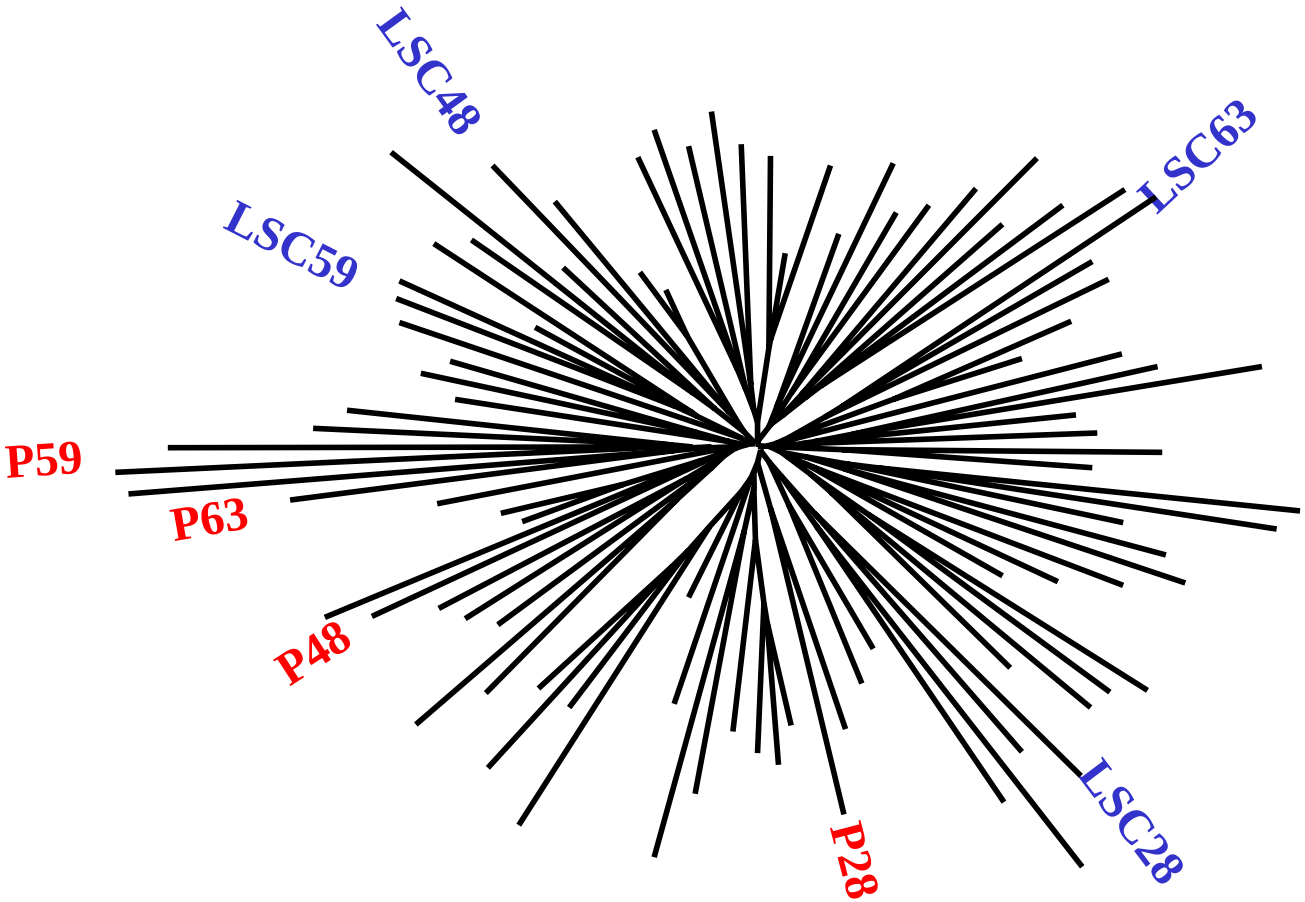


Mazzoli et al, 1999, JID

Acquired protective Immunity ?



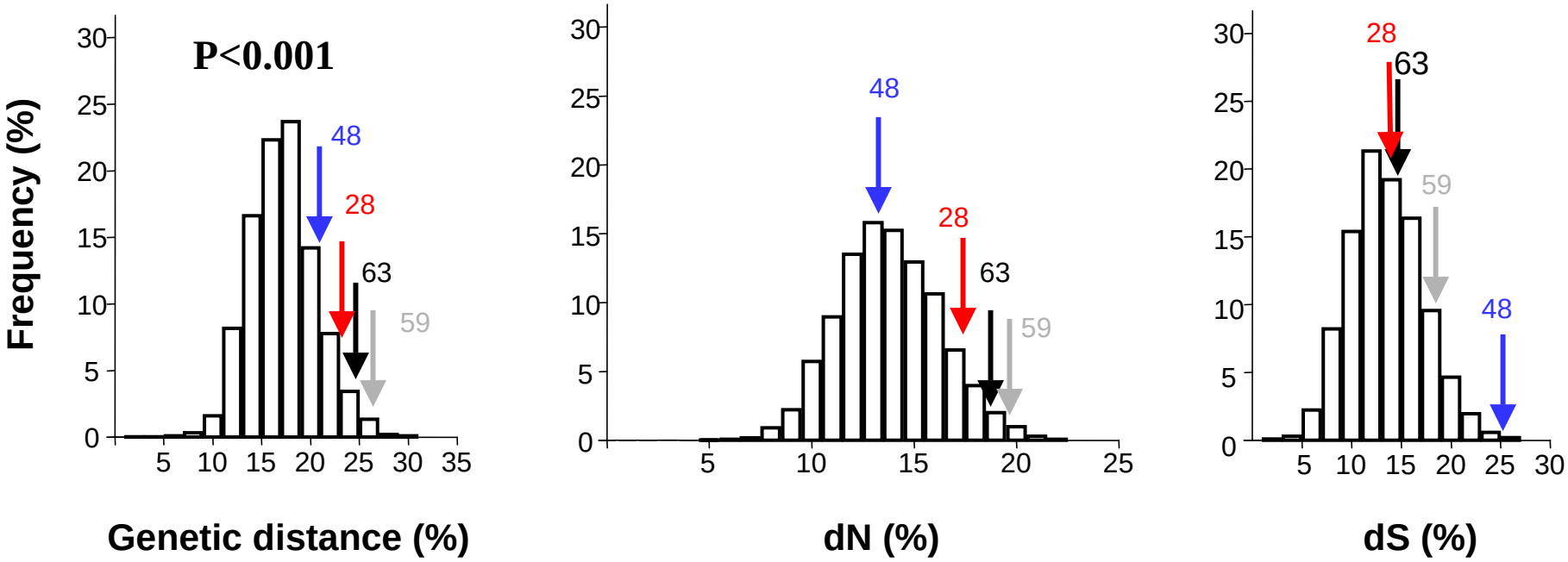
Phylogenetic Relationship of HIV-1 C2-V5 Consensus Sequences of LSC, their Long-term Sexual Partners and Control Sequences (n=82) of Subtype B HIV-1 from the Los Alamos Database Published from 1997-2002



