# PEP and PrEP

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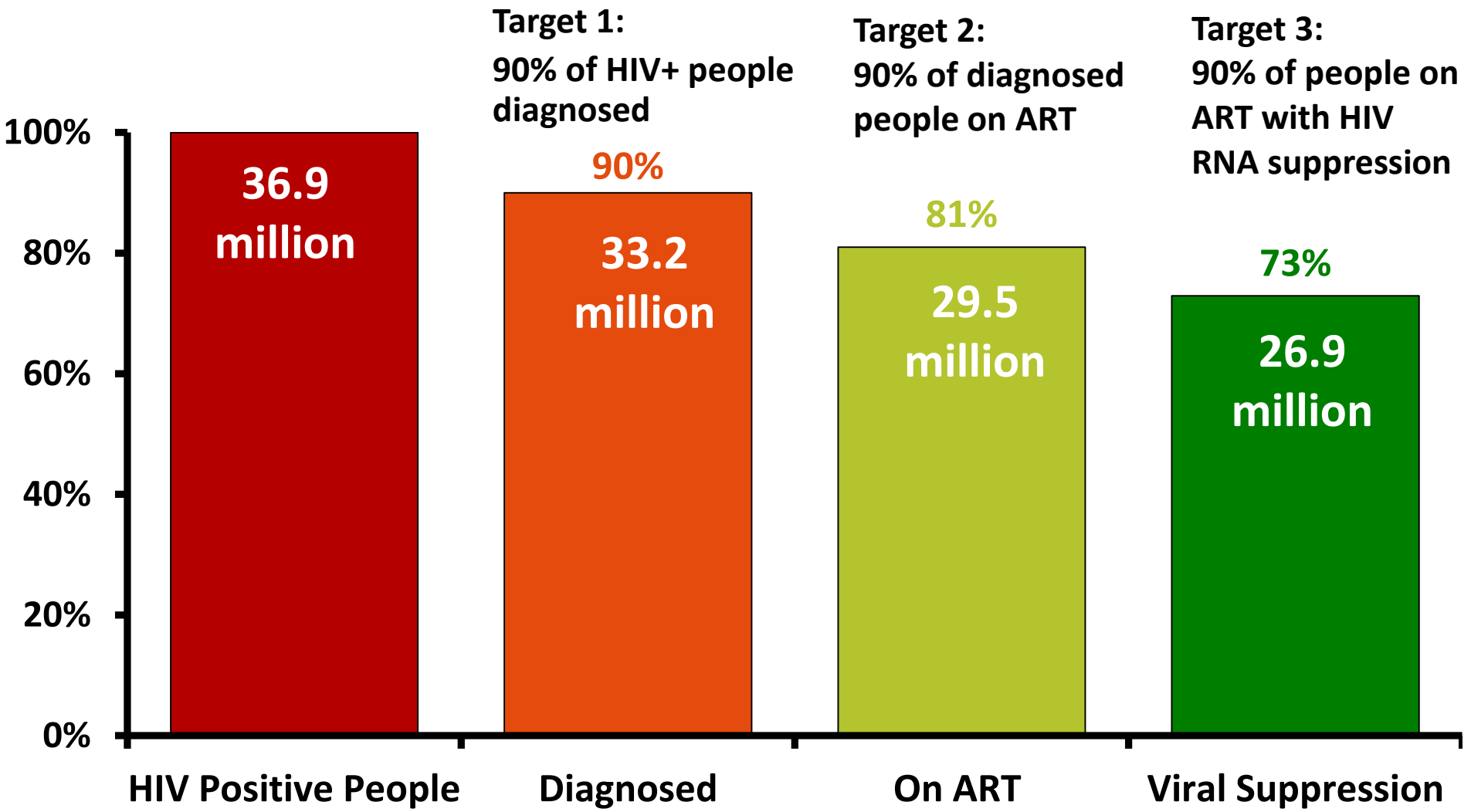
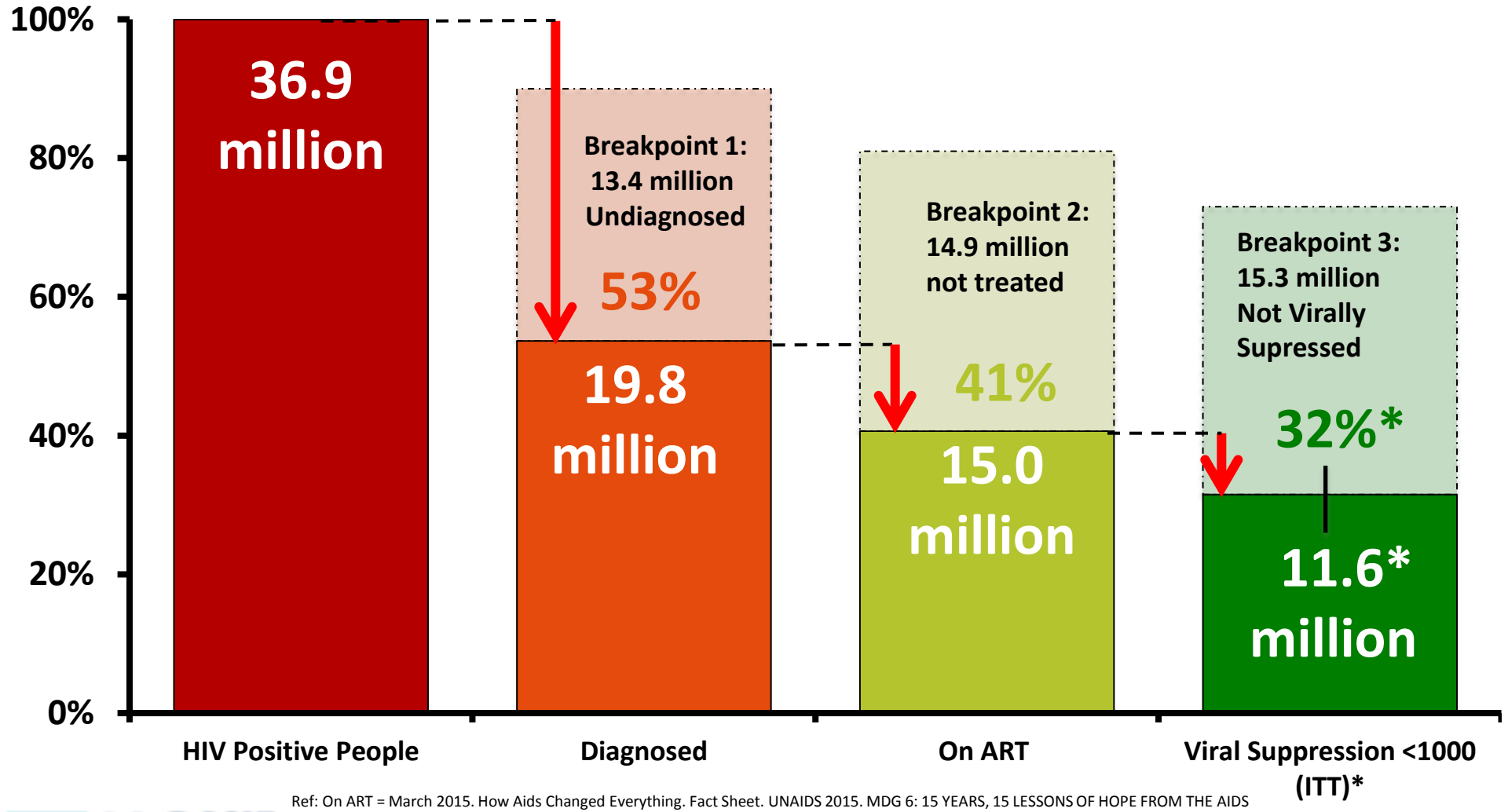
# UNAIDS 90-90-90:
## HIV Treatment Targets for 2020 with Global Estimates (2014)






