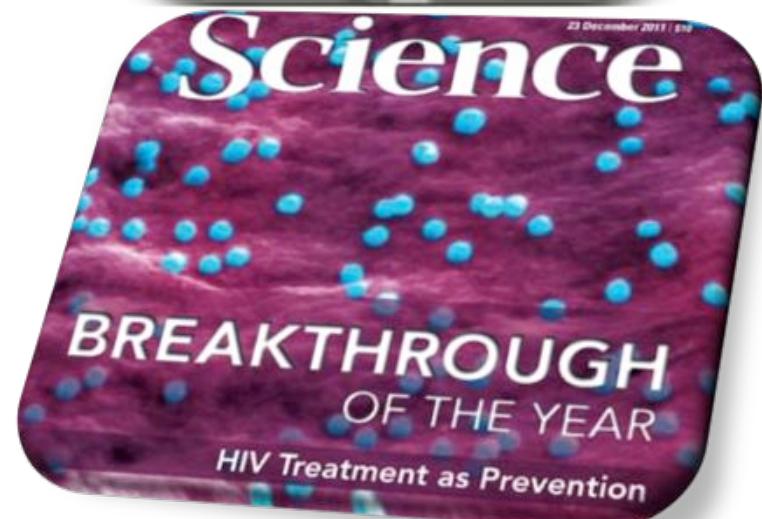


Traitements comme prévention L'expérience Suisse

Enos Bernasconi

Service des maladies infectieuses
Département de médecine interne
Lugano et Genève

Virosem, Bordeaux, 27-09-2013



Disclosure

- Advisory boards and speaker's bureau:
BMS, Boehringer Ingelheim, Gilead, Janssen,
MSD, ViiV Healthcare, and Pfizer
- Research grants: Gilead, MSD
- A special thank to Pietro Vernazza who kindly provided several slides

Outline

- The beginning
- The Swiss experience
- Recent data on Treatment as Prevention (TasP)



The beginning

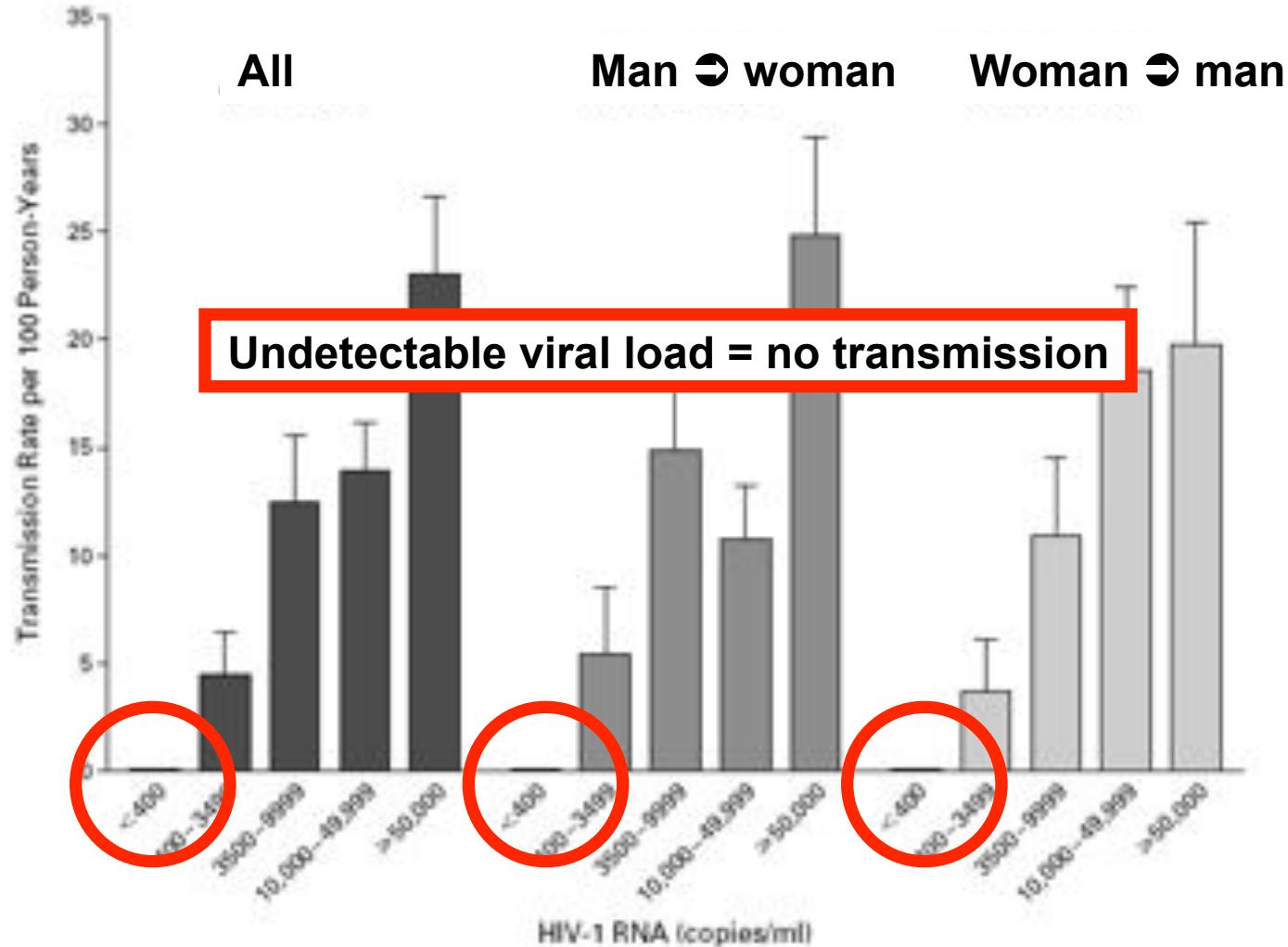
Background of the Swiss statement

- Increasing evidence for low risk on combined antiretroviral therapy (cART):
 - Epidemiological data
 - Biological plausibility
 - *Lack of case reports*

The « Rakai » study

Quinn et al. N Engl J Med 2000;342:921-9



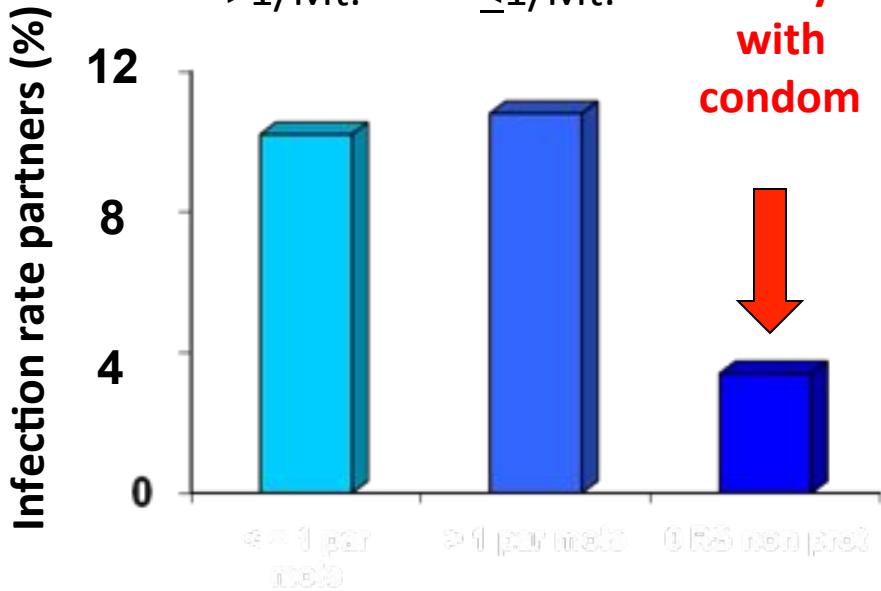


« Rakai » study: The risk of HIV transmission depends on the viral load in the blood