Zhu et al, CROI 2004

Pairwise Distance Distributions of HIV-1 C2-V5 Sequences

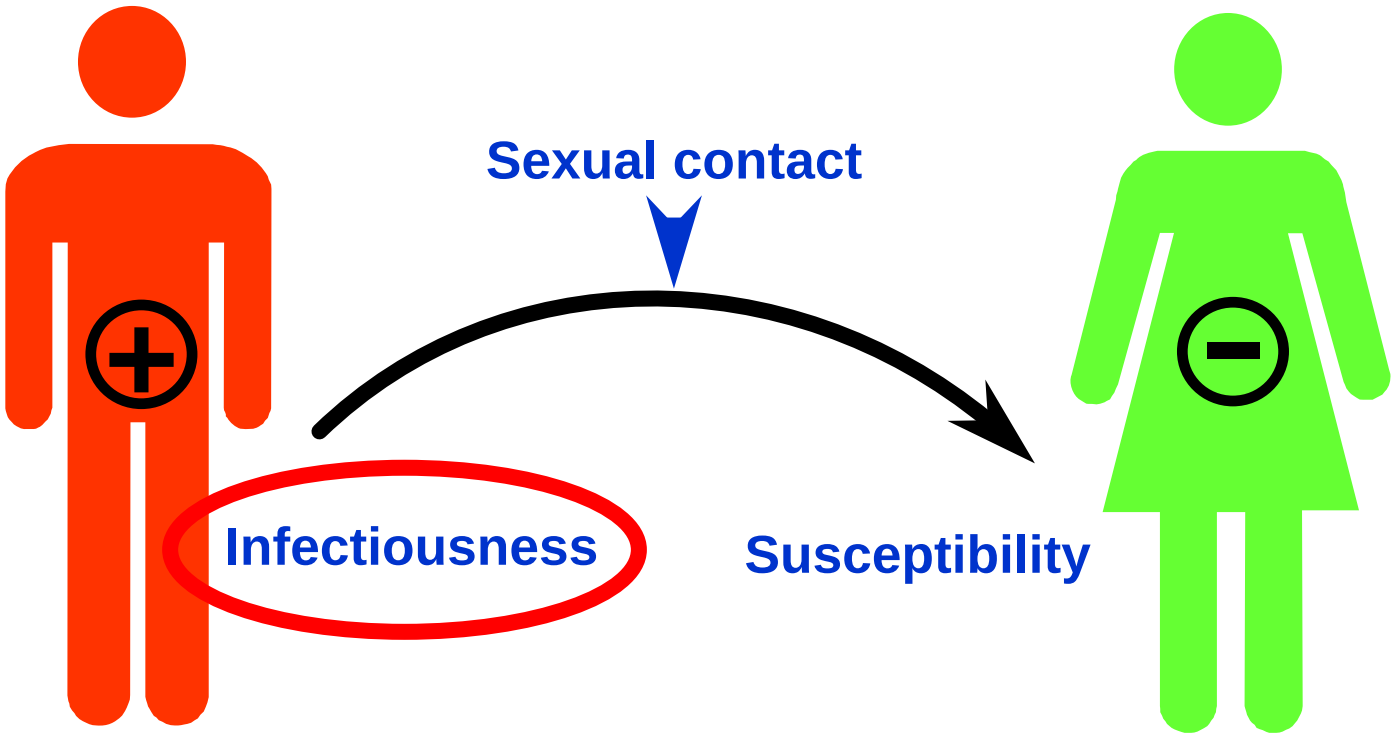
US (n=82, published 1997-2002)



Conclusion

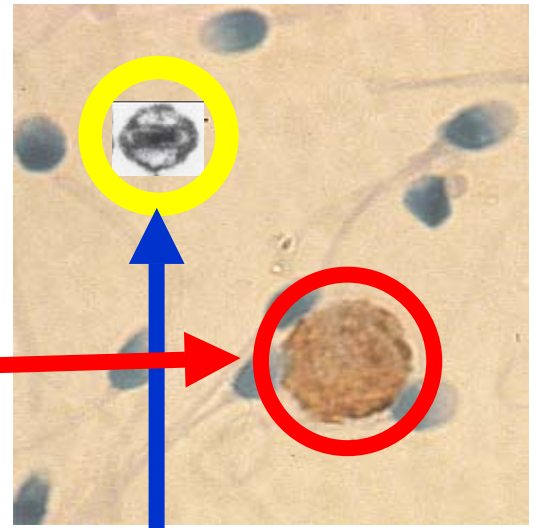
- **HIV transmission risk highly heterogenous**
- **Immune response may reduce risk**

Sexual Transmission of HIV



Sexual Transmission of HIV

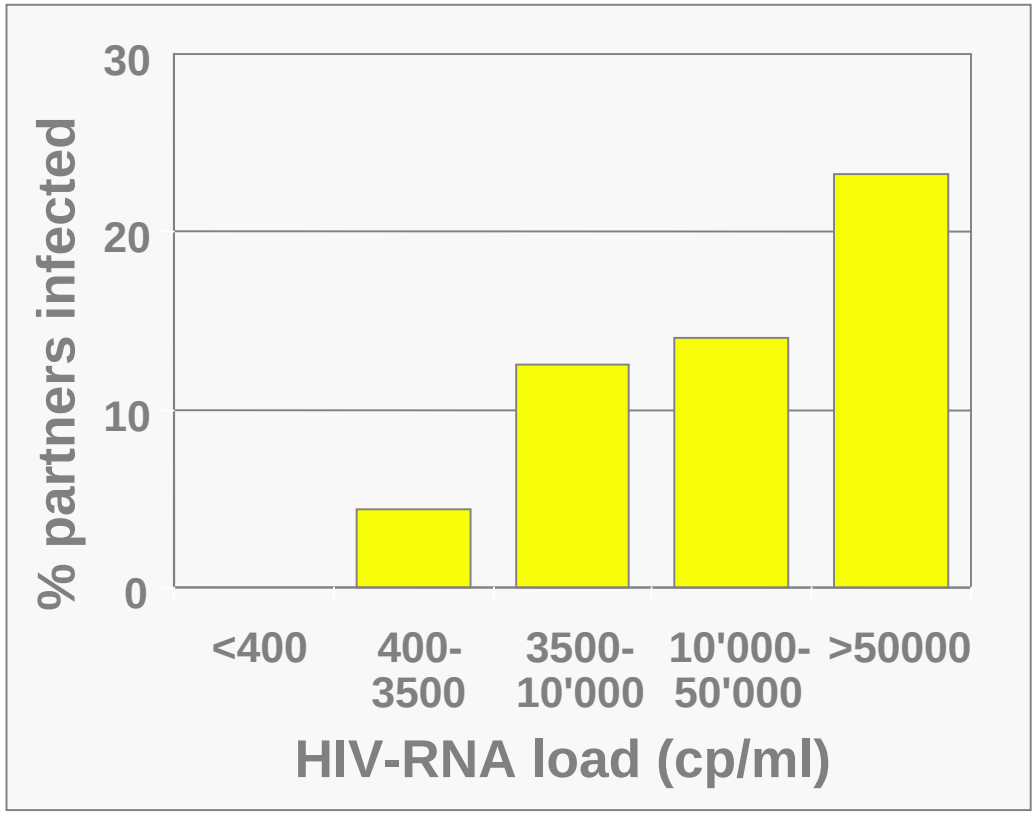
- **Risk of transmission enhanced with:**
  - **Low CD4 counts**
  - **Symptomatic disease**
  - **High blood viral load**
  - **Genital inflammation**
  - **PHI**