Ref: The Joint United Nations Programme on HIV/AIDS. 90-90-90 An ambitious treatment target to help end the AIDS epidemic. 2014; JC2684 (Numbers as of March 2015) How Aids Changed Everything. Fact Sheet. UNAIDS 2015. MDG 6: 15 YEARS, 15 LESSONS OF HOPE FROM THE AIDS RESPONSE July 2015.

# Global Estimates (2014-15) vs the Gap to reach 90-90-90 Targets

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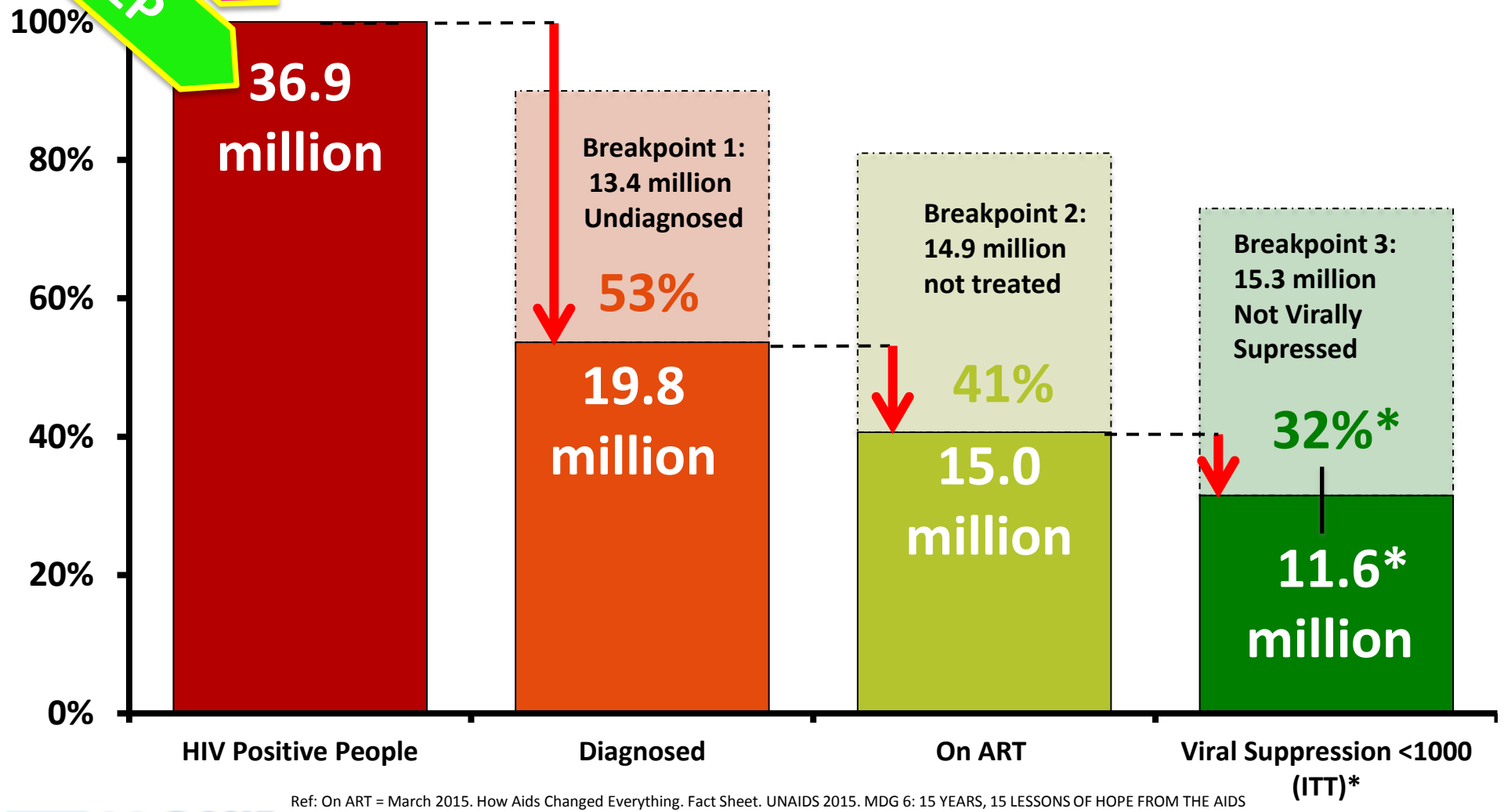
PrEP

