

Factors influencing HIV transmission

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Factors influencing (sexual) HIV transmission

- What is known
- Why do we still not know everything?
- Antiretroviral therapy and transmission
- Statement by Swiss AIDS Commission

HIV transmission routes and risks

- Blood transfusion Close 100%
- Mother-to-child 10% – 25%
- Intravenous drug use ?
- Sexual ?
- Oro-genital Very low, but not 0%
- Needle stick injuries 0,1% – 0,2%

Why so few scientific studies?

- Difficult to study, therefore few good studies
- The average transmission risk per sexual contact is low, means that large studies are needed for reliable results
- Many different cooperate risk factors have to be taken into account
- Studies on sero-discordant couples are easily biased for low transmission risk
 - Couples where transmission occurred early are not discordant
 - Unethical to not try to reduce transmission

Some factors that may influence the risk of sexual transmission

Biological

- Stage of HIV infection
- Virus levels
- Other STIs (part. HSV-2)
- Male circumcision
- Host genetics
- Sex
- Viral factor
- Antiretroviral therapy

Behavioral

- Type of sexual contact:
anal or vaginal
active or passive MSM
- Condom use
- Number and concurrency
of partners
- Serosorting

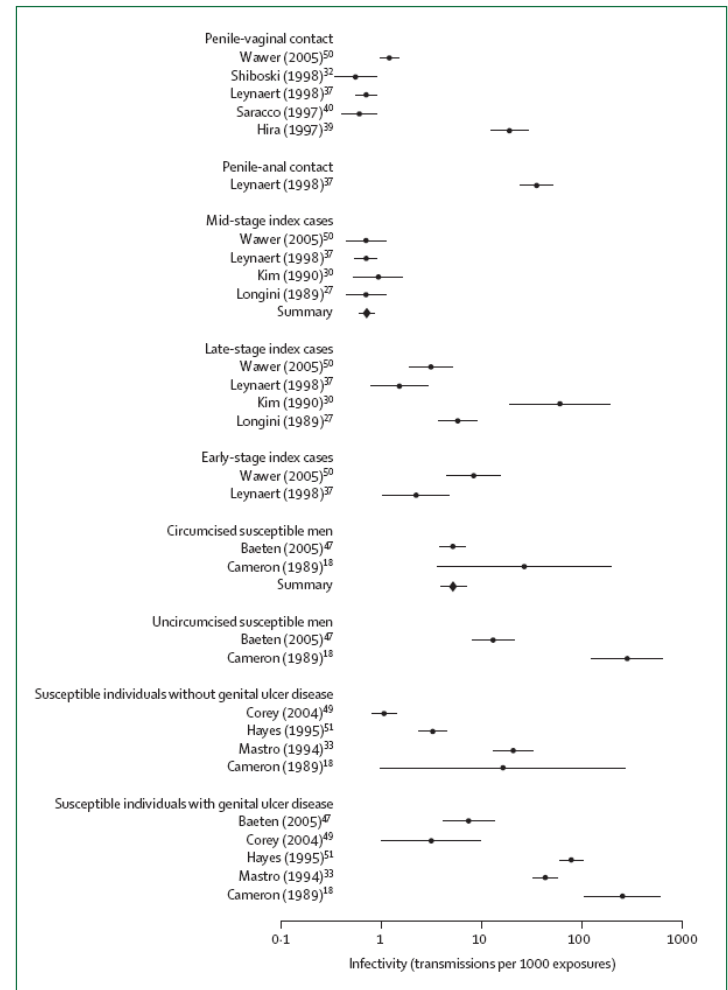
Large individual variations. Often misleading to look at average risk

Heterosexual transmission risk

- Meta-analysis (Powers, Lancet Infect, Aug 2008)
- Based on 27 published studies
- Transmission risk per contact is highly variable and depends on a number of underlying factors
- The often cited risk of 1 in 1000 is estimated in stable, discordant couples with few high risk factors
- 1 in 1000 is therefore often an underestimation of real risk
- For many contacts the risk is considerably larger