r = 0.5-0.6

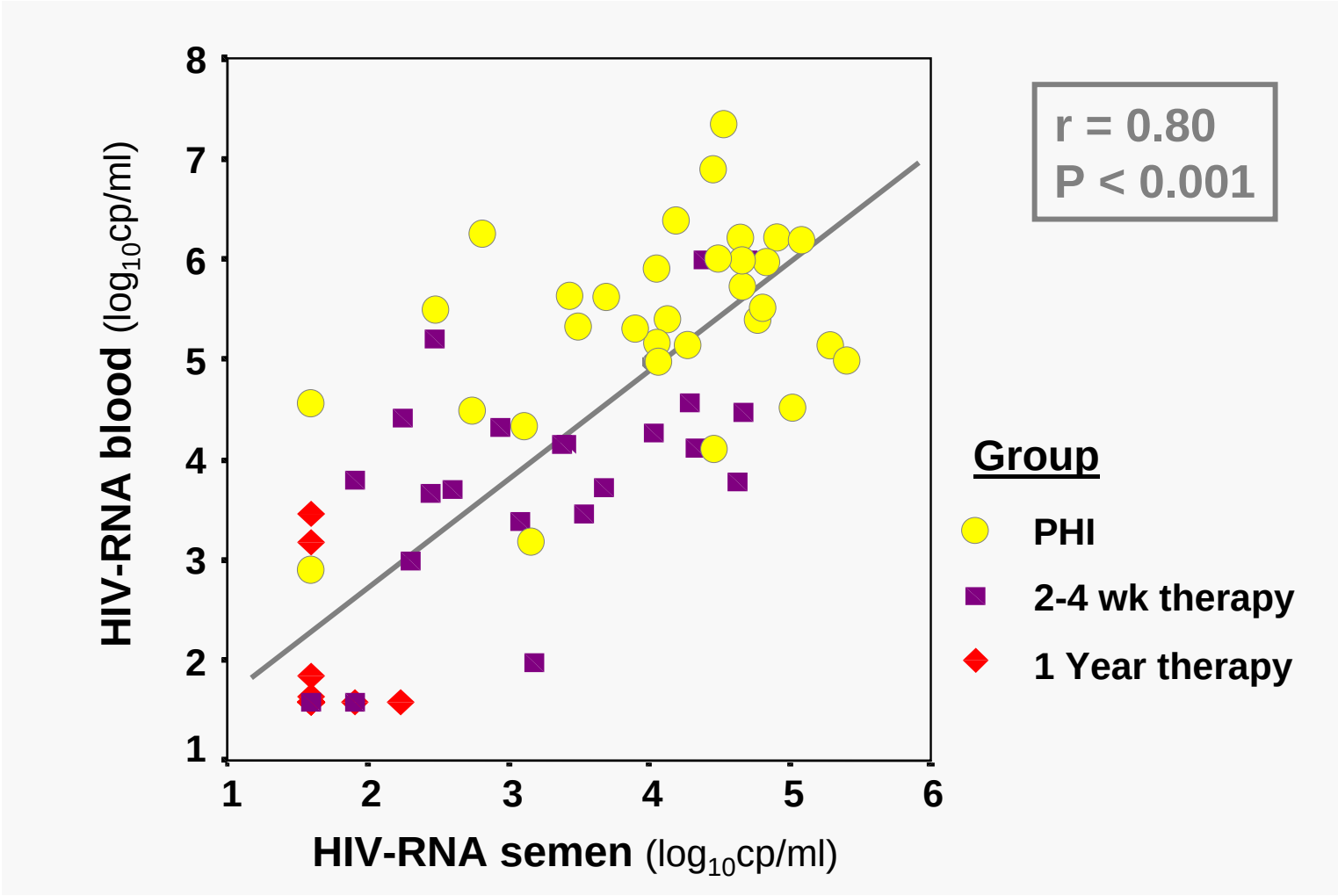
VL and HIV-Transmission

- **Rakai (Uganda)**
- **453 HIV-disk. couples**
- **11.6 % TR / year**



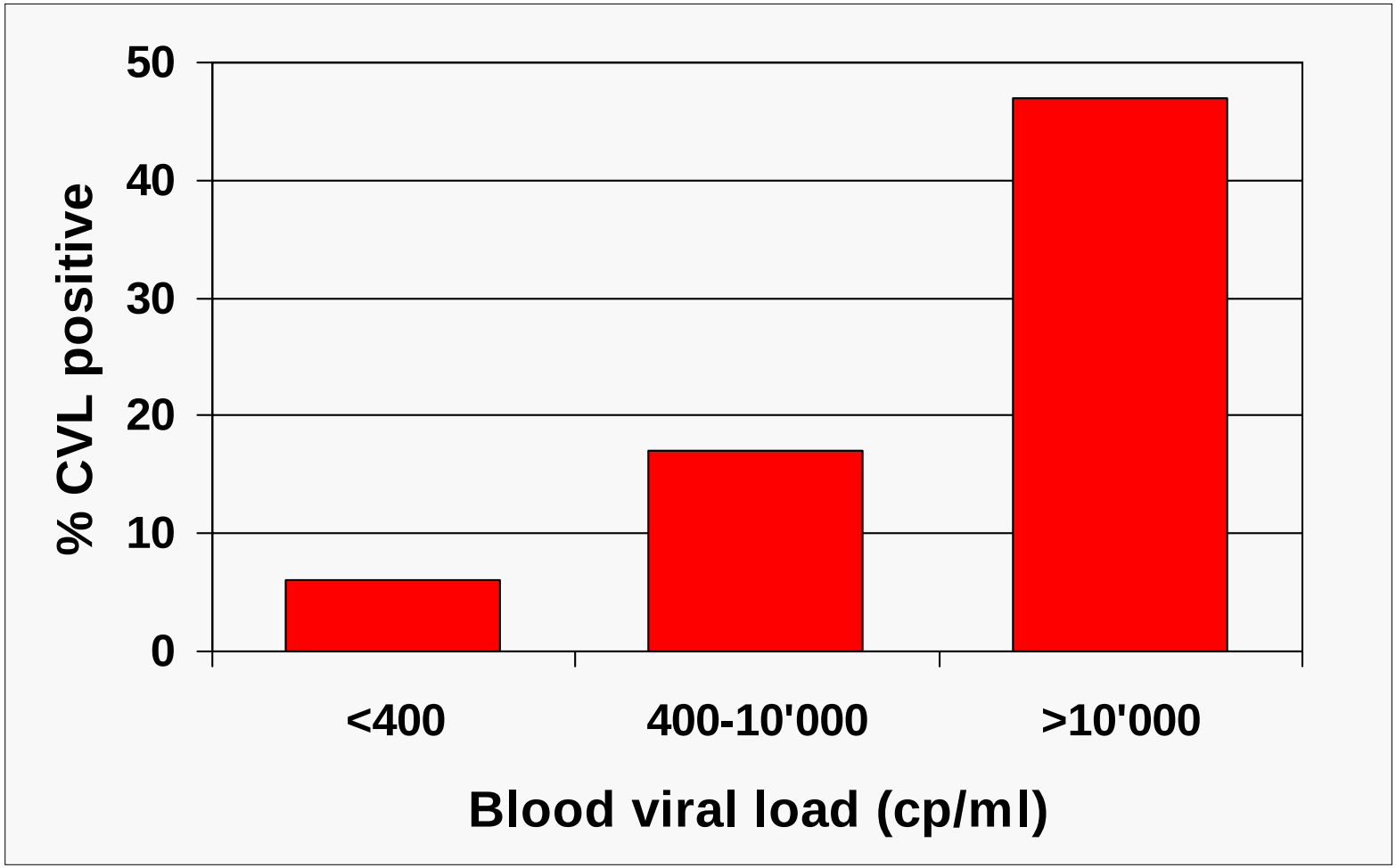
Quinn et al, NEJM, 2000,342:921

HIV- Primary Infection



Vernazza et al., CROI, 2000; Abst 564

Cervical viral load and HAART



Cu-Uvin et al., AIDS, 2000; 14:415

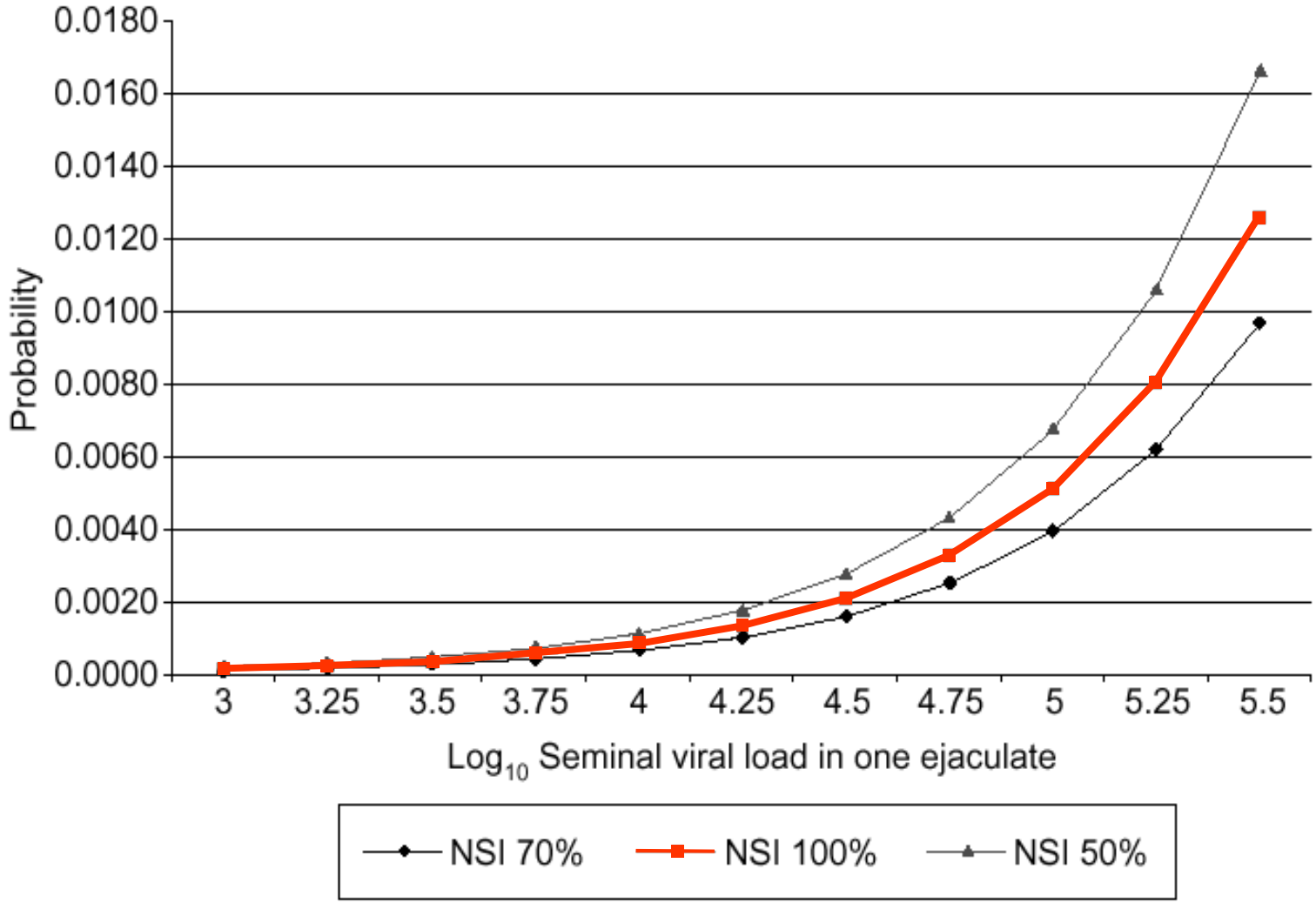
HIV in Semen and Risk of Tx

Viral burden in genital secretions determines male-to-female sexual transmission of HIV-1: a probabilistic empiric model

Hrishikesh Chakraborty, Pranab K. Sen[a], Ronald W. Helms[a], Pietro L. Vernazza[b], Susan A. Fiscus[c], Joseph J. Eron[d], Bruce K. Patterson[e], Robert W. Coombs[f], John N. Krieger[g] and Myron S. Cohen[d]