PEP

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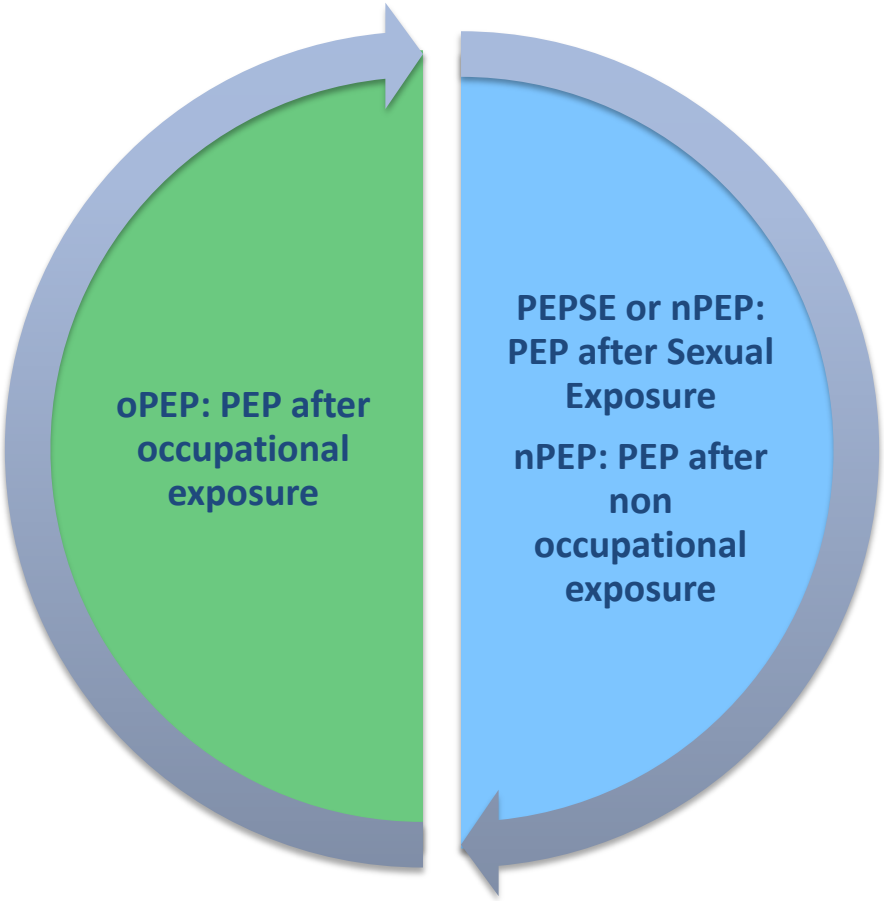
# Post Exposure Prophylaxis
# PEP

# Post Exposure Prophylaxis



# What is considered substantial risk?

**Substantial Risk**

• Exposure of

- Vagina, rectum, eye, mouth or other mucous membrane, non intact skin, or percutaneous

contact

• With

- Blood, semen, vaginal secretions, rectal secretions, breast milk, or any body fluid

that is visibly contaminated with

blood

• When

- The source is known to be HIV infected

**Negligible risk**

• Exposure of

- Vagina, rectum, eye, mouth or other mucous membrane, intact or non intact skin, or percutaneous contact

• With

- Urine, nasal secretions, saliva, sweat, or tears if not visibly contaminated with blood

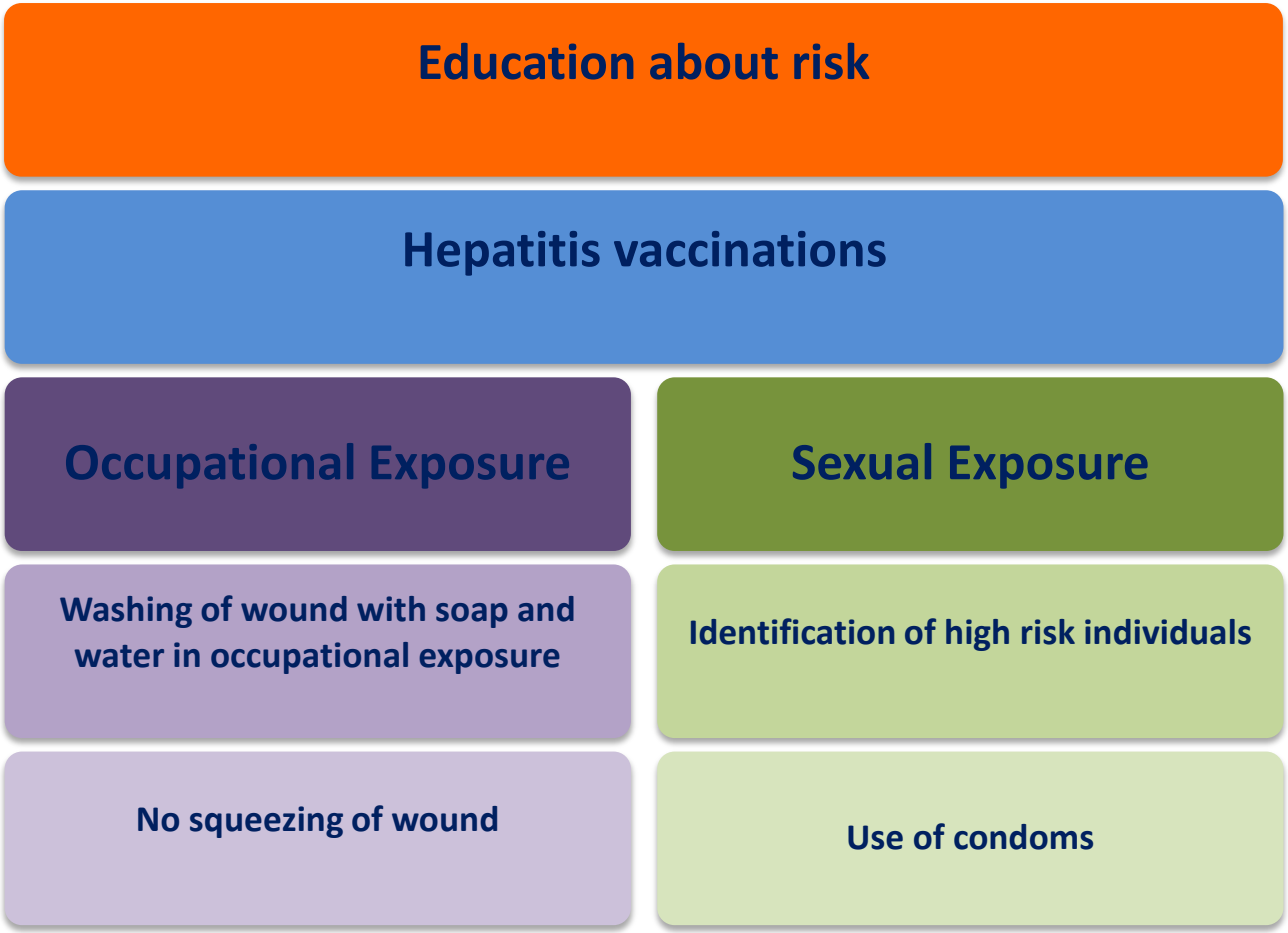
• Regardless

- Of the known or suspected HIV status of the source

# Risk of exposure

| Type of exposure | Estimated risk of HIV transmission |
|---|---|
| Receptive anal intercourse | 1.1 (0.042– 3%) |
| Receptive vaginal intercourse | 0.1 (0.004– 0.32%) |
| Insertive vaginal intercourse | 0.082 (0.011– 0.38%) |
| Insertive anal intercourse | 0.06 (0.06-0.065%) |
| Receptive oral sex | 0.02 (0– 0.04%) |
| Insertive oral sex | 0 |
| Needle-stick injury | 0.3 (0.2-0.5%) |
| Sharing injecting equipment | 0.67% |
| Mucous membrane exposure | 0.63 (0.018-3.47%) |