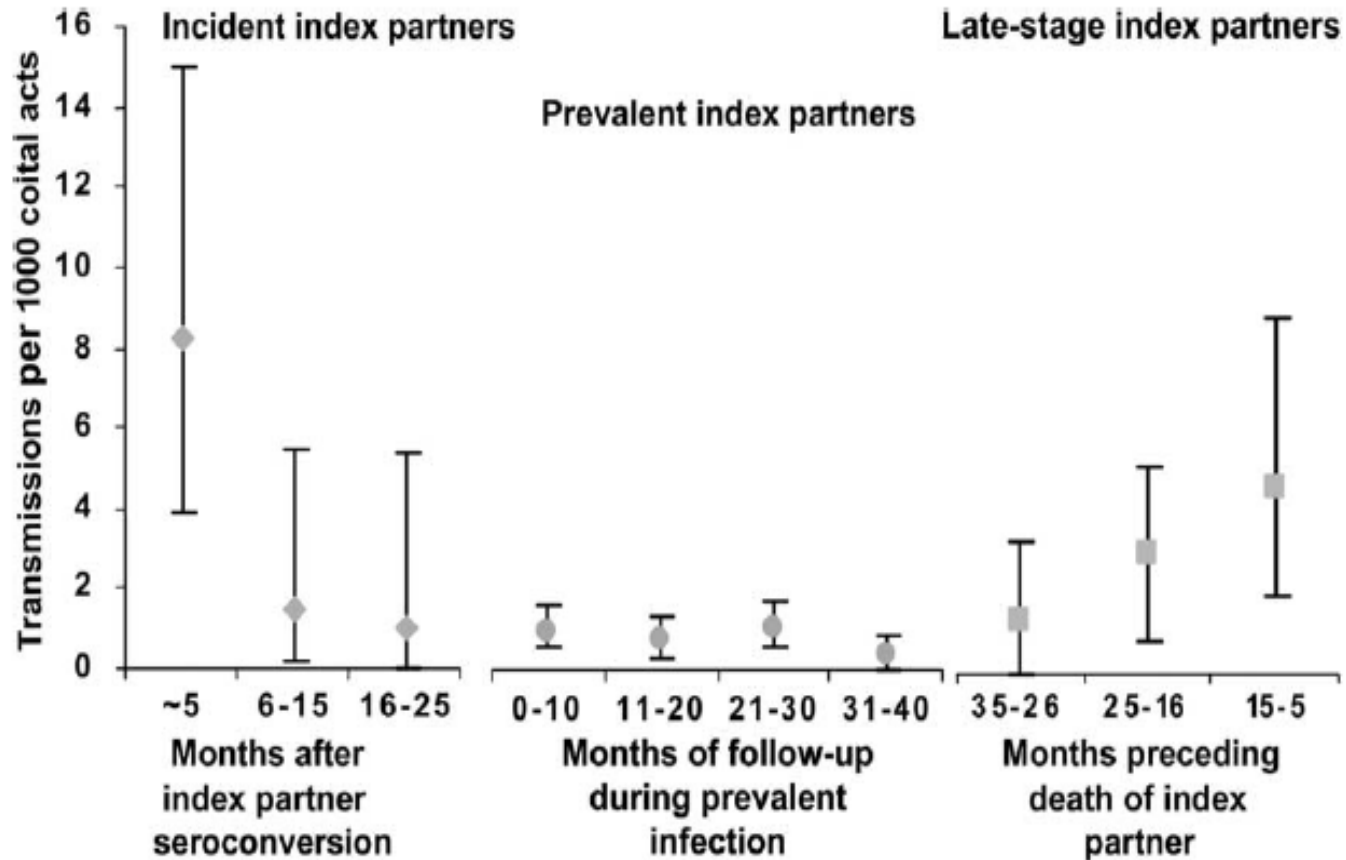
Heterosexual HIV transmission risk

- Transmission risk per heterosexual contact
Meta-analysis (Powers, Lancet Infect, Aug 2008)
- Up to 1 transmission per 3 contacts during heterosexual anal intercourse and many other "bad" risk factors
- Down to < 1 transmission per 1000 contacts during vaginal intercourse and few "bad" risk factors