AIDS 2001,15: 621-7

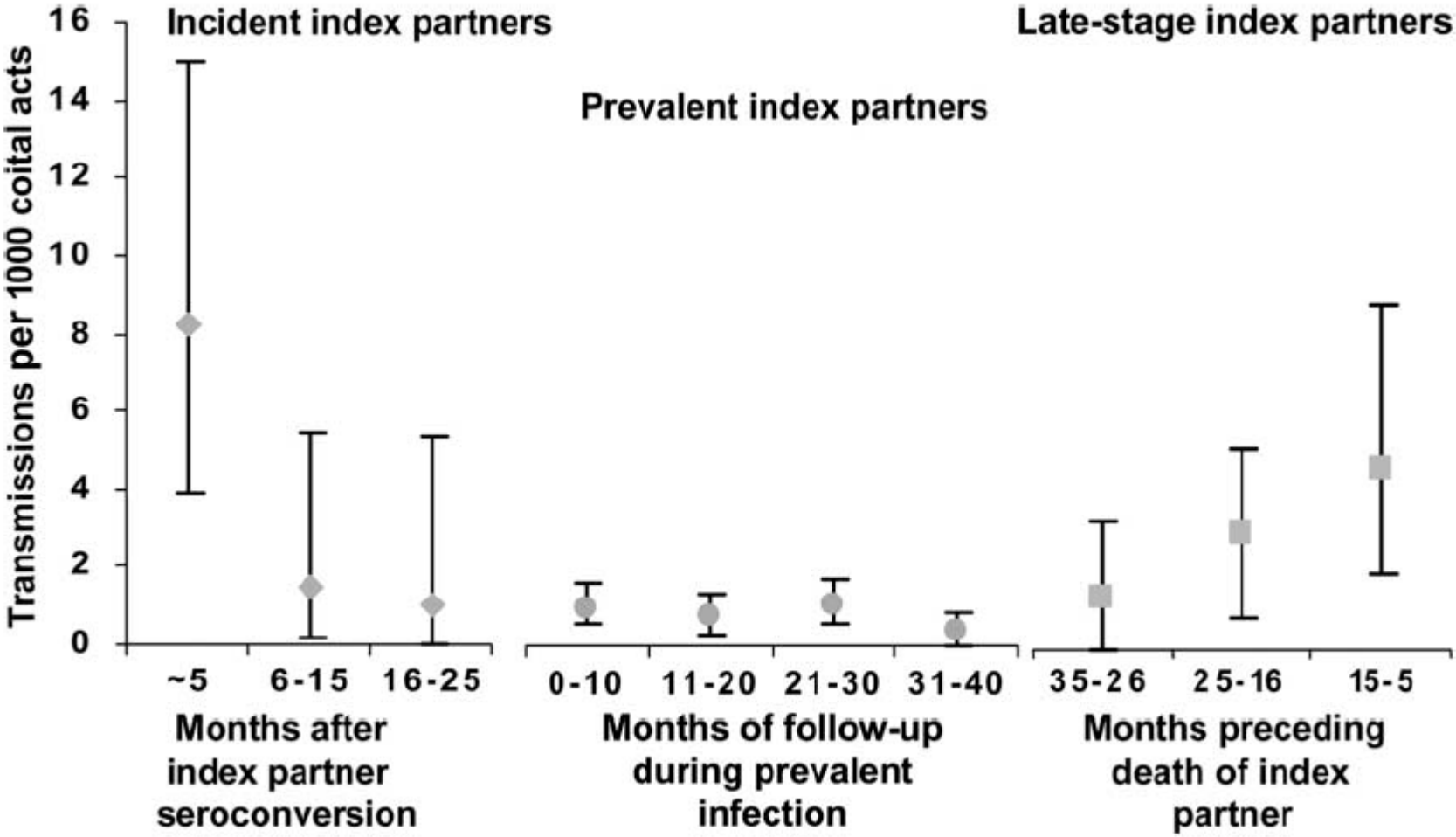
HIV in semen & risk per coital act



Chakraborty et al. AIDS 2001,15: 621-7

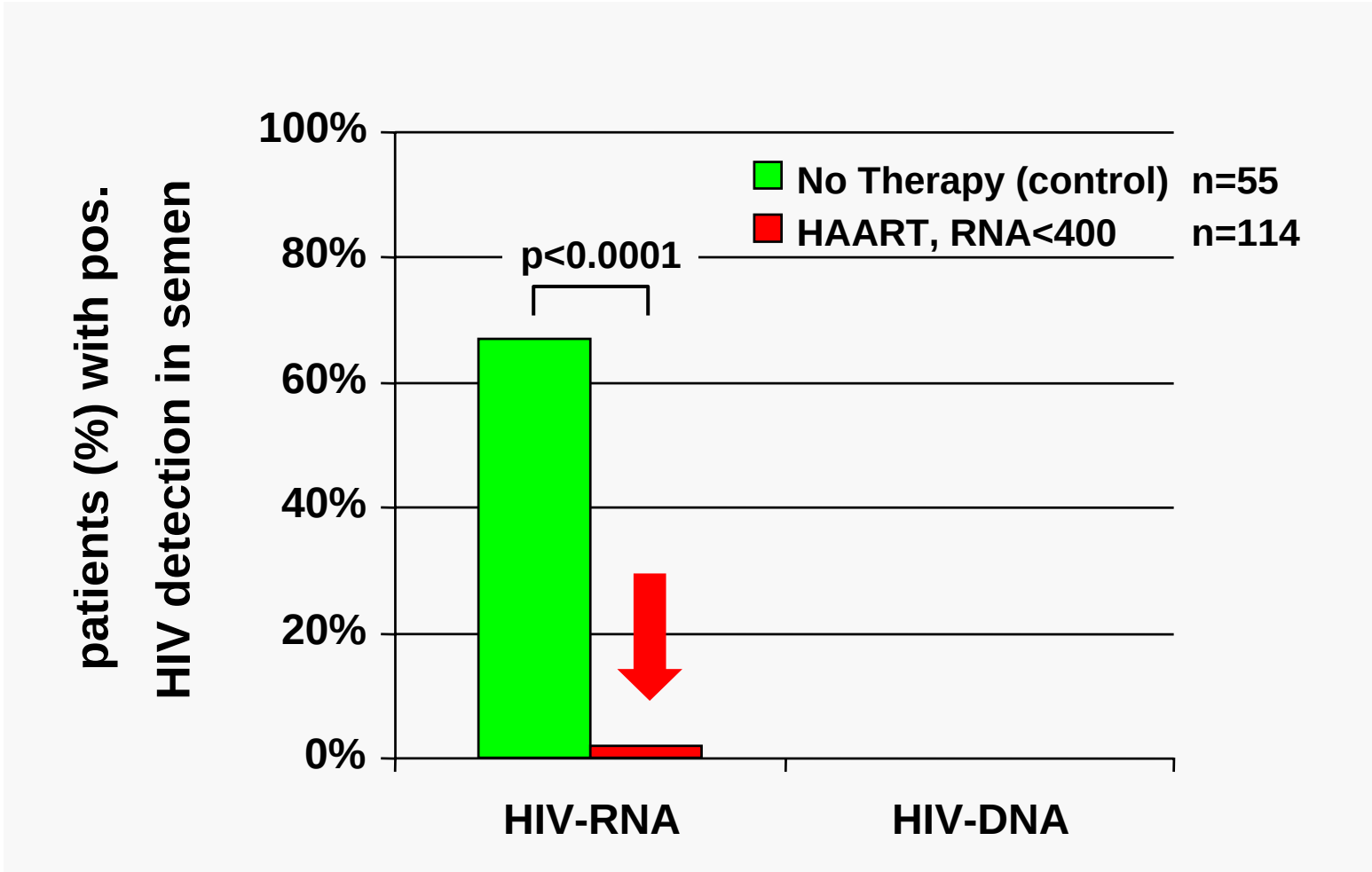
Risk per coital act in couples

- 235 monogamous, discordant couples, Uganda



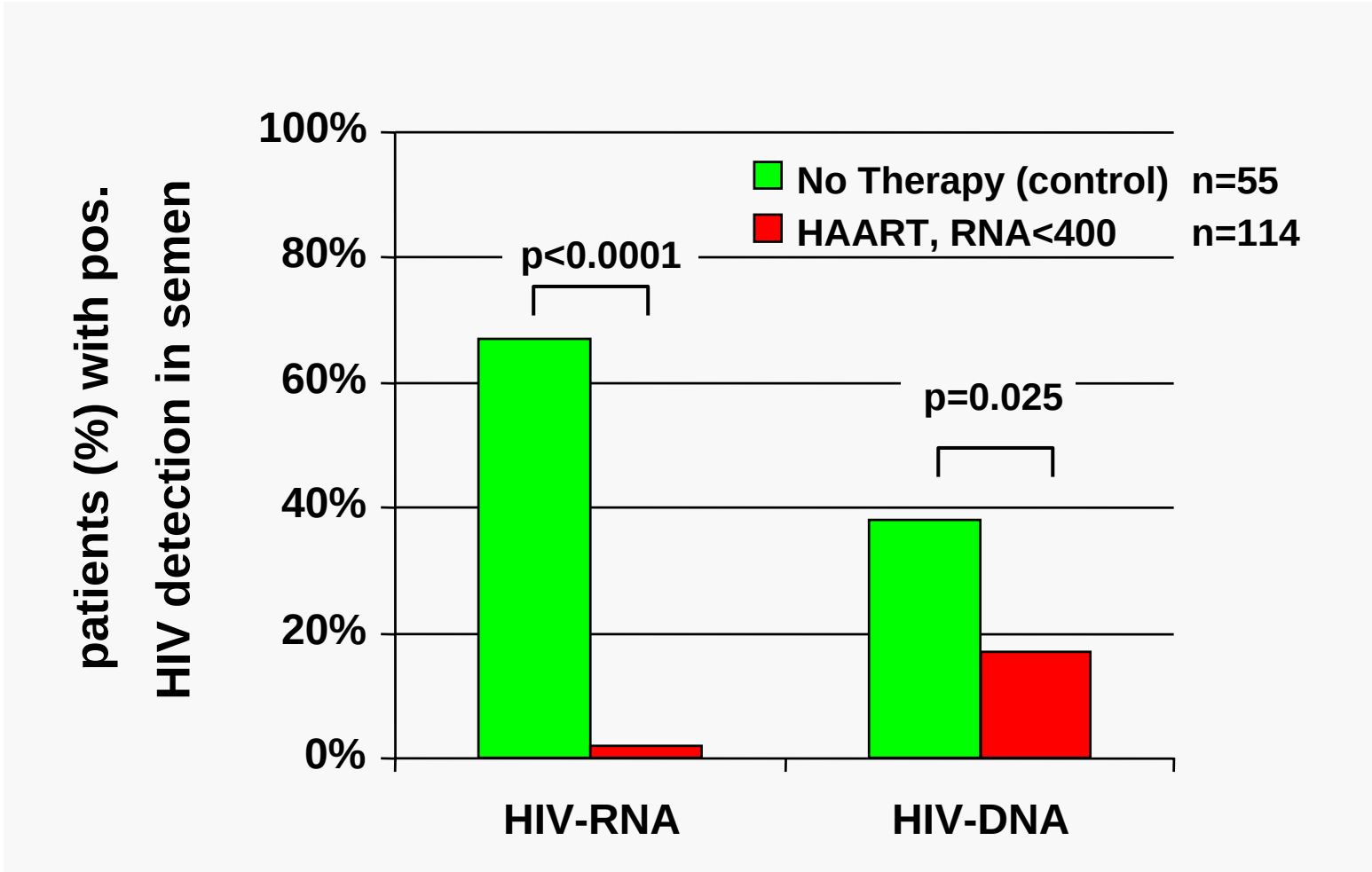
Waver et al. JID 2005,191: 1403-9

HIV in Semen during HAART



Vernazza et al., AIDS, 2000; 14:117-21