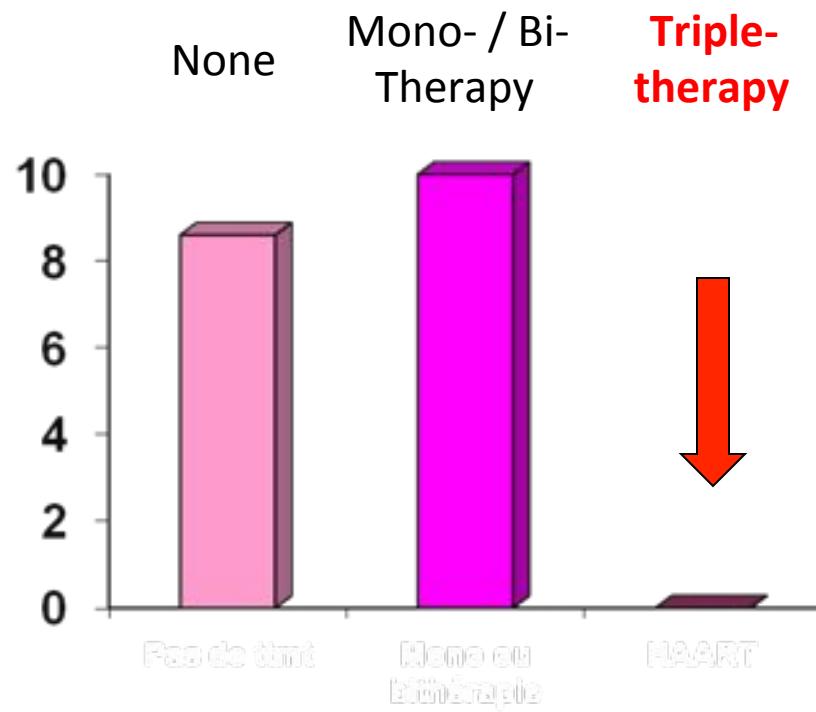
Activity of ART for Prevention

ART is comparable to condom use

Sex w/o Condom

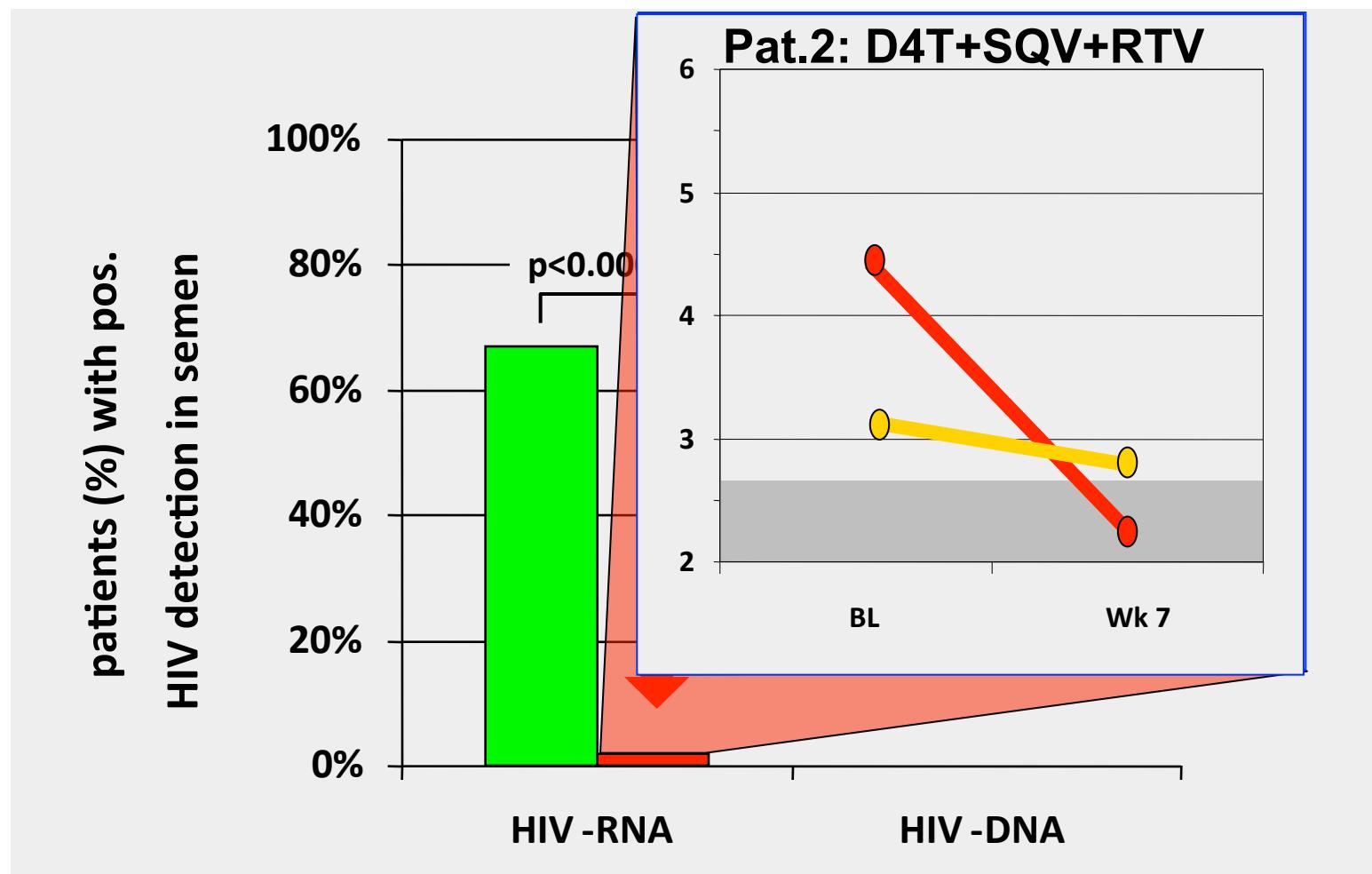


Partner under HAART

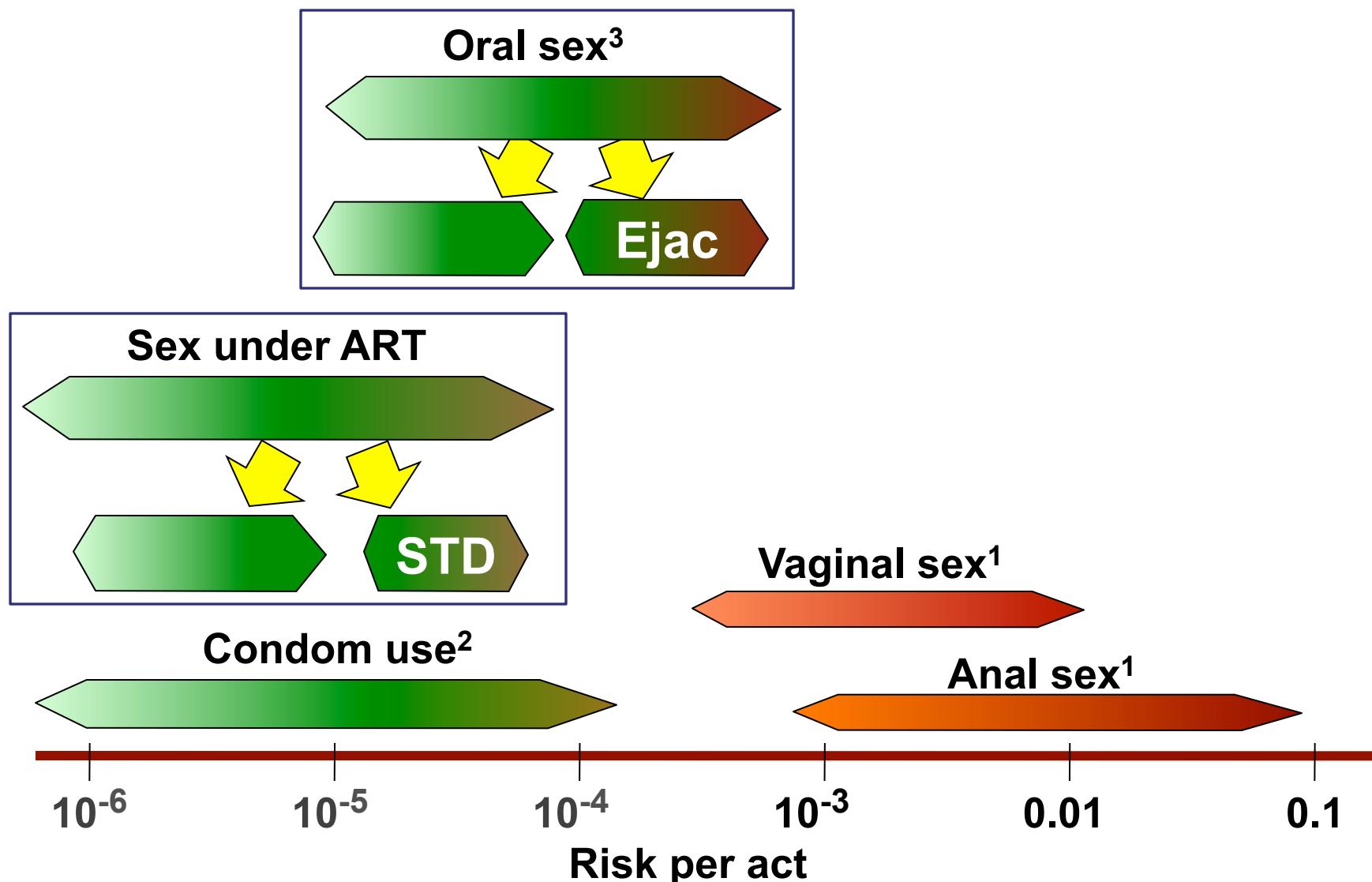


Castilla, et al. JAIDS 2005

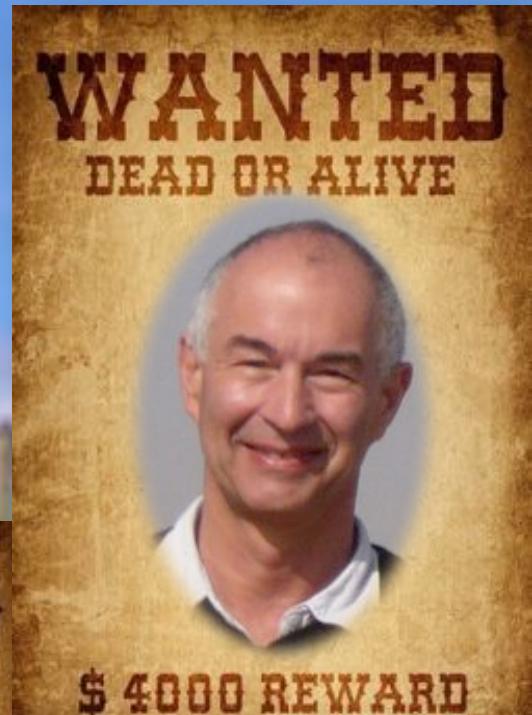
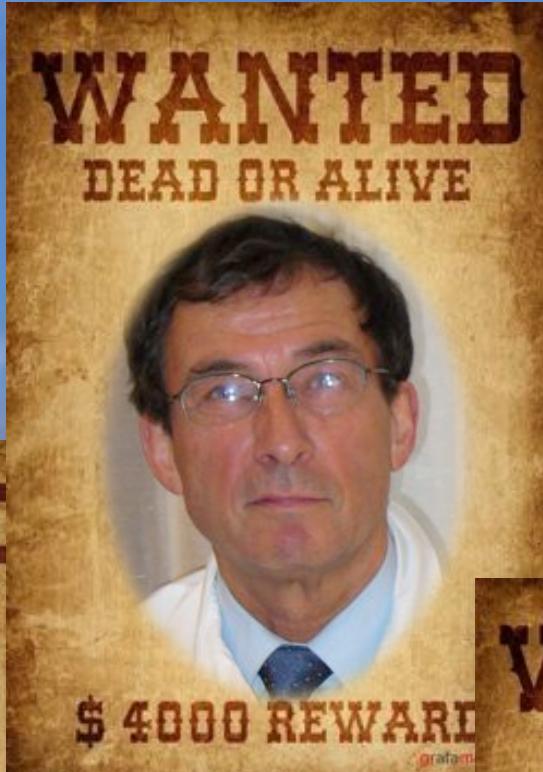
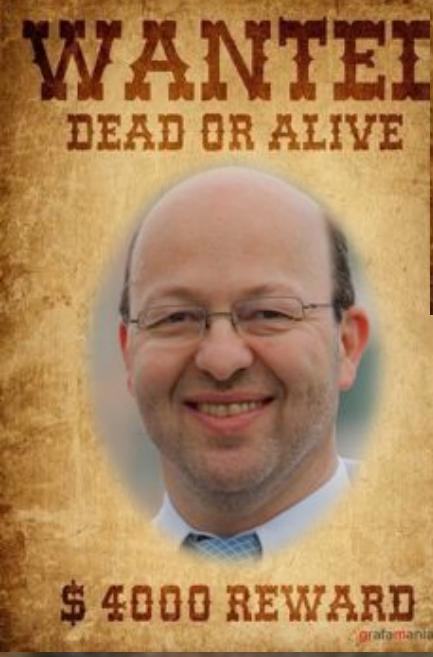
HIV in semen during cART