# In addition to PEP

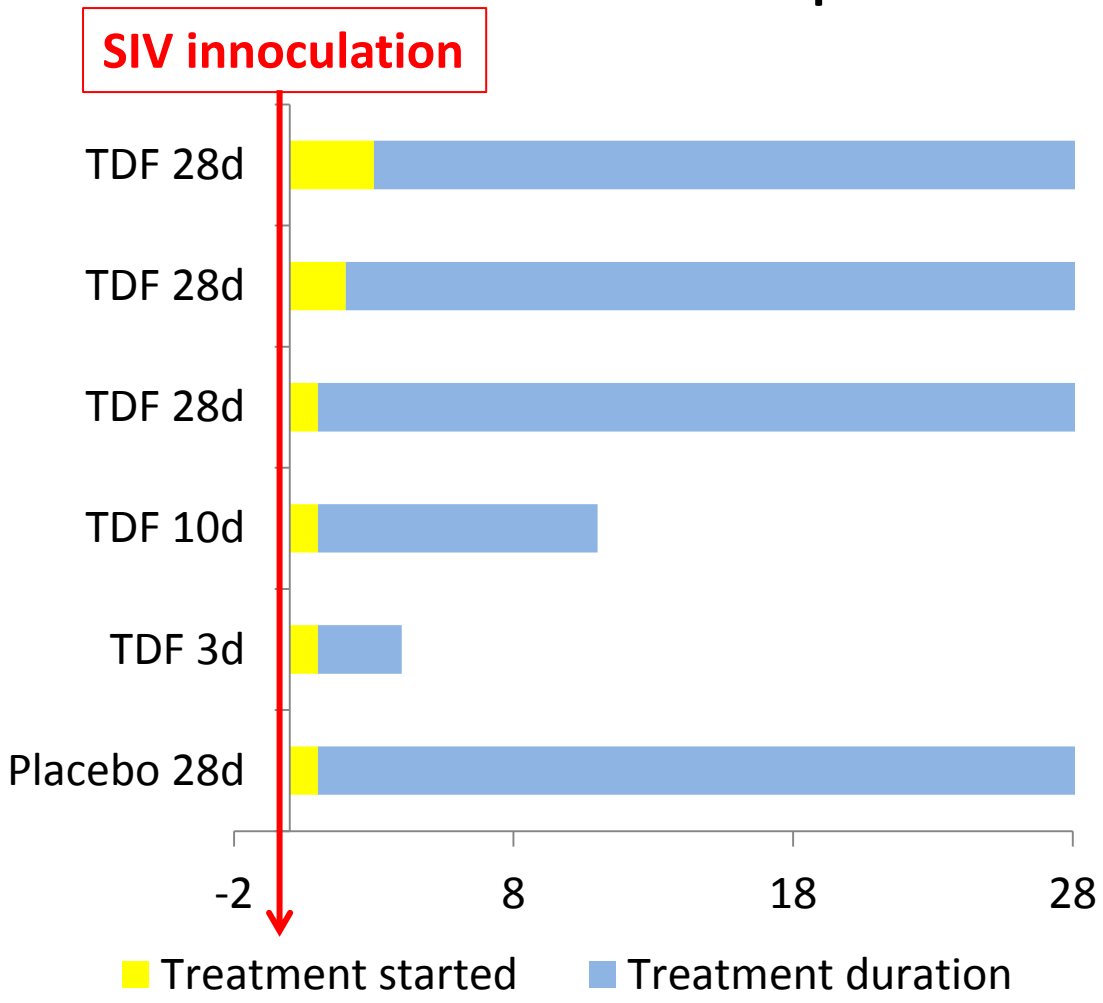


# Post Exposure Prophylaxis

- No randomized, placebo-controlled clinical trial of PEPSE has been conducted
- Data relevant to PEP guidelines are evolved from
  1. Animal transmission models
  2. Perinatal clinical trials MTCT
  3. Observational studies of health care workers receiving prophylaxis after occupational exposures
  4. Observational and case studies of PEPSE use

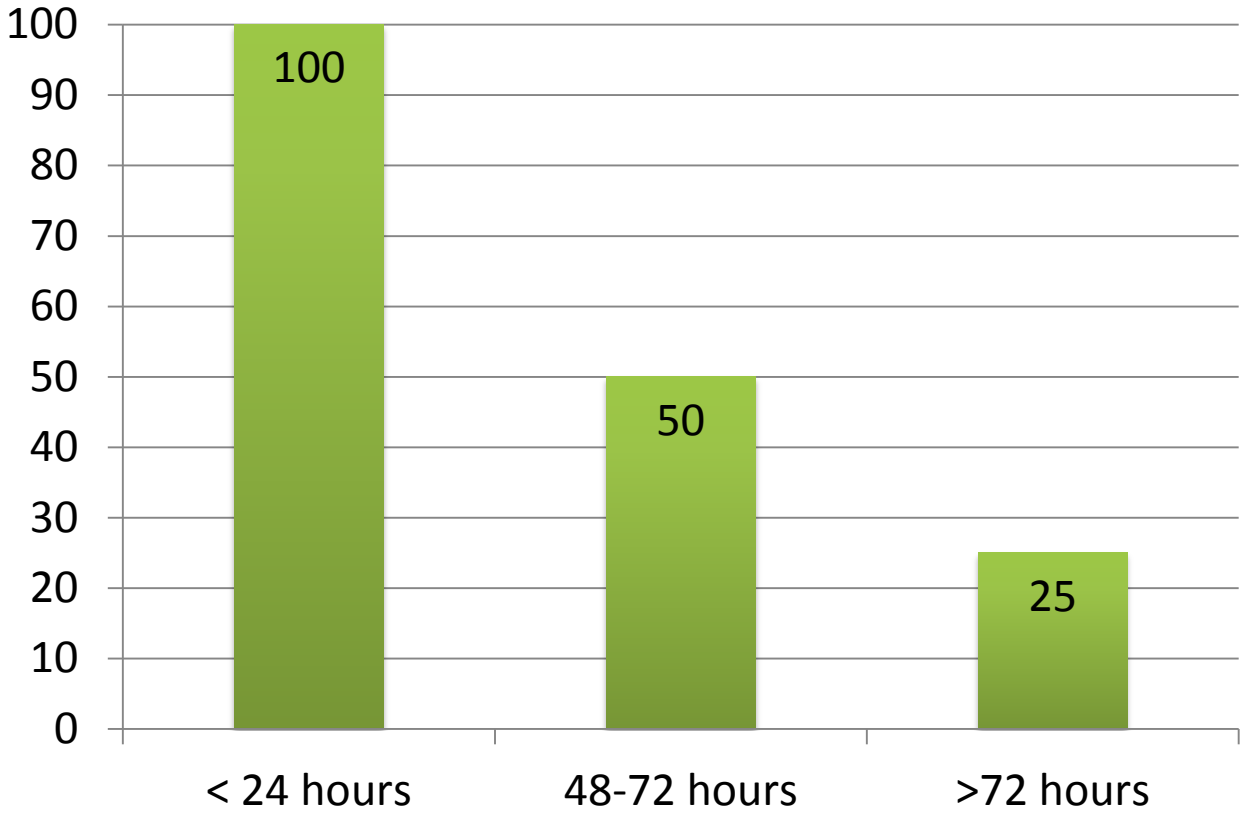
# 1. Animal Model Data
# Effectiveness of Tenofovir PEP in Macaques