Contagiousness and virus levels

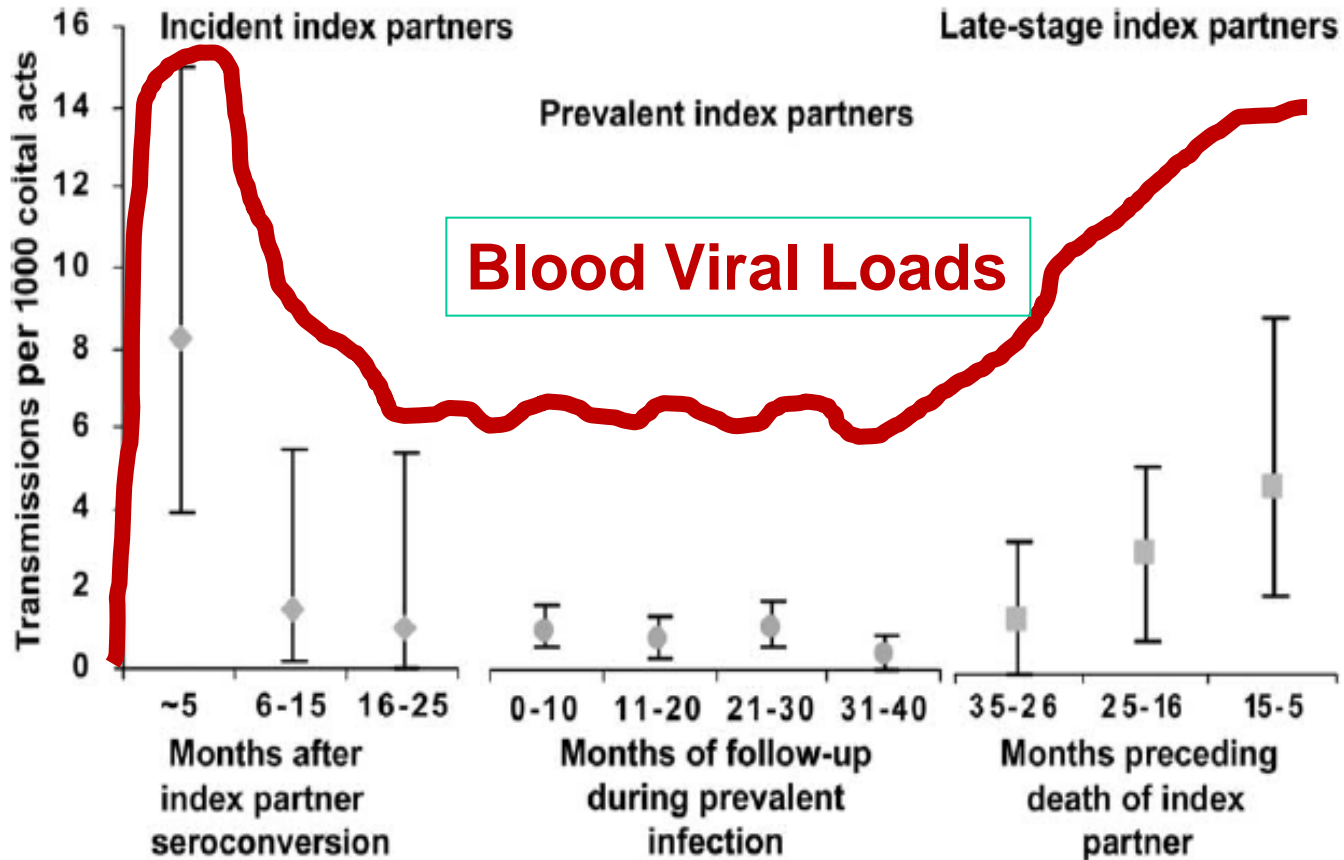
Rakai study



Wawer, MJ., et al., JID: 2005

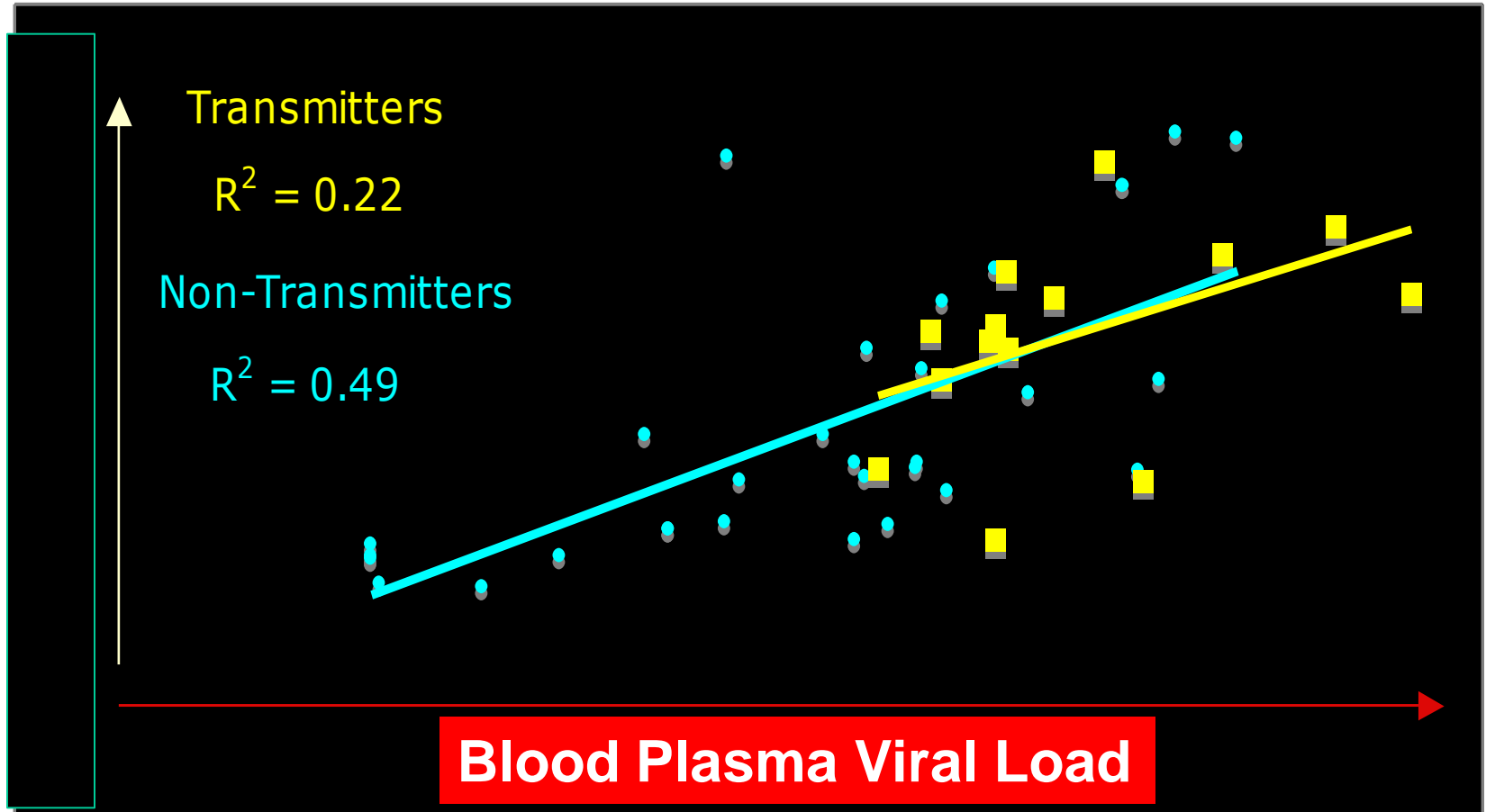
Contagiousness and virus levels

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Blood VL Correlates with Seminal VL



Kindly provided by Davey Smith, UCSD

Butler DM et al. CROI 2008

Jan Albert, KI and SMI

QUESTION:
DOES YOUR
UNIVERSAL HEALTH
CARE PLAN
COVER STD'S?