HIV transmission risks are fuzzy



¹Royce RA et al, 1997; ²Davis KR et al, 1999; ³Vittinghoff E et al, 1999



Une personne séropositive, suivant un traitement antirétroviral (TAR) et avec une virémie indéetectable, ne transmet pas le VIH, par voie sexuelle

Validité de l'affirmation:

- 1) TAR appliqué “à la lettre” et suivi régulier par un médecin;
- 2) Charge virale en dessous du seuil de détection ≥ 6 mois (< 40 cp/ml);
- 3) Aucune autre maladie sexuellement transmissible (urétrite, syphilis...)

The EKAF (“Swiss”) statement

What the statement described

- It's ok to talk about risk estimates
- Under optimal conditions, risk is in the range of daily life („negligible“)
 - Long term maximal suppression
 - Perfect adherence, regular checks
 - Absence of STDs
- Only the informed partner can decide on condom use

Other “negligible” risk situations:

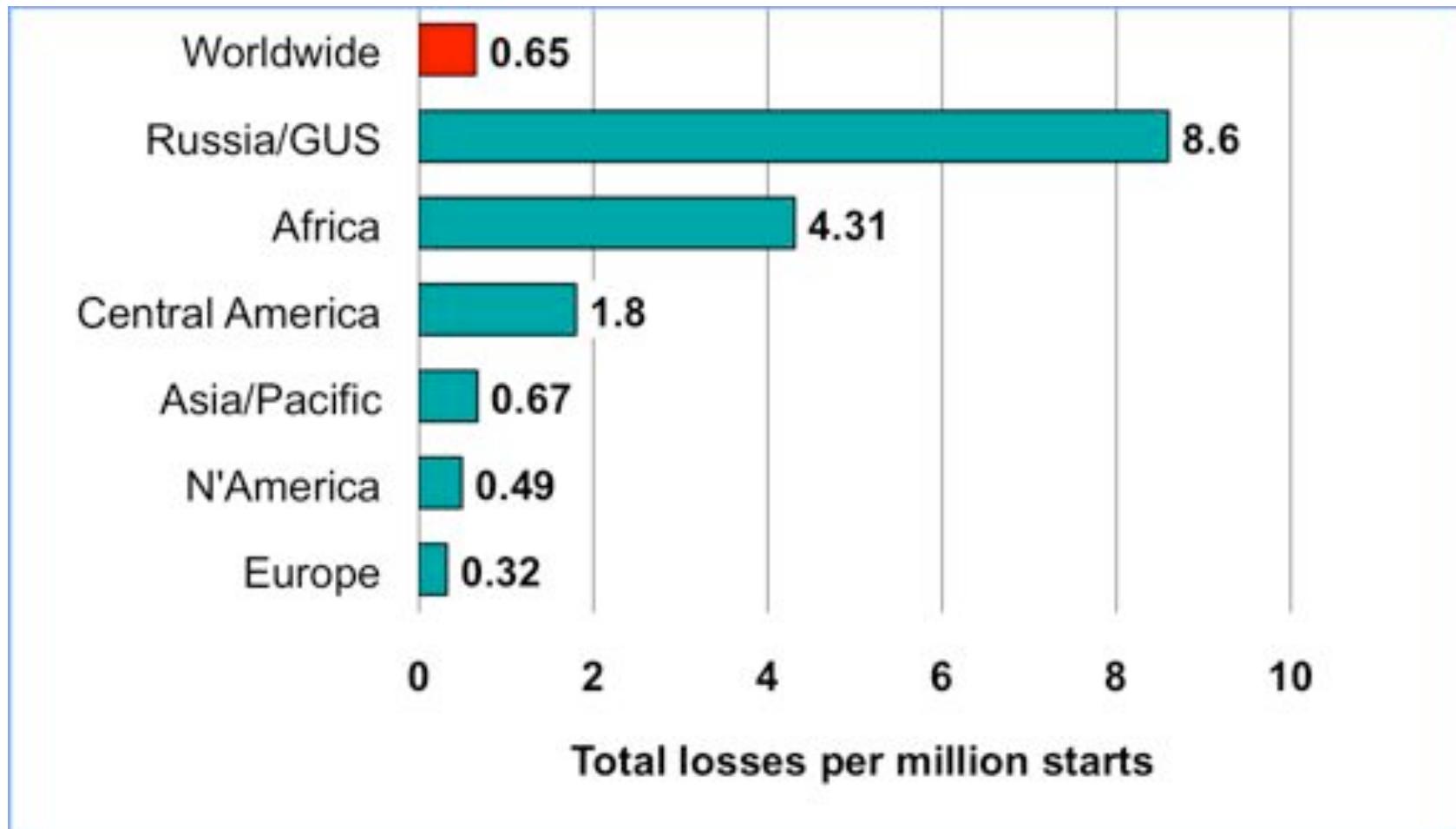
1. Condom-protected vaginal sex:
→ 0.9 / 100 py for always users

Davis, 1999, Fam Plan Perspectives

2. Receptive oral sex (MSM):
→ 0.0004 / act (= 1/2'500)

Vittinghoff, 1999, Am J. Epid

Risk airline crash 2006



Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis

Deborah Donnell, Jared M Baeten, James Kiarie, Katherine K Thomas, Wendy Stevens, Craig R Cohen, James McIntyre, Jairam R Lingappa, Connie Celum, for the Partners in Prevention HSV/HIV Transmission Study Team*

| | Follow-up during which HIV-1 infected partner had not initiated ART | | | Follow-up after HIV-1 infected partner initiated ART | | |
|----------------------|---|------------------------------------|---|--|------------------------------------|---|
| | Number of HIV-1 transmissions | Length of follow-up (person-years) | HIV-1 incidence per 100 person-years (95% CI) | Number of HIV-1 transmissions | Length of follow-up (person-years) | HIV-1 incidence per 100 person-years (95% CI) |
| Overall | 102 | 4558 | 2.24 (1.84-2.72) | 1 | 273 | 0.37 (0.09-2.04) |
| By CD4 cell count† | | | | | | |
| <200 cells per µL | 8 | 91 | 8.79 (4.40-17.58) | 0 | 132 | 0.00 (0.00-2.80) |
| 200-349 cells per µL | 41 | 1467 | 2.79 (2.06-3.80) | 1* | 90 | 1.11 (0.27-6.19) |
| 350-499 cells per µL | 24 | 1408 | 1.70 (1.14-2.54) | 0 | 30 | 0.00 (0.00-12.30) |
| ≥500 cells per µL | 29 | 1592 | 1.82 (1.27-2.62) | 0 | 21 | 0.00 (0.00-17.57) |

* HIV-neg 18 days after Tx start of index patient,
but HIV-pos. at next visit (day 90)

Jorge Del Romero, clinical researcher,¹ Jesús Castilla, consultant medical epidemiologist,² Victoria Hernando, epidemiologist,³ Carmen Rodríguez, research scientist,¹ Soledad García, clinical researcher¹

Combined antiretroviral treatment and heterosexual transmission of HIV-1: cross sectional and prospective cohort study

| Prevalence | Tx Index | |
|--------------|----------|------|
| | No ART | cART |
| Partners (n) | 476 | 149 |
| Partner pos. | 9.2% | 0%* |

*p<0.001

| Incidence | Tx Index | |
|-----------------|----------|--------|
| | No ART | cART |
| Partners (n) | 341 | 144 |
| Sex acts** (n) | 11'000 | >7000 |
| Pregnancies | 50 | 47 |
| Seroconversions | 5 | 0 |
| s/c per sex act | 0.0004 | 0 |
| Upper 95%-CI | 0.001 | 0.0005 |

** without condoms

The NEW ENGLAND
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

AUGUST 11, 2011

VOL. 365 NO. 6

- 1 763 couples, one partner HIV+ and the other HIV negative; HIV+ with CD4+ counts between 350 and 500/ μ L
- Randomization 1:1 to immediate ART (early) or after CD4+ declined below 250/ μ L
- After a median follow up of 1.7 years, 38 HIV

Lancet editorial 2011: It would be unethical not to offer immediate ART to serodiscordant couples