- Study Features
- N = 24 macaques
- Randomized to 6 treatment arms
- SIV inoculated intravenously
- SIV dose 10x 50% infective dose
- PEP started at 24, 48 or 72 hours
- PEP duration: 3, 10, or 28 days
- PEP regimen: tenofovir (TDF) SQ
- Analyzed for antibody and viremia




*Tsai CC, Fransen K, Diallo MO et al. J Virol 1998;72:4265–73*

# Macaque animal models – timing of PEP




- Systemic viral dissemination does not occur immediately → window of opportunity

*Tsai CC, Fransen K, Diallo MO et al. J Virol 1998;72:4265–73*

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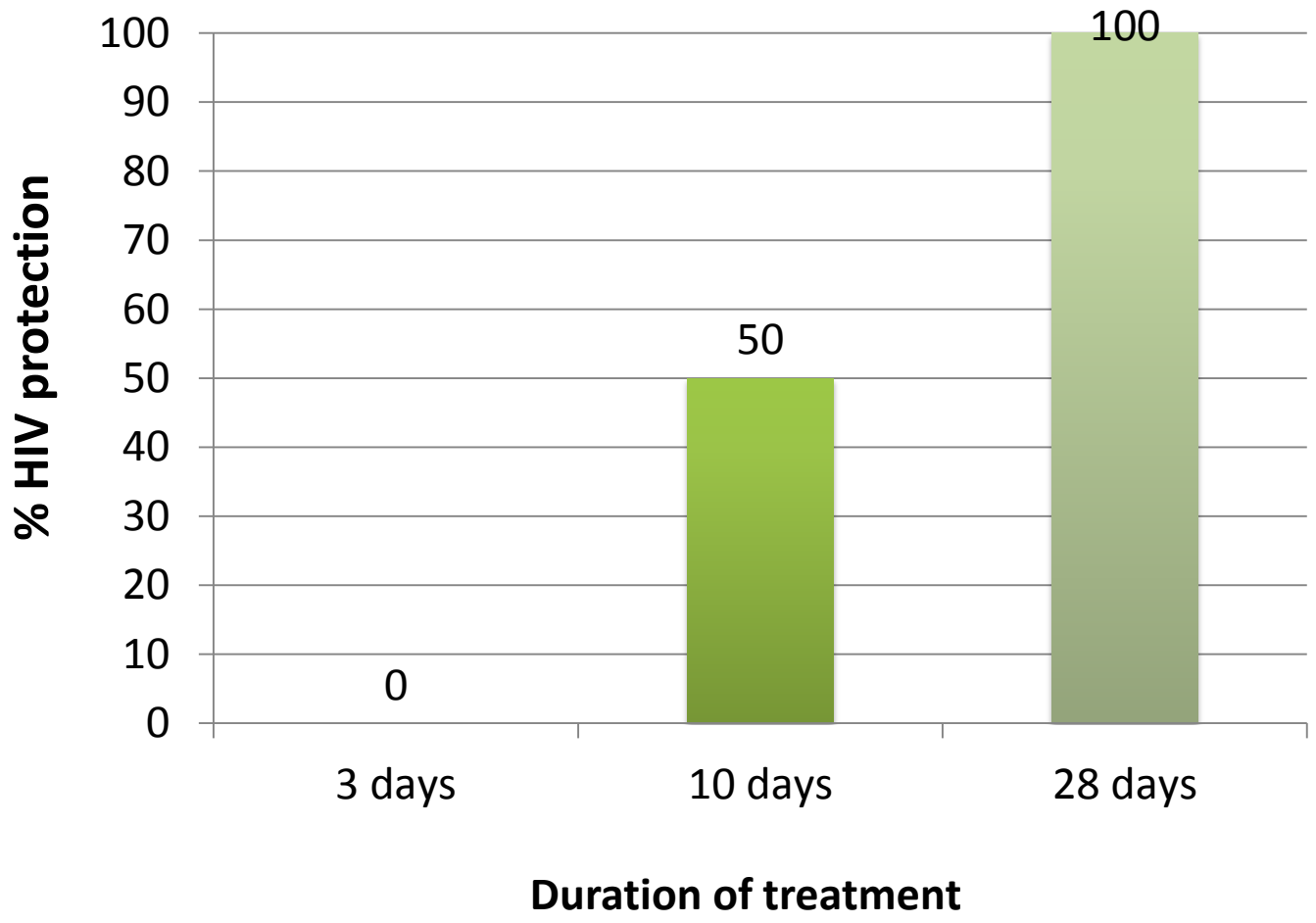