HIV in Semen during HAART



Vernazza et al., AIDS, 2000; 14:117-21

Decline in infectivity* w. HAART

- **HIV incidence in SF-MSM during 1994-1999**

Time period at risk for infection	No. of Subjects	**Infectivity**	Mean no. of unprotected RAI partners	Crude incidence rate/year
4/94 – 9/95	534	**0.12**	0.6	1.36%
9/95 – 11/96	481		0.75	1.29%
11/96 – 9/97	445	**0.048**	0.8	0.78%
9/97 – 3/99	320		1.3	1.02%

- 60%

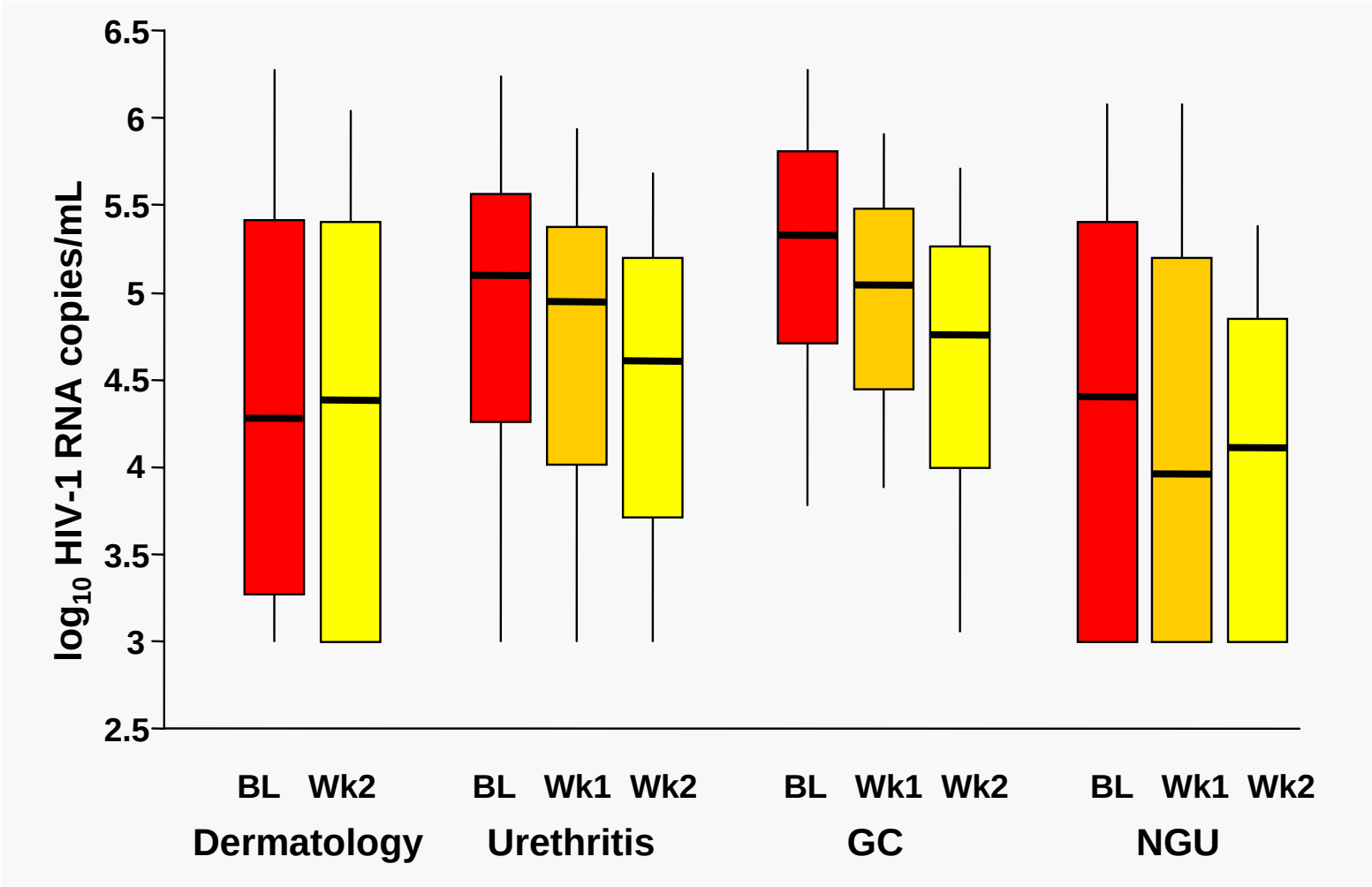
* per-partnership probability of trx from HIV+ partner

Porco et al, AIDS 2004, 18:81–88

Conclusion 2

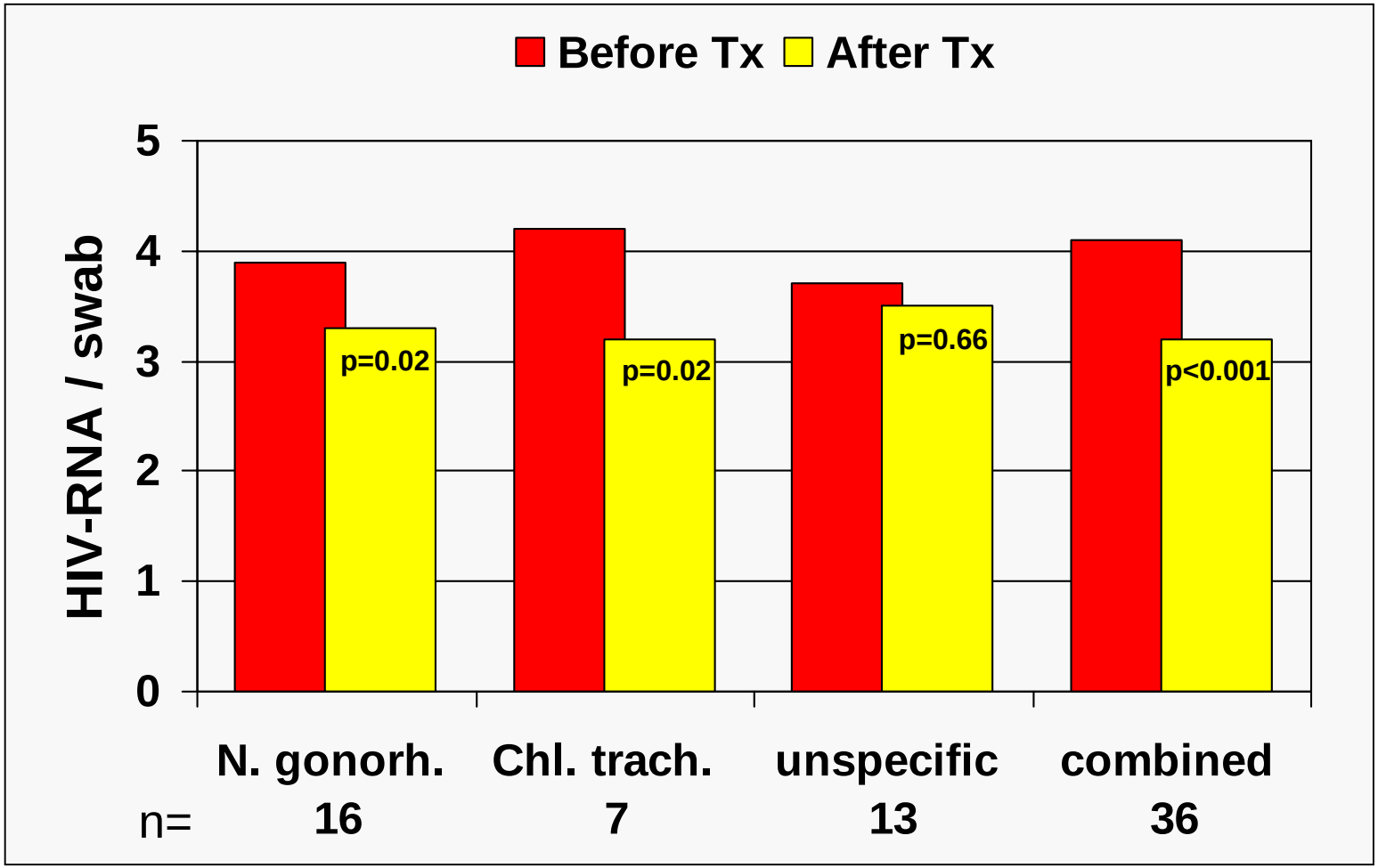
- **HIV transmission risk highly heterogenous**
- **Immune response may reduce risk**
- **Viral load (genital / blood) most potent predictor of trx risk**