HPTN 052: HIV-1 Transmission

>6 Months of therapy

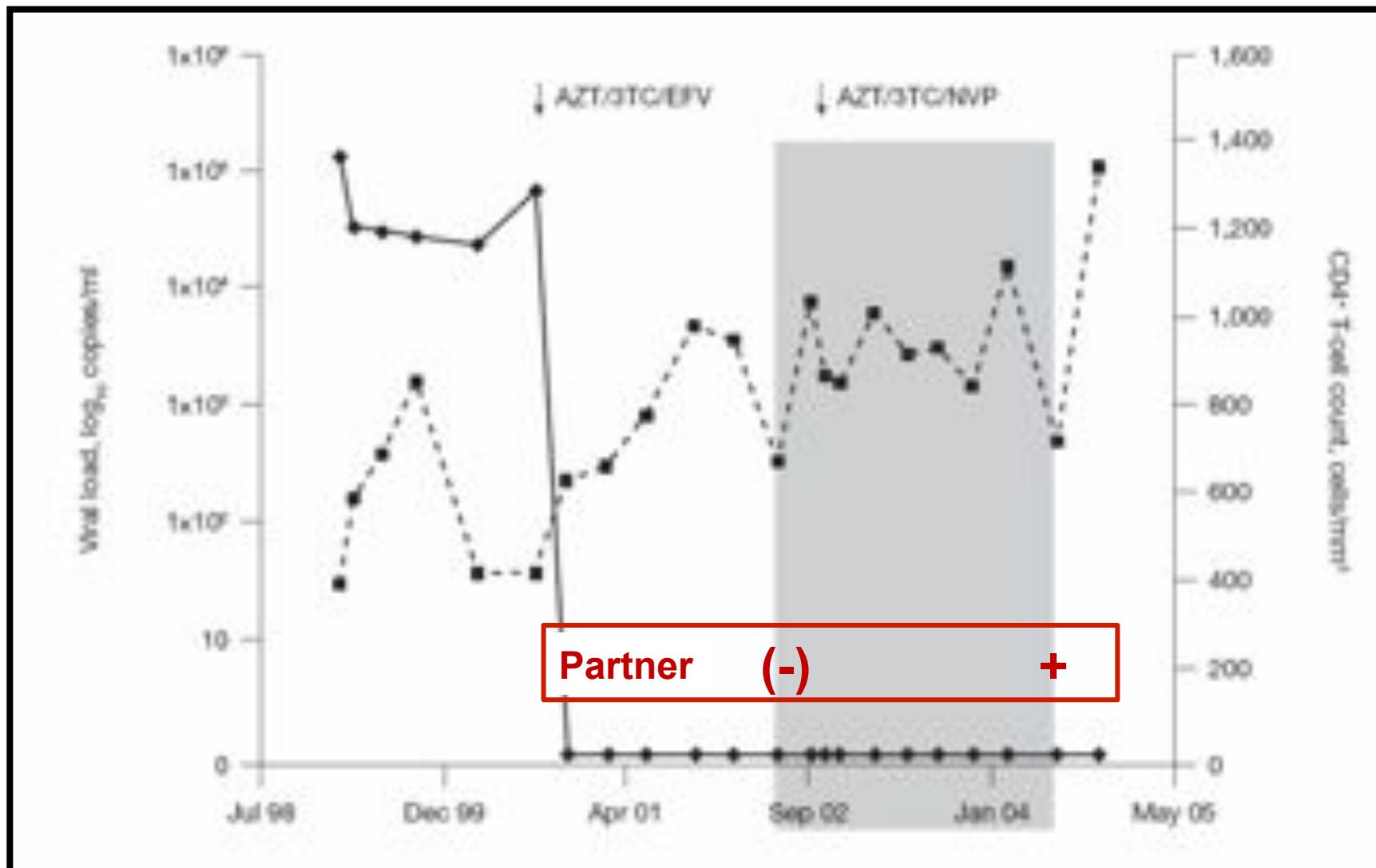
| Study Arm | Follow-up (PY)* | Incidence/100PY [95% CI] | |
|-----------|-----------------|-----------------------------|--------------------|
| | | Linked | > 6 Mth Th |
| Immediate | 1585 / 1145 | 0.1 [0.0 – 0.4] | 0.0 [0.0 – 0.3] |
| Delayed | 1567 | 1.7 [1.1 – 2.5] | |

*Person-years specific for transmission events

Median follow-up: 1.7 (1.1) years

The ultimate proof: Lack of reported transmission on cART after 2008

One swallow does not make a summer





The Swiss experience
(or: 5 years after the statement)

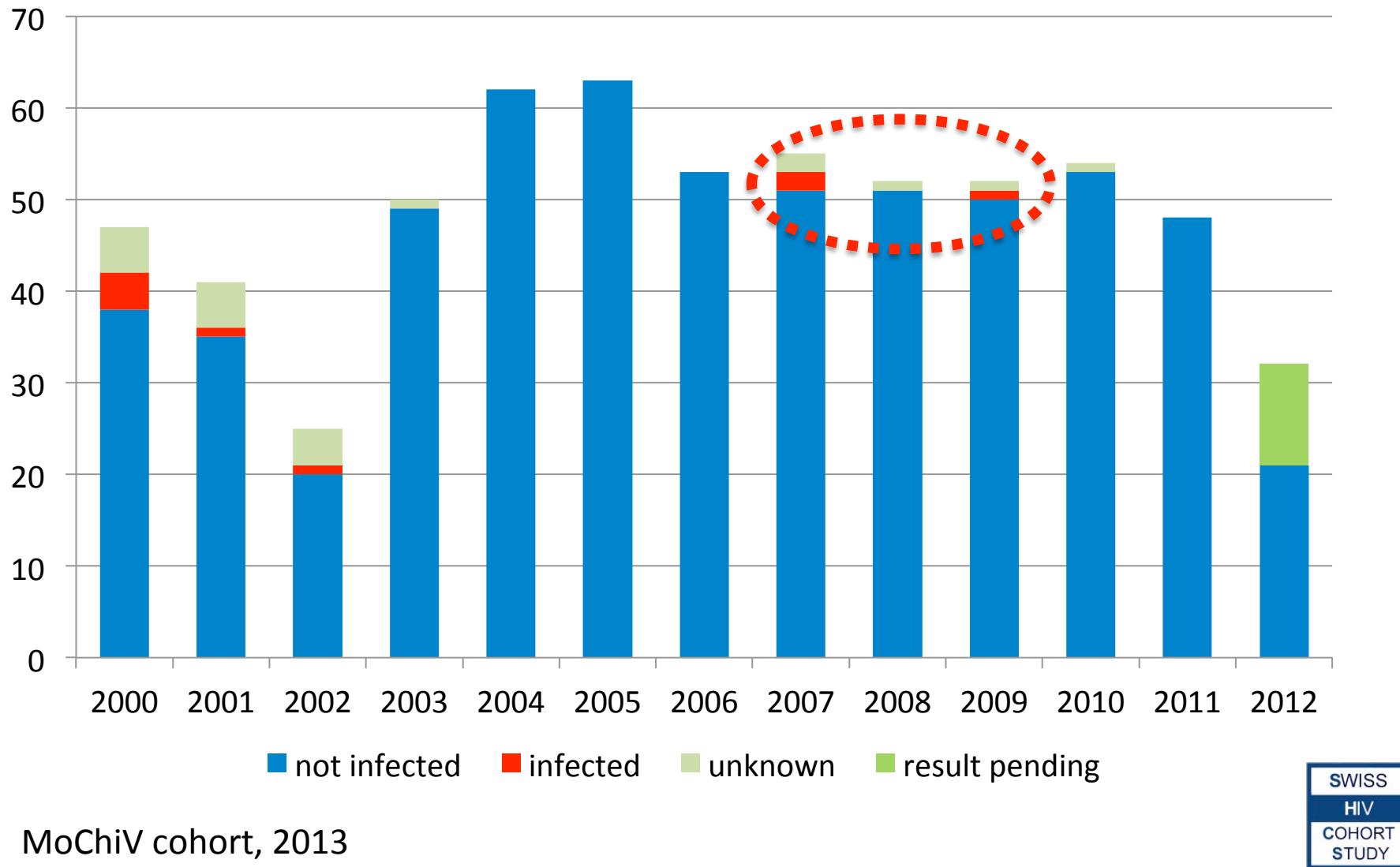
Swiss made

- Counselling of serodifferent couples
- No mother to child transmission of HIV
- Swiss court decision
- Impact of the Swiss statement on sex practices
- Discussion on PreP

Counselling activity

- What does it mean “lack of infectiousness on cART”
 - The concept of negligible risk
- Consequences for the serodiscordant couple
 - Heterosexual couple with desire of procreation
- The seronegative partner must be involved in the discussion and she/he has the last word

Mother to Child transmission



✓ Change in the application of Swiss legislation

Man not guilty for sex under cART

World News

Issue: 142

Swiss court accepts that criminal HIV exposure is only 'hypothetical' on suc

In the first ruling of its kind in the world, the Geneva Court of Justice has quashed an 18-month prison sentence given to a 34-year-old HIV-positive African migrant who was convicted of HIV exposure by a lower court in December 2008, after accepting expert testimony from Professor Bernard Hirschel – one of the authors of the Swiss Federal Commission for HIV/AIDS consensus statement on the effect of treatment on transmission – that the risk of sexual HIV transmission during unprotected sex on successful treatment is one in 100,000.