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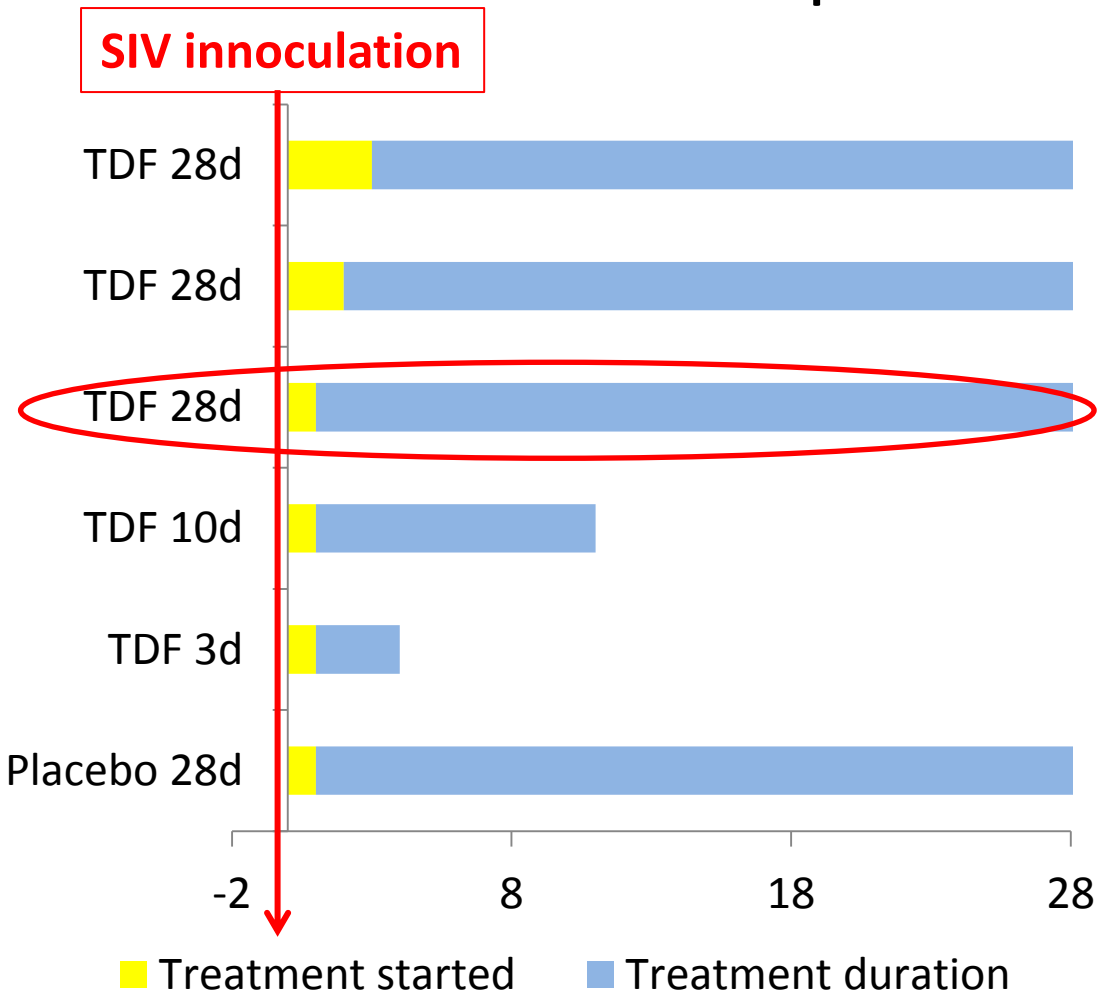


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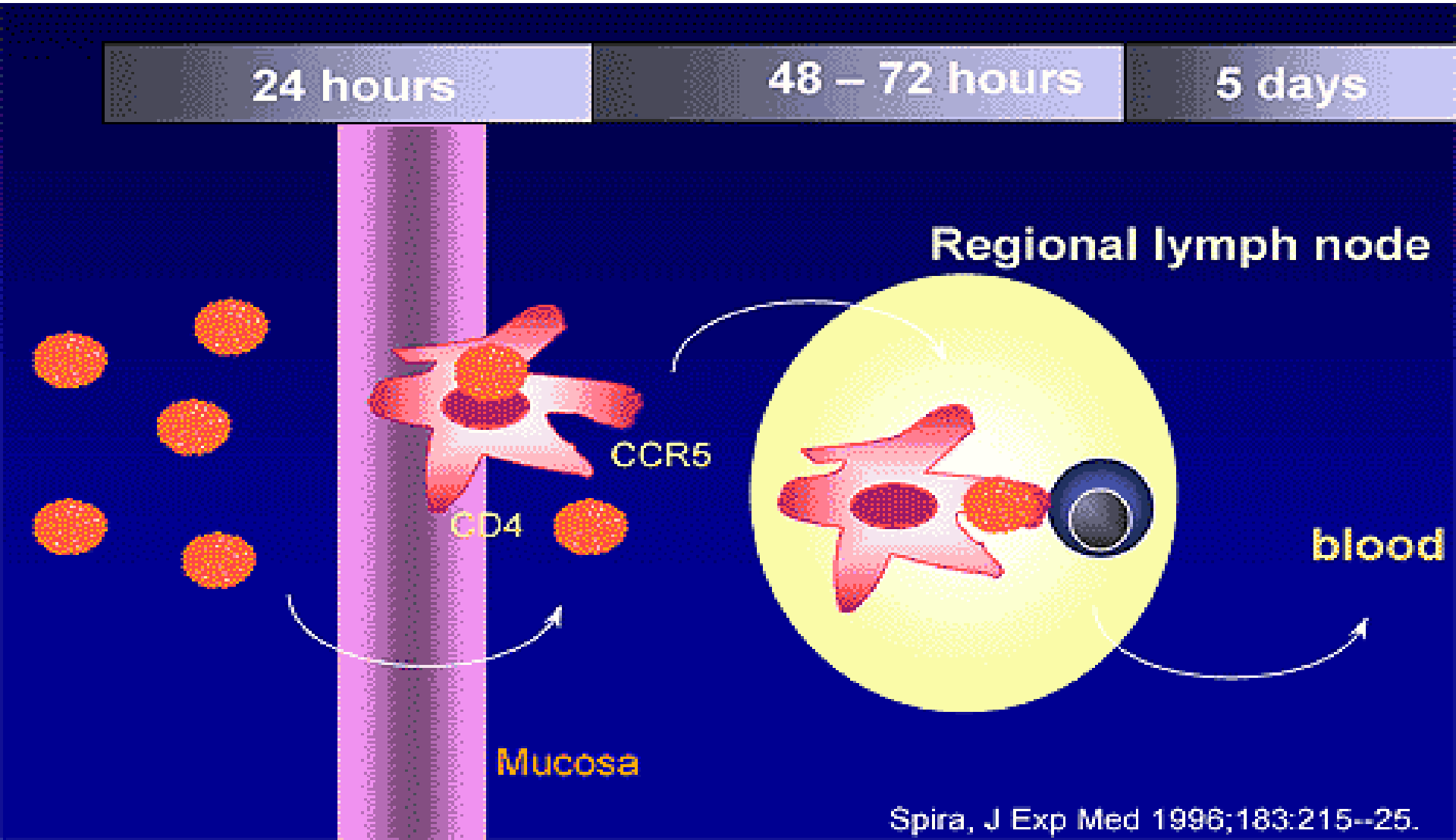
# Dynamics following exposure to HIV