Malawi urethritis project: HIV-RNA in semen



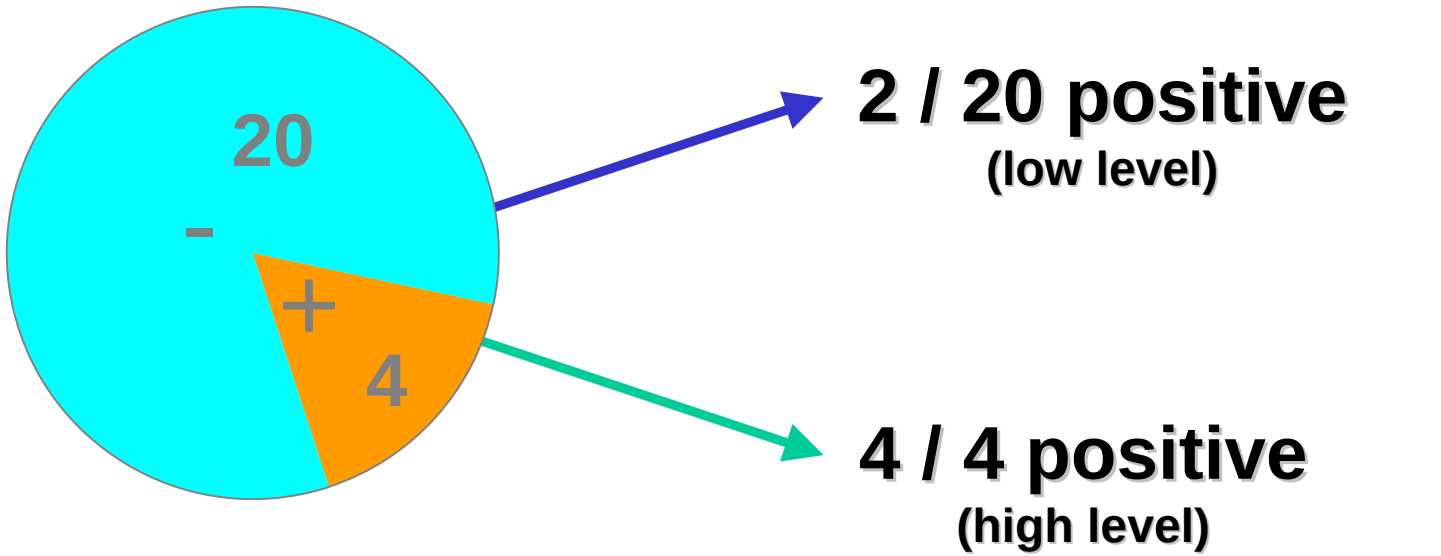
Cohen et al, Lancet 1997; 349:1868-73

Tx of Cervicitis and Shedding of HIV



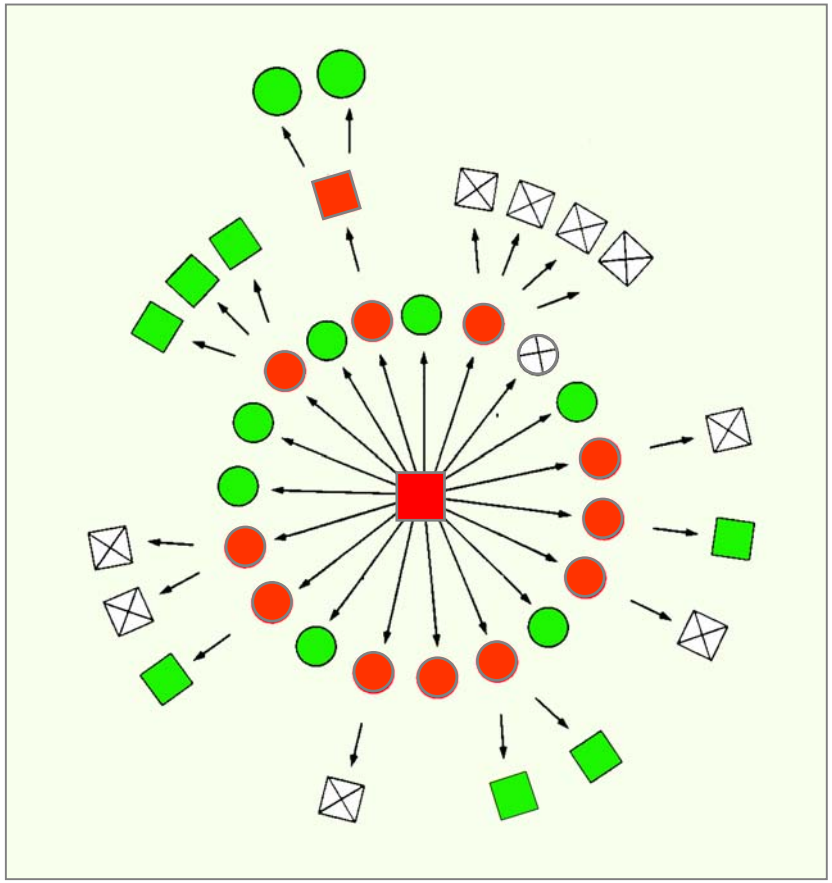
McClelland et al, AIDS 2001; 15:105-110

Urethritis during HAART (n=24)



Sadiq et al, AIDS 2002, 16:219-25

Heterosexual Transmission



HIV-pos.