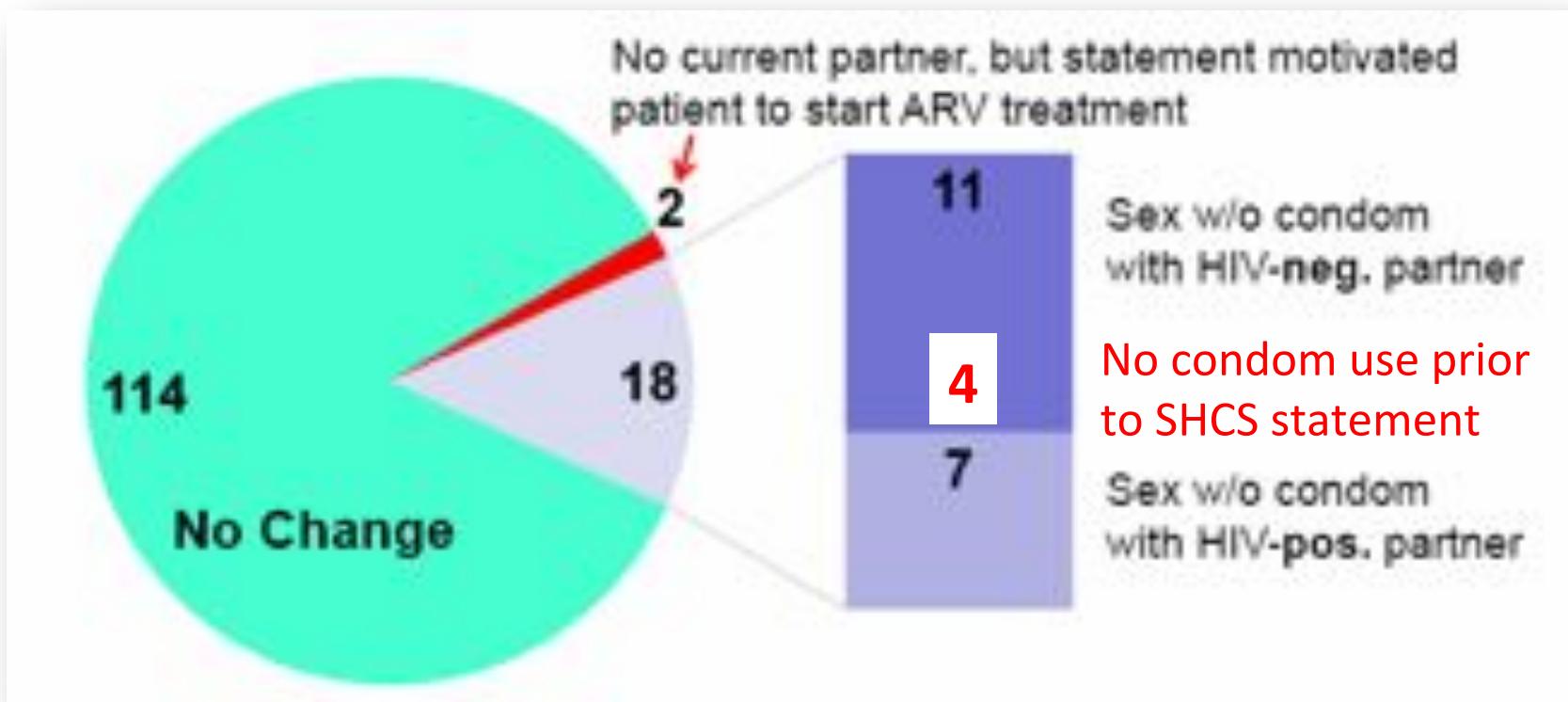


March 2009

http://www.positivenation.co.uk/news_world/article.php?article_id=159

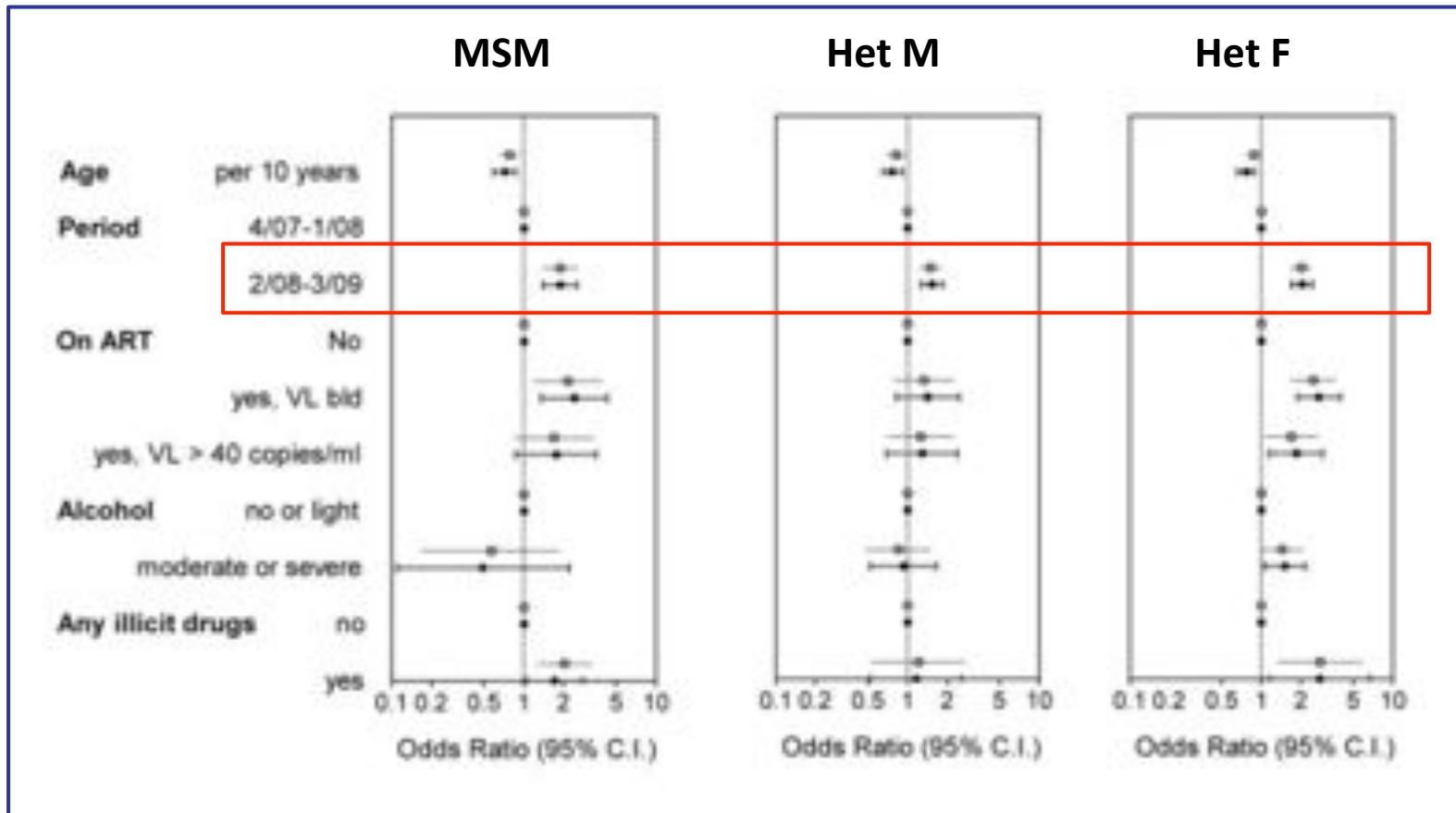
Little behavioural changes

Anonymous Survey in selected SHCS sites
3 months after the Swiss Statement



Unprotected Sex in SHCS after the Swiss statement

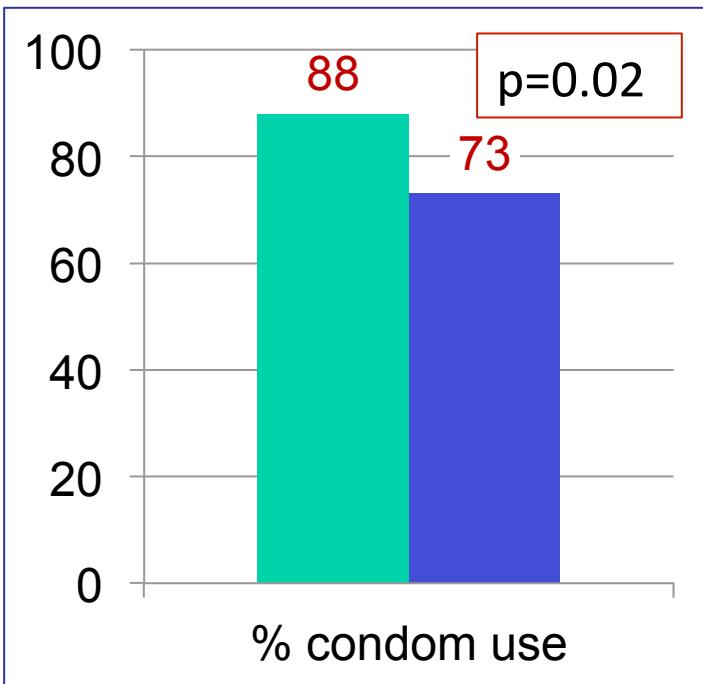
More reports of sex w/o condom



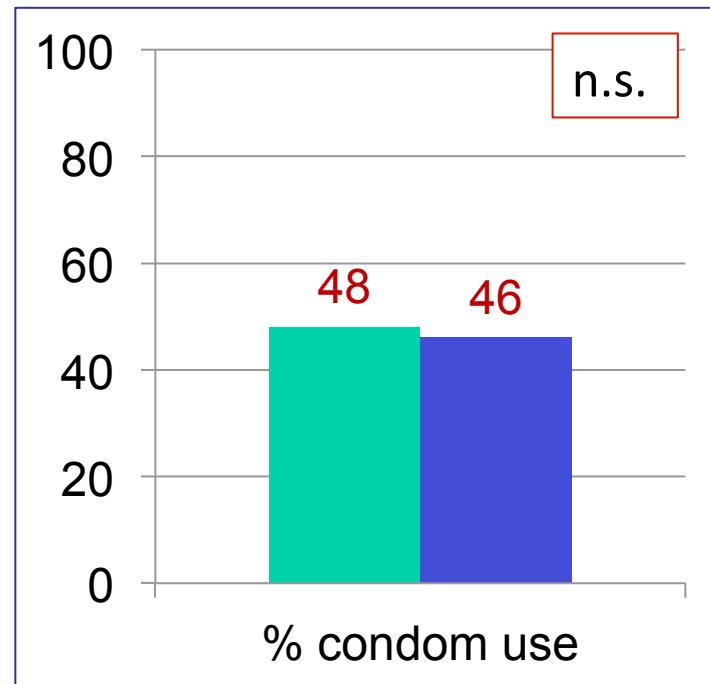
Sexual History questionnaires in Swiss HIV cohort study