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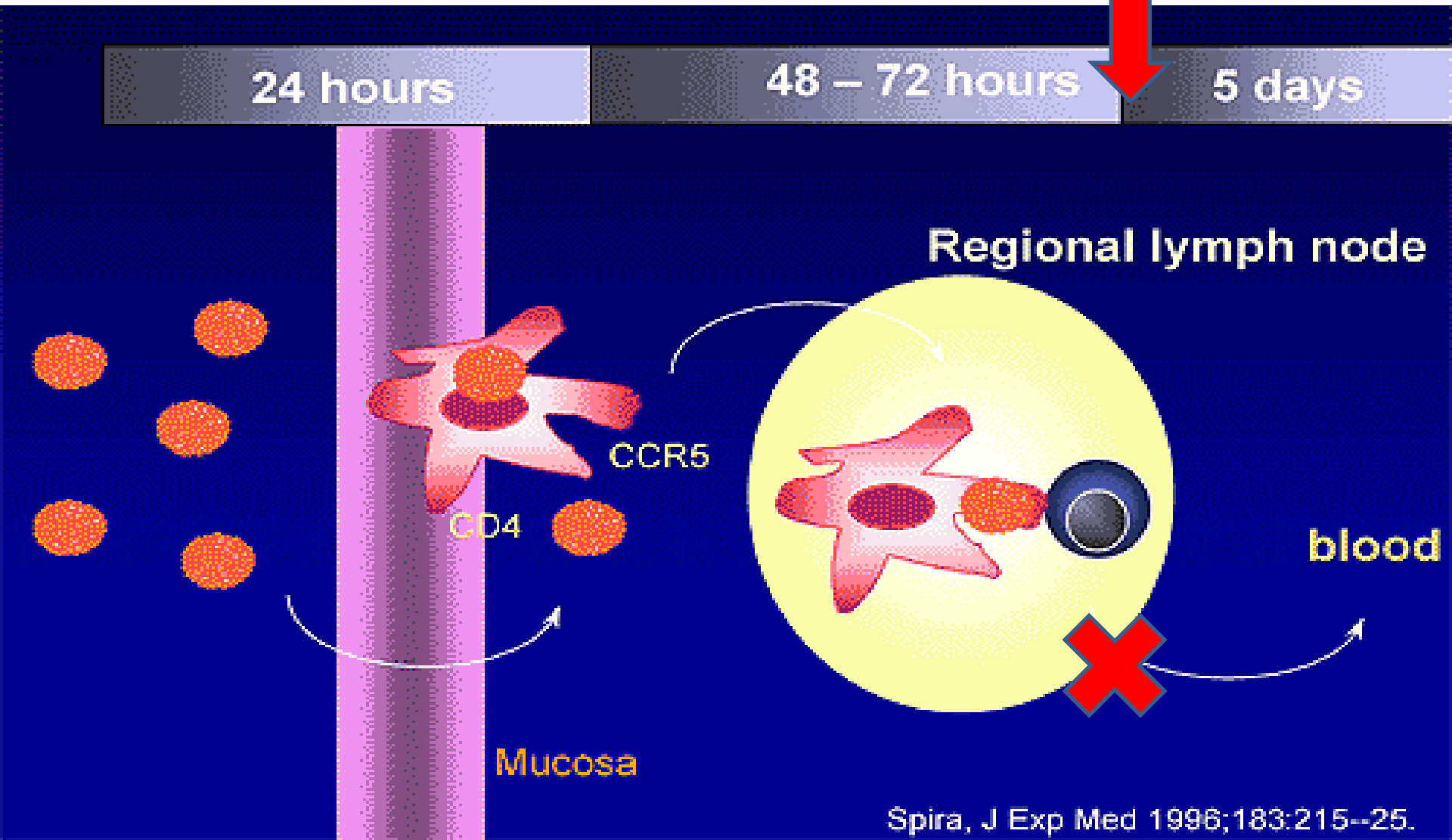
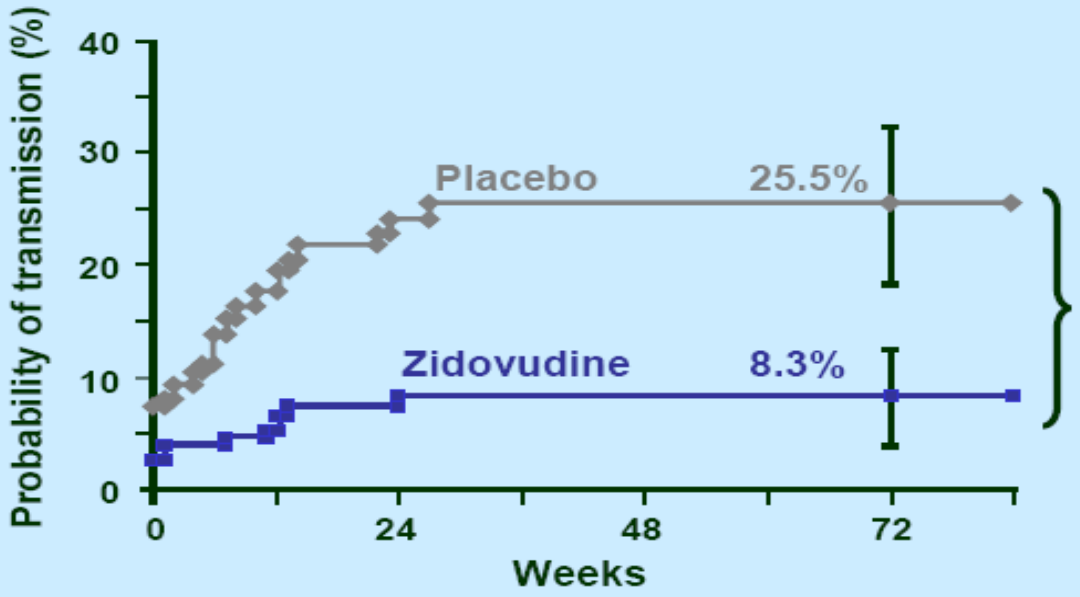