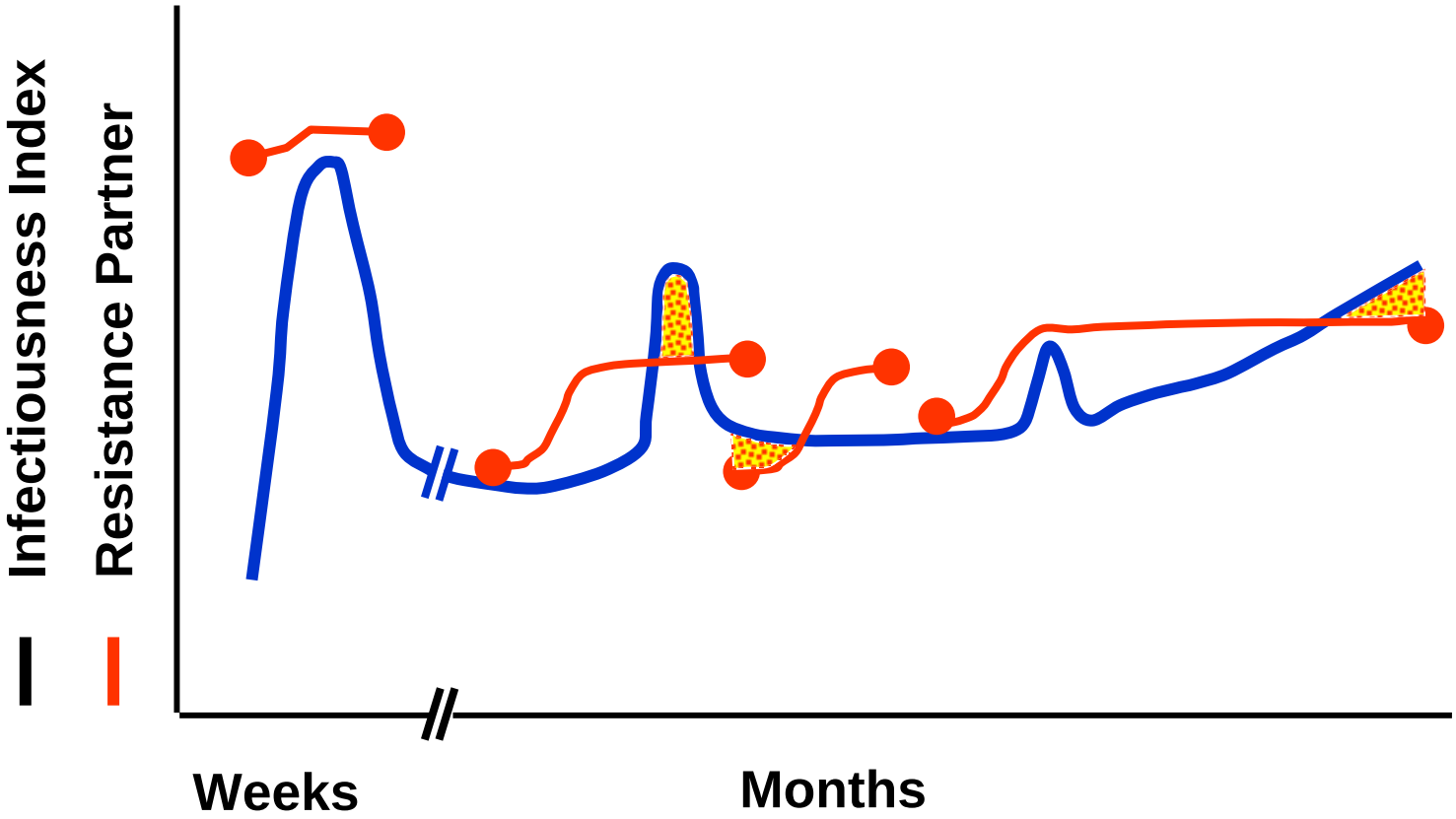
HIV-neg.

Clumeck N, et al, NEJM, 1989;321:1460

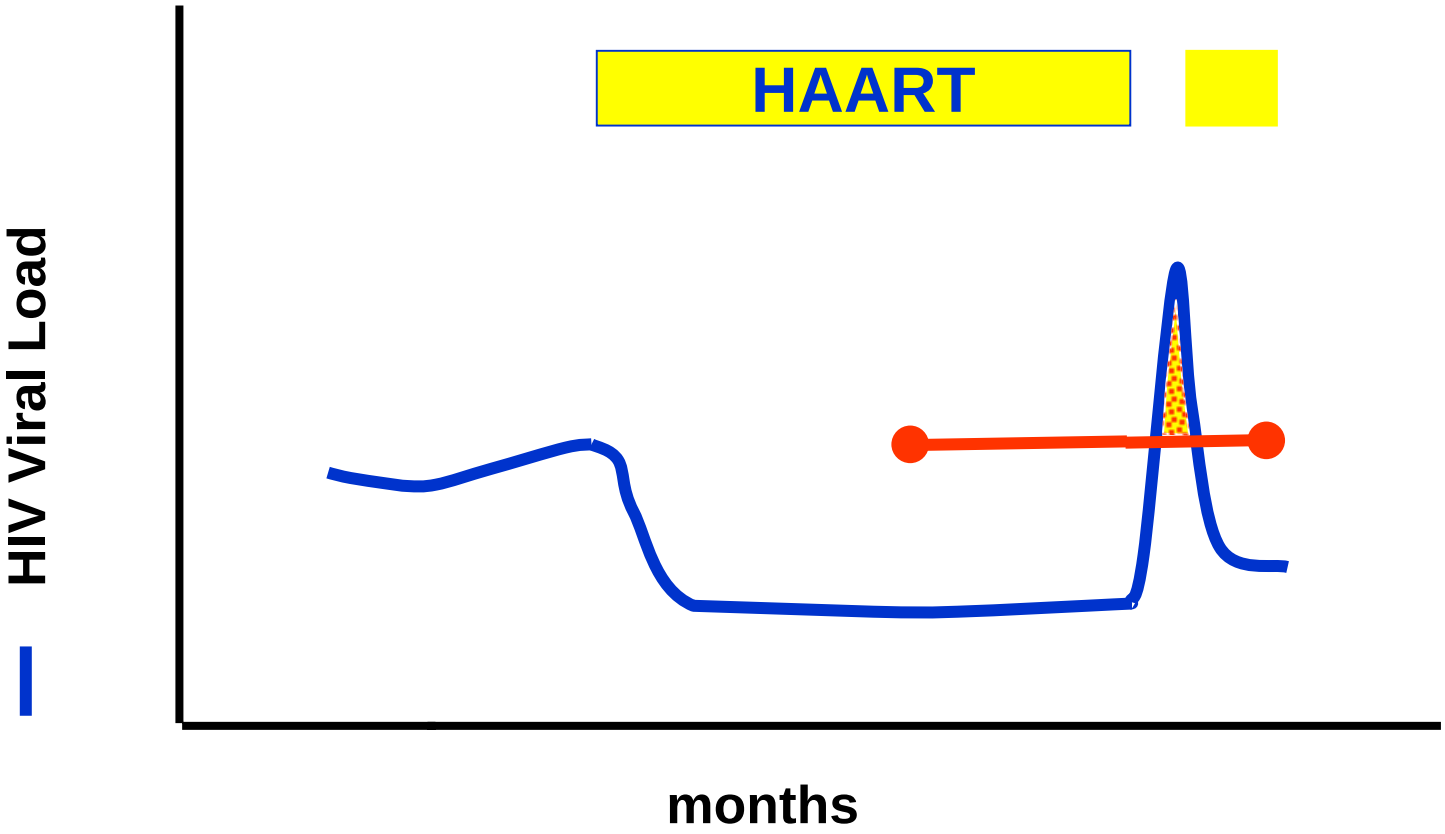
Conclusion 3

- **HIV transmission risk highly heterogenous**
- **Immune response may reduce risk**
- **Viral load (genital / blood) most potent predictor of trx risk**
- **STDs enhance trx risk**

Infectiousness & Susceptibility



Cave: Treatment interruption



Bernasconi et al, JAIDS, 2001; 27:209–211

Consequences for clinical practice

- **STD‘s should be carefully monitored**
- **STD prevention remains a key issue**
- **Transmission risk likely to be highly varible over time**

? Effect of HAART on txm risk