Interview vs. Anonymous

2002 – before EKAF¹



2010 – after EKAF²

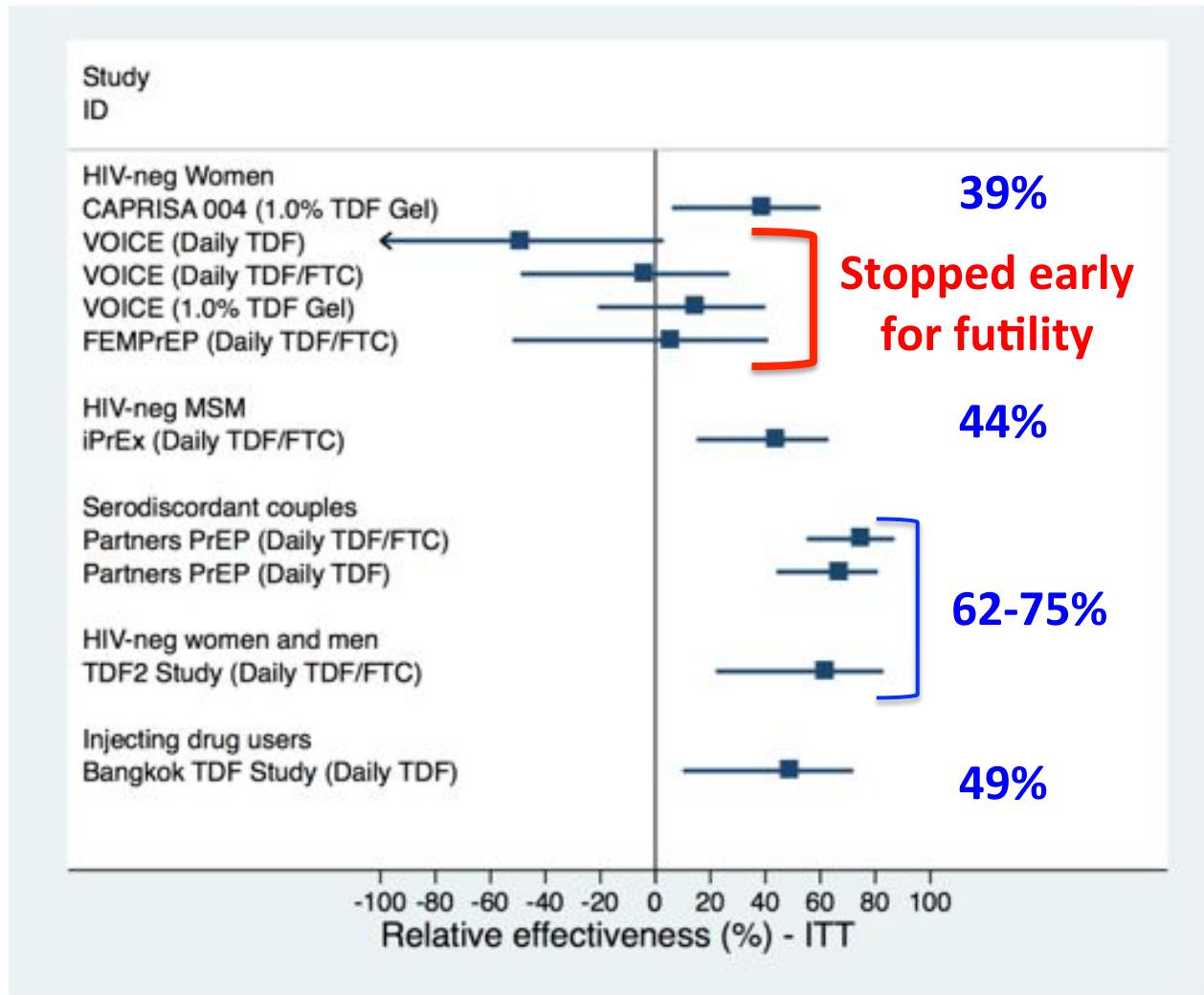


■ Interview ■ Anonymous

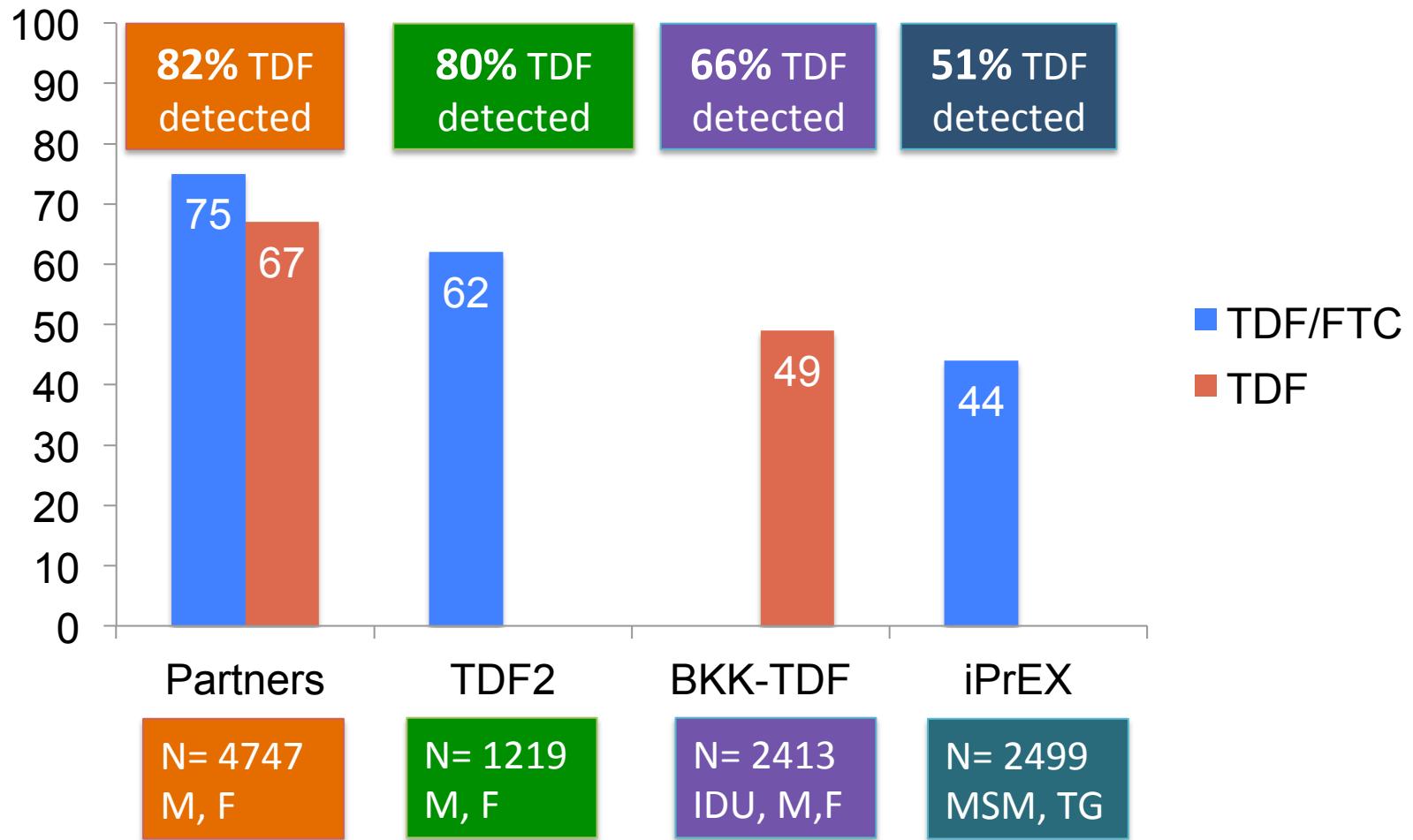
¹Panzo et al, SMW 2003

²Nagel et al, 2012 (personal comm.)