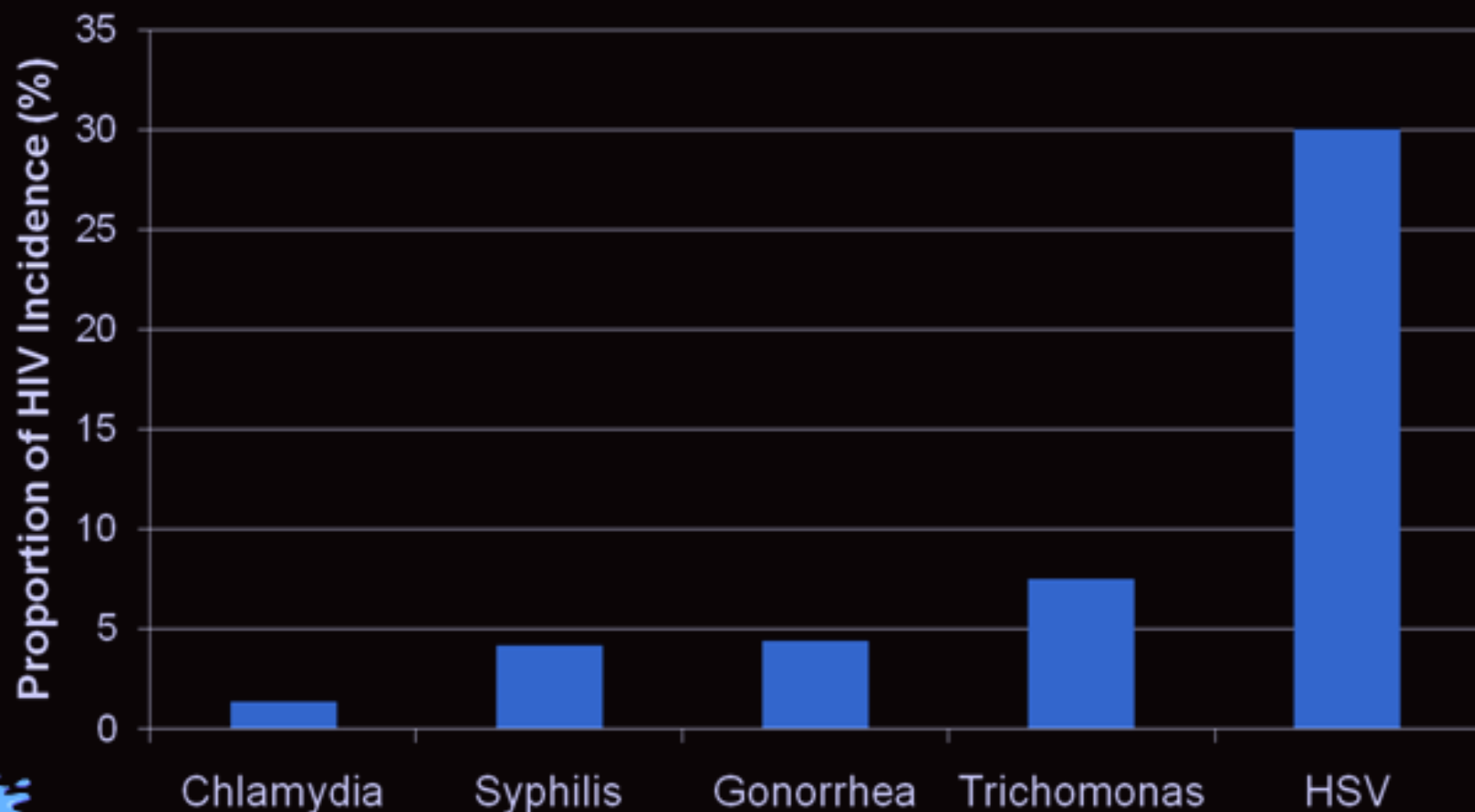
Hillary
FOR PRESIDENT

SIT
DOWN,
BILL...