PreP: Discordant results



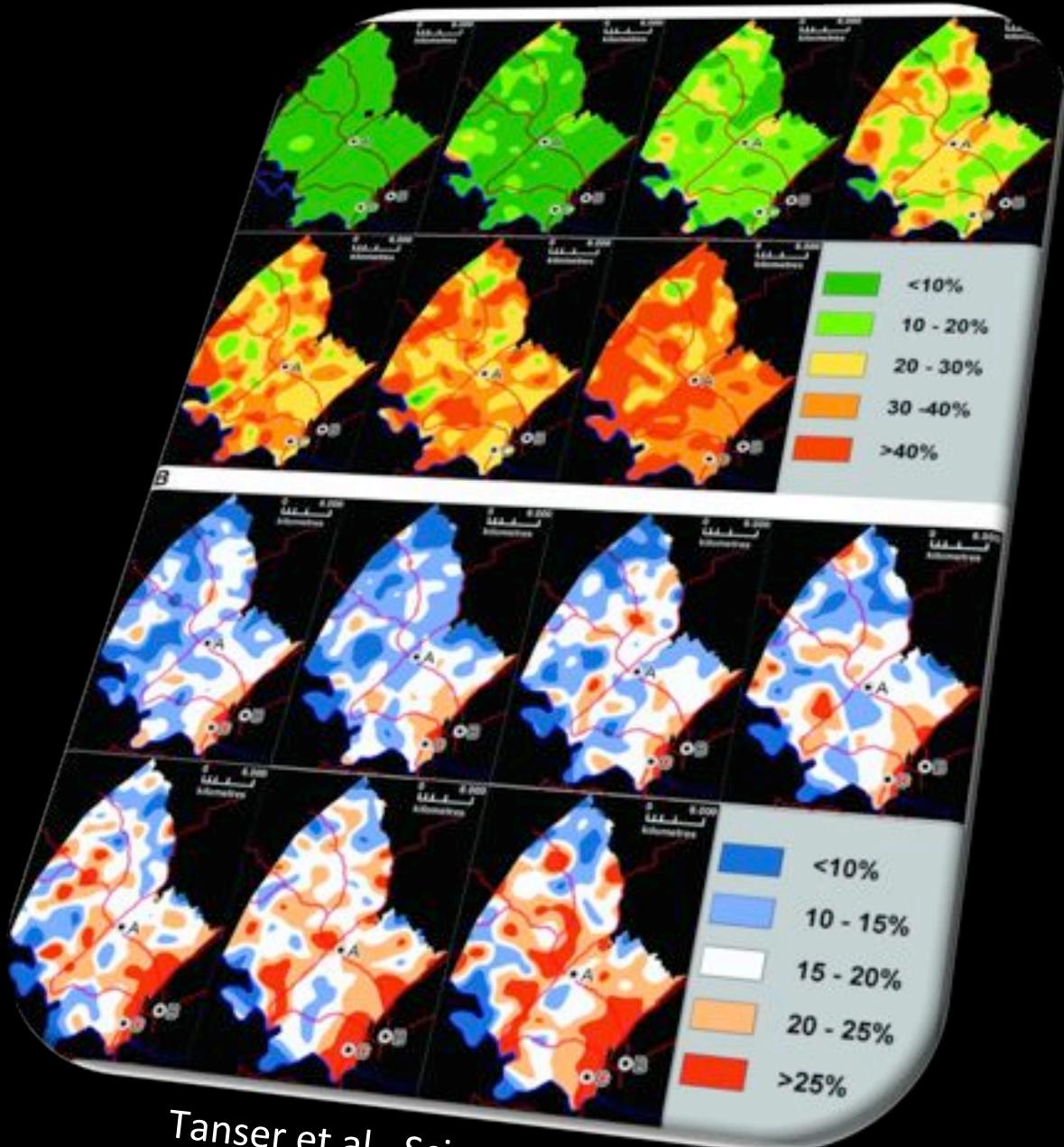
PreP: it works...when you take it



New drugs for PrEP

| | Mechanism | Dosing route | Frequency | Stage of developm. |
|--------------------|---------------------------|--------------|------------|--------------------------------|
| Maraviroc | CCR5 antag. | ORAL | once daily | Phase 2, enrolling |
| Rilpivirine | NNRTI | IM | monthly | Phase 1; Phase 2 planned |
| Dapivirine | NNRTI | RING | monthly | Phase 3, enrolling |
| Ibalizumab | CD4 attachm. inhibitor | SC | weekly | Phase 1, pilot |
| 744-LAP | Integrase inhibitor | IM | quarterly | Phase 1; Phase 2 planned |

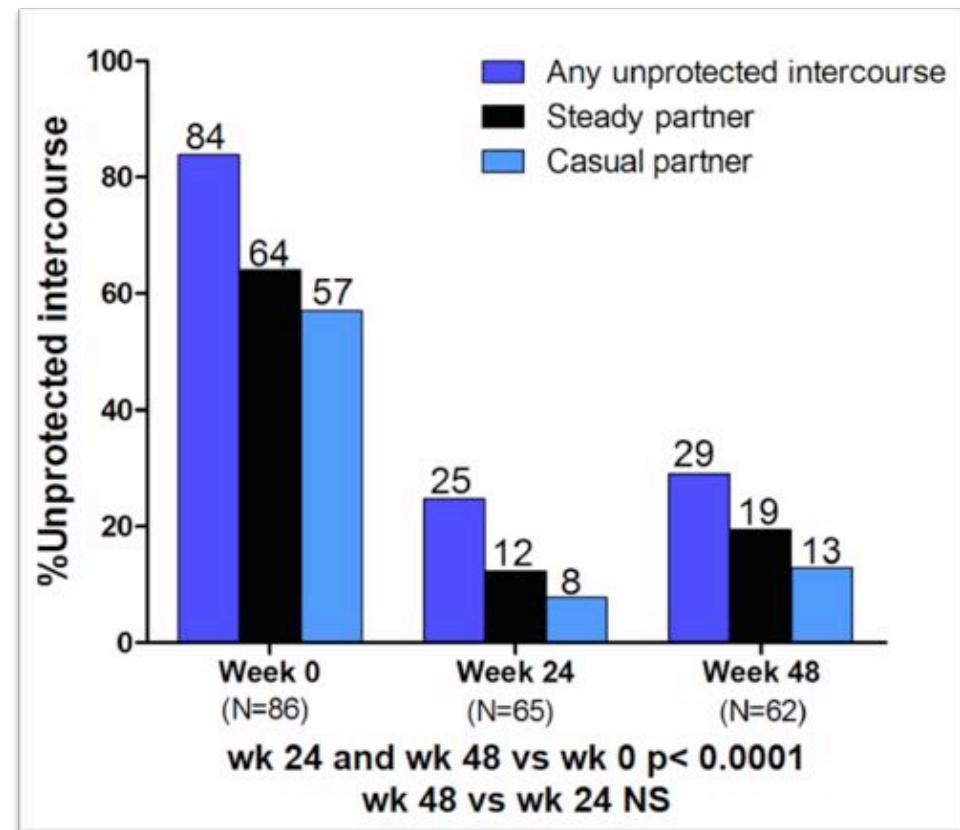
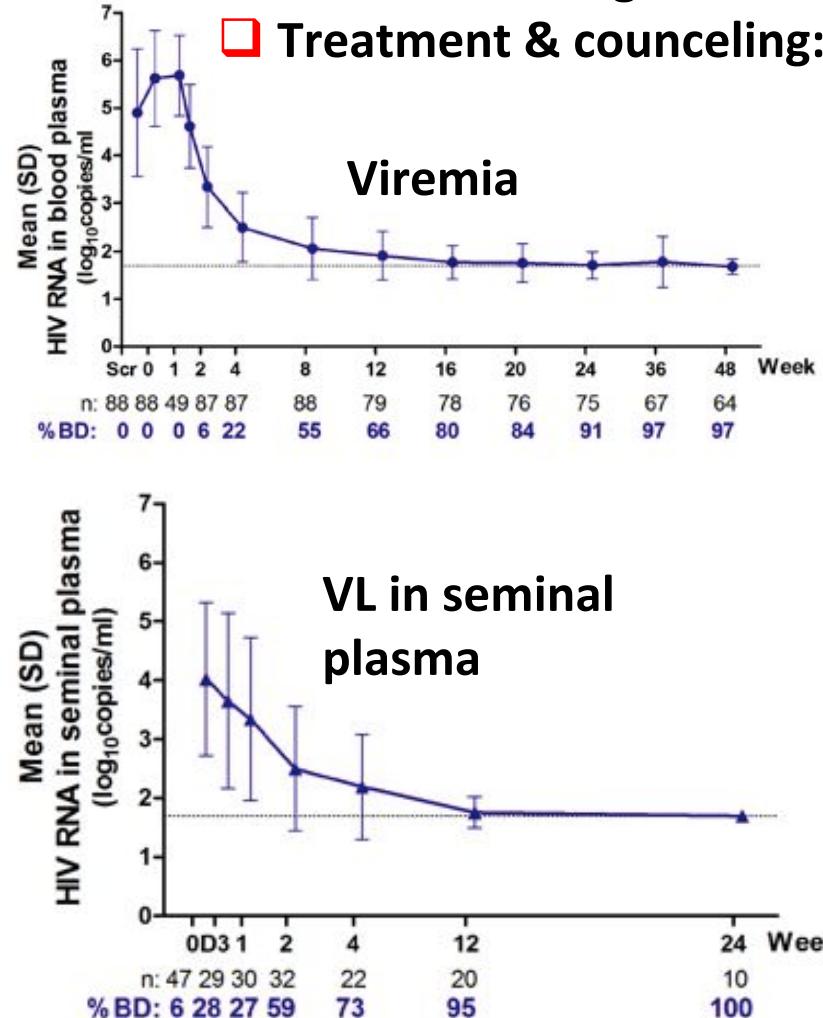
Recent Data on TasP



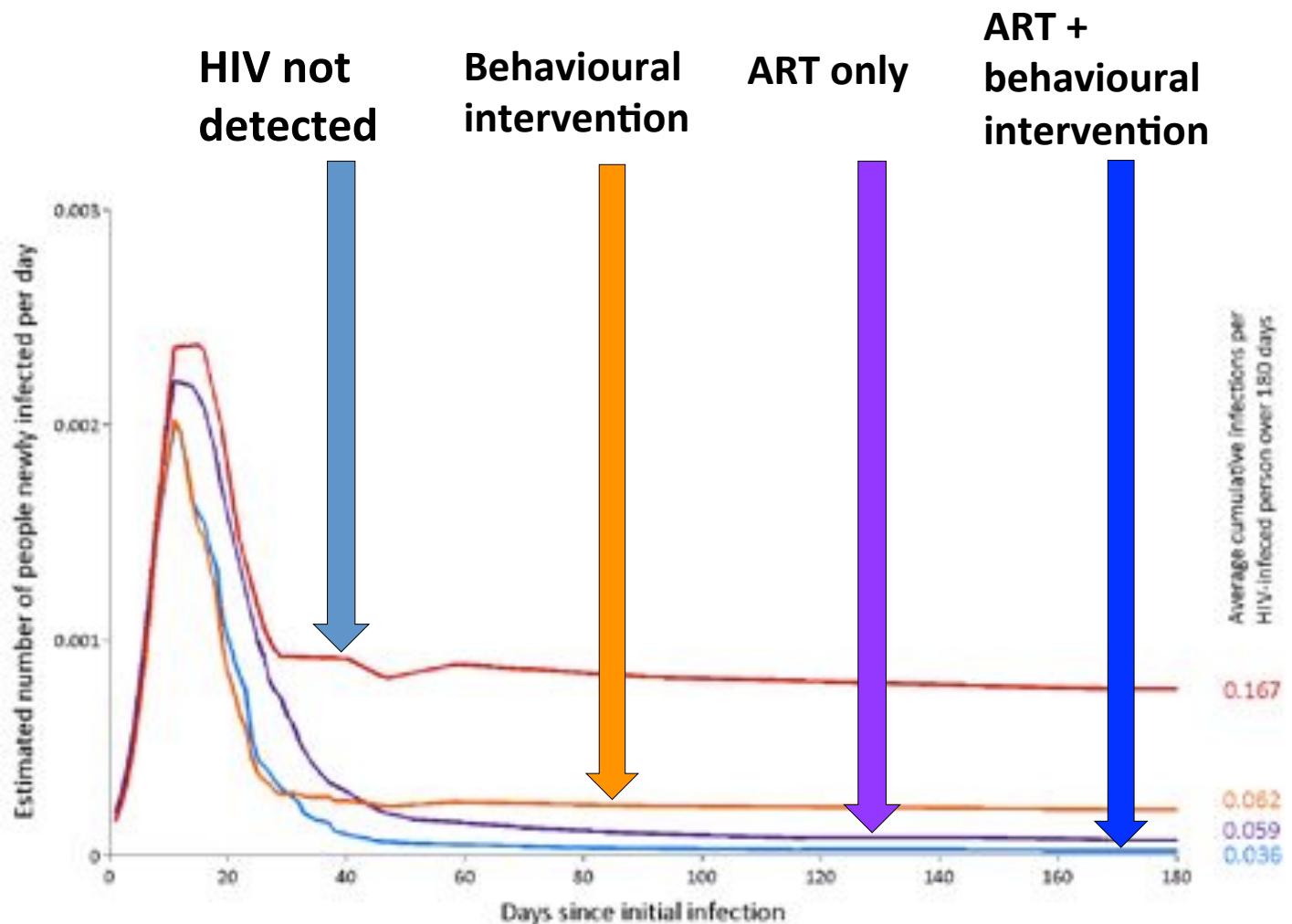
Tanser et al., Science 2013

Treatment: a successful prevention tool

- 88 MSM in Bangkok with acute HIV infection
- Treatment & counceling: Virologic outcome and behaviour