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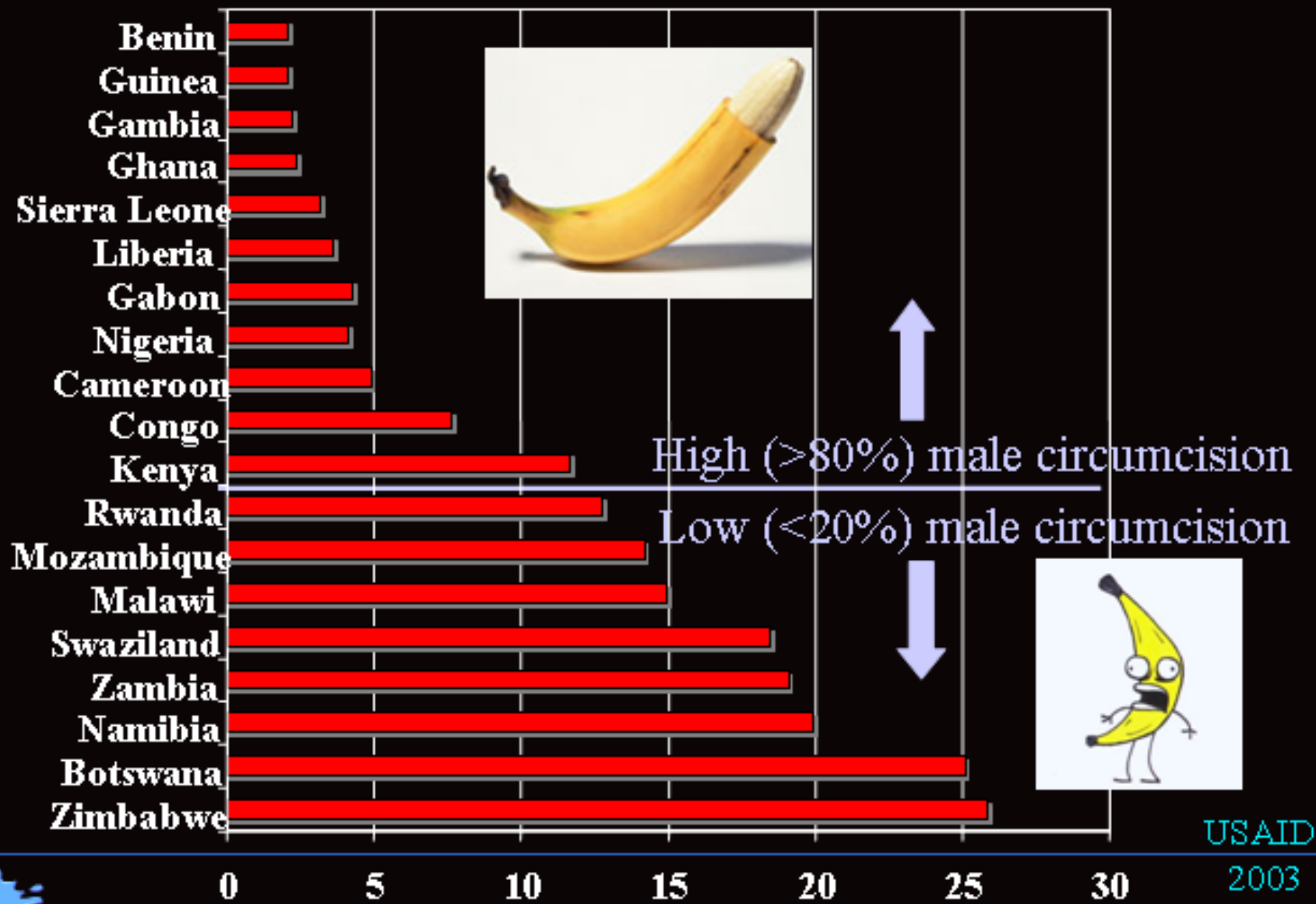
Population Attributable Fraction of HIV Acquisition due to STIs



Rottingen JA, et al. STD 2001; Gray RH, et al. AIDS 2001; Freeman et al. STI 2007,

Kindly provided by Davey Smith, UCSD

Male Circumcision and HIV Prevalence in Africa



Kindly provided by Davey Smith, UCSD

Statement by the Swiss AIDS Commission

An HIV infected person, who has effective therapy and "undetectable" virus (<40 copies) is not sexually infective given that:

- The person is fully adherent to therapy and the effect of therapy is regularly checked
- The virus levels have been "undetectable" in plasma for at least 6 months
- The person has no other STIs

Position of the Swiss AIDS Commission

- Quite controversial
- Not internationally accepted

The scientific basis for the position

- 1) One study in Rakai (415 patients) shows that the risk of transmission is closely correlated with virus levels in plasma (Quinn).
- 2) One prospective study on 393 heterosexual discordant couples showed no transmissions from patients on therapy (ART), compared to 8,6% transmission from untreated patients (Castilla).
- 3) In one study on 92 discordant couples, 6 infections occurred, all from untreated patients (Melo).
- 4) In 62 discordant couples (man infected and treated) who had unprotected intercourse to become pregnant, no infections occurred (Barreiro).

No transmission if plasma virus levels are less than 1500 copies/ml?

- **In the Rakai study 415 discordant couples were followed for up to 30 months**
- **90 transmissions occurred**
- **No transmissions were observed from patients with < 1500 copies/ml**

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- 90 transmissions occurred
- No transmissions were observed from patients with < 1500 copies/ml
- **This does not prove that transmissions cannot occur if virus levels are <1500 copies/ml**
- **There are 2,5 million transmissions every year, of which 90 (0.004%) were studied**

Other data on contagiousness when virus levels are undetectable?

- Case report (Sturmer, Antiviral Ther, juli 2008)
- Monogamous MSM couple, one HIV infected
- Transmission despite undetectable virus
- Index patient had therapy and undetectable virus since July 2000 and regular checks
- Partner was HIV negative in June 2002, but HIV positive July 2004
- Interviews, epidemiology and molecular typing of the viruses indicate that transmission occurred from the index patient to the partner

Other data on contagiousness when virus levels are undetectable?

- Two presentations at the CROI conference in Montreal 2009
- 31% and 5%, respectively, of men with successful therapy (plasma virus levels <50 copies/ml) had detectable virus in semen
- However, it is not shown that this virus is infectious

Pre-exposure prophylaxis (PrEP)?

- Microbicides – some promising primate studies on using antiretroviral drugs in microbicides
- Universal PrEP?

Lancet 2009; 373: 48–57

Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model

Reuben M Granich, Charles F Gilks, Christopher Dye, Kevin M De Cock, Brian G Williams

Interpretation Universal voluntary HIV testing and immediate ART, combined with present prevention approaches, could have a major effect on severe generalised HIV/AIDS epidemics. This approach merits further mathematical modelling, research, and broad consultation.

One of many replies

Harold Jaffe, Adrian Smith, Tony Hope

The World Medical Association international code of medical ethics states that “A physician shall act in the patient’s best interest when providing medical care.” If we are to deviate from this basic principle, we will need a robust ethical model for balancing individual and societal benefits.

Conclusions

- Risk of HIV transmission depends on a number of biological and behavioral factors
- It is often difficult to predict the risk of transmission in an individual sexual encounter
- HIV transmission illustrates that scientific questions often are more complicated than they appear at first