...with additional potential



On ART:
100% VL
undetectable at
weeks 12 and 24
in seminal plasma
(100% correlation
with blood)

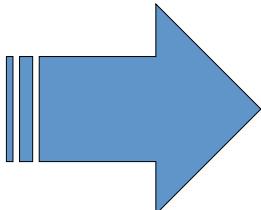
Further studies on TasP at IAS 2013

- Metanalysis of observational studies: **ART linked to lower sexual risk taking and fewer new STI diagnoses** (Doyle et al, WEPDB0105)
- French longitudinal study: 153 MSM on stable ART, viremia < 50 cp/ml > 6 months, **HIV detected in 23/304 semen samples** (7.6%) (Ghosn J, MOPE142)
- Australian study: **Perceived undetectable viral load strongly predicted condom-free anal intercourse** in 76 HIV-discordant gay couples (and the perception was wrong (7%) (Bavinton, MOLBPE30)

What ART for TasP ?

Criteria endorsed by 19 French experts for ART selection and applicability for a “test & treat” approach:

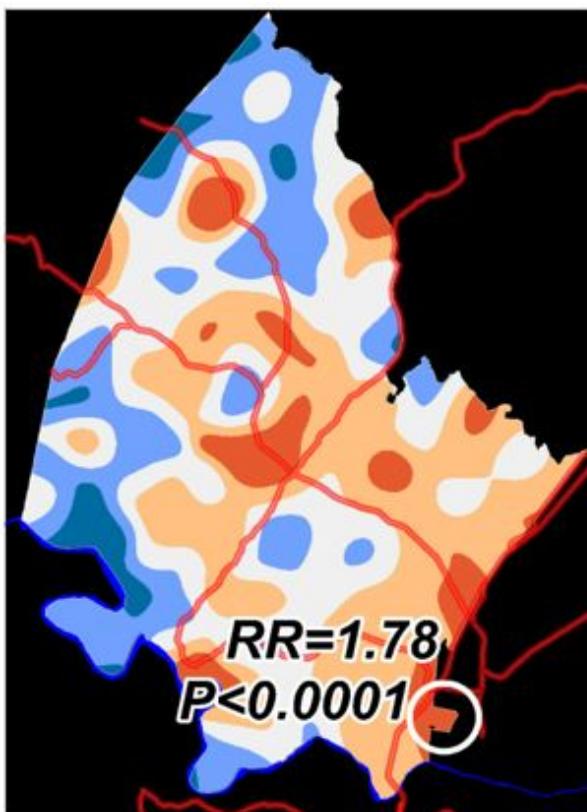
- **Tolerance, side effects, and/or toxicity profile** of ART
- **Simplicity** (e.g. Rx schedule, dosage form)
- **Individualization** of Rx (eg. adapted to lifestyle, perceptions of Rx)



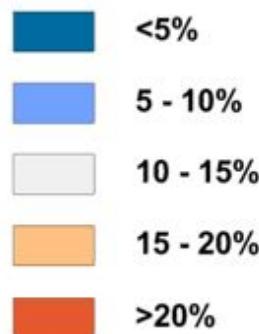
“Minimal interference”: ART for TasP should have optimal tolerance, low toxicity and simple administration
BUT
No one-size-fits-all approach

ART, viremia & HIV transmission

Population prevalence of detectable virus (PPDV) in rural KwaZulu-Natal



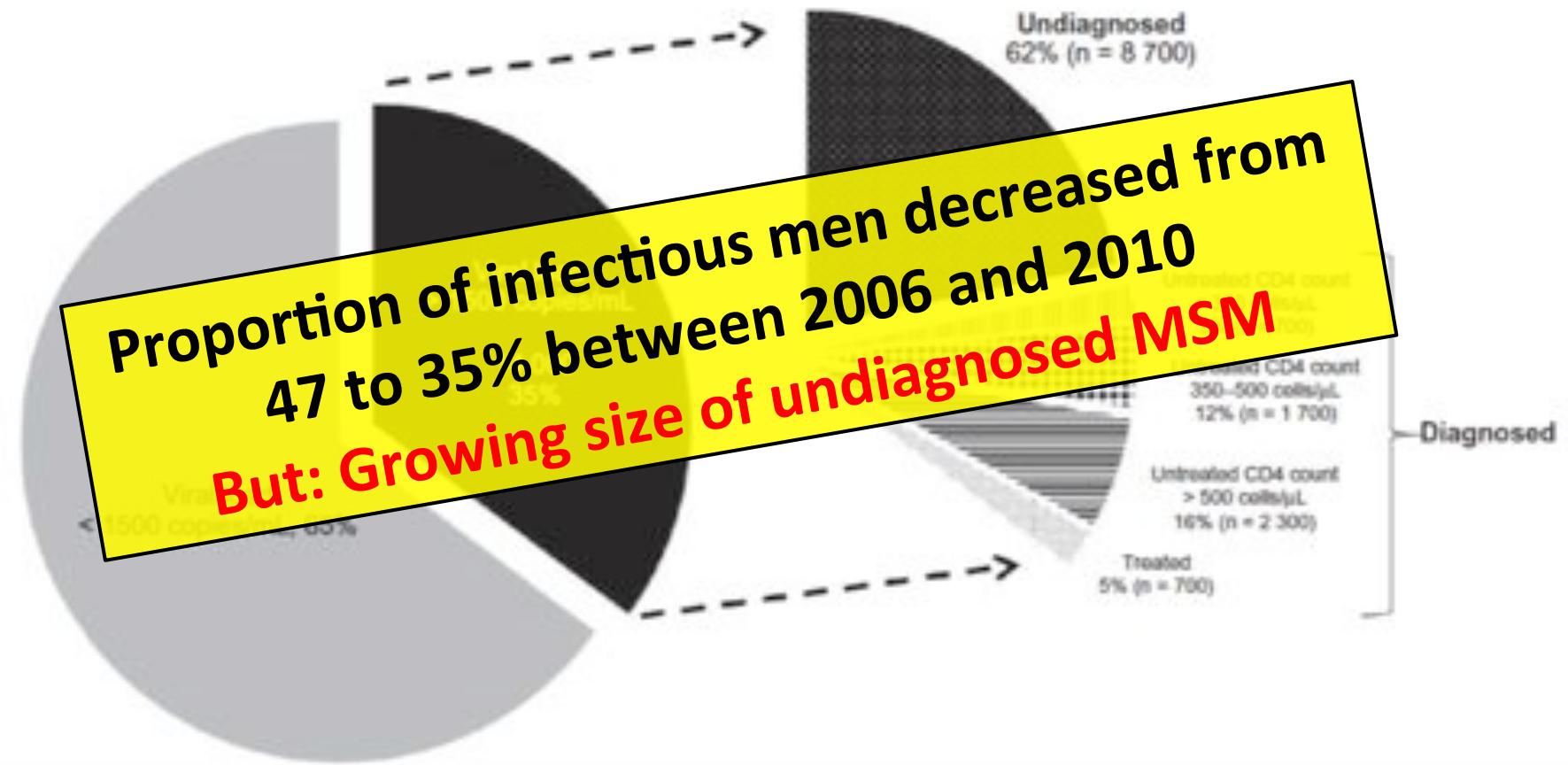
Prevalence (%)



Population prevalence of detectable virus (PPDV) successfully identified known areas of continued high HIV incidence

Tanser* et al., TUSY0405 (author of the Science paper on reduction of HIV acquisition with increasing ART coverage)

Viral load distribution in MSM, UK 2010



What is the PARTNER Study

The PARTNER study is enrolling couples where one partner is HIV-positive and the other is HIV-negative. This new study is looking at the risks of HIV transmission when someone is taking effective HIV treatment.

We know that condoms are the safest and most effective way of protecting against transmission. But we also know that not everyone uses a condom every time.

The PARTNER study particularly focuses on partnerships that do not always use a condom when having sex. The study is also looking at why condoms are not always used.



The PARTNER study is an international collaborative study taking place in several European countries. It is funded by the National Institute for Health Research in England and is coordinated by Copenhagen HIV Programme (CHIP) in collaboration with University College London (the sponsor) and The Royal Free Hampstead NHS Trust, London.

Study Coordinating Centre contact:

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Copenhagen HIV Programme
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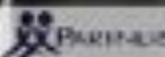
www.partnerstudy.eu

For information in your country,
please contact:

HIV Treatment
Sexual
Transmission
Condom
Use



The PARTNER
Study:
a new study for
sero-discordant
couples



www.partnerstudy.eu

Kindly provided by P. Vernazza

Summary

- 5 years after the “Swiss statement” no sign for an increase of HIV infection due to failure of TasP
- TasP has become a “politically correct” matter worldwide
- In Switzerland we acknowledge some major achievements like natural procreation and change in the legislation



Merci pour l'attention !