# 2. Perinatal Studies MTCT
# Zidovudine significantly reduces MTCT

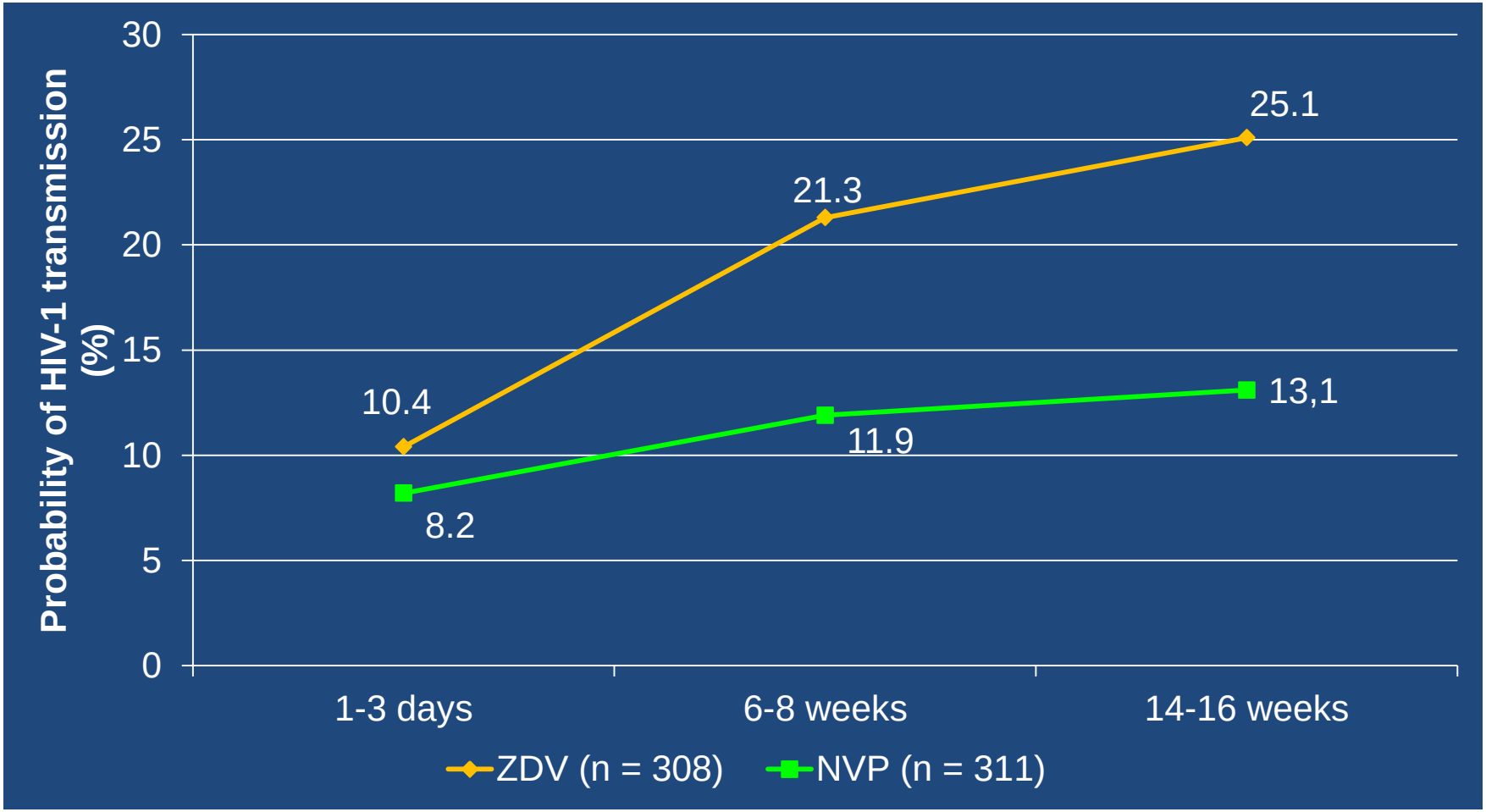
## PACTG 076 Study




| | | | | |
|---|---|---|---|---|
| Placebo (n) | 183 | 84 | 42 | 37 |
| Zidovudine (n) | 180 | 105 | 51 | 43 |

Connor EM *et al. NEJM* 1994;331:1173–1180

# HIVNET 012: HIV transmission
# Intrapartum/postpartum nevirapine vs zidovudine




**Stat dose NVP for mother and infant vs ZDV for mother in labour and neonate 1/52**

*Adapted from Guay et al. Lancet 1999;354:795–802.*

# 3. Occupational PEP (oPEP) study

- An observational case-control study
- HCW with occupational percutaneous exposure to HIV infected blood
- The case patients (n=33) were those who became seropositive after exposure to HIV, as reported by national surveillance systems in France, Italy, the United Kingdom, and the United States
- The controls (n=665) were HCWs in a prospective surveillance project who were exposed to HIV but did not seroconvert
- The case patients were significantly less likely than the controls to have taken zidovudine after the exposure (odds ratio=0.19; 95 percent confidence interval, 0.06 to 0.52)
- The first study to describe the efficacy of oPEP

Cardo DM, Culver DH, Ciesielski CA, et al. A case-control study of HIV seroconversion in health care workers after percutaneous exposure. *New Engl J Med.* 1997;337(21):1485-1490.

# 4. MSM PEPSE Observational study Brazil

- 2-year prospective study in Brazil
- 200 seronegative MSM at high risk of HIV were provided with
  - education regarding PEPSE
  - a 4-day starter pack with instructions to initiate its use for a suspected eligible exposure
  - a follow-up 24-day pack (to complete a 28-day course) but only for those men with eligible exposures
  - 68/200 MSM initiated PEPSE
  - Adherence to PEPSE medications was estimated on the basis of questions at the 28-day visit and remaining pill counts
  - The entire 28-day PEPSE regimen was completed by 89% of men with eligible exposures including 1 participant who seroconverted
  - Ten of 11 seroconversions occurred among men who did not initiate PEPSE despite risk exposure

Schechter M, do Lago RF, Mendelsohn AB, et al. Behavioral impact, acceptability, and HIV incidence among homosexual men with access to postexposure chemoprophylaxis for HIV.
*J Acquir Immune Defic Syndr*. 2004;35(5

# PEPSE failure in Men who have Sex with Men (MSM)

- 49 seroconversions were reported after PEPSE use based on 1 case report 13 and 6 studies

- The case report from Italy described a PEPSE failure in an MSM despite
  - self-reported 100% adherence
  - Use of a 3-drug medication regimen consisting of ZDV, lamivudine (3TC), and indinavir (IDV)
  - denial of ongoing HIV risk transmission behaviors after completing PEPSE
  - concomitant hepatitis C virus (HCV) seroconversion was also diagnosed

Terzi R, Niero F, Iemoli E, Capetti A, Coen M, Rizzardini G. Late HIV seroconversion after non-occupational postexposure prophylaxis against HIV with concomitant hepatitis C virus seroconversion. *AIDS.* 2007;21(2):262-263.
Donnell D, Mimiaga MJ, Mayer K, Chesney M, Koblin B, Coates T. Use of non-occupational post-exposure prophylaxis does not lead to an increase in high risk sex behaviors in men who have sex with men participating in the EXPLORE trial. *AIDS Behav.* 2010;14(5):1182-1189..
Sonder GJB, Prins JM, Regez RM, et al. Comparison of two HIV postexposure prophylaxis regimens among men who have sex with men in Amsterdam: adverse effects do not influence compliance. *Sex Transm Dis.* 2010;37(11):681-686.
16.):519-525.

# PEPSE failure in Men who have Sex with Men (MSM)

- 6 studies of 1535 MSM with 48 HIV seroconversions despite PEPSE use (31.3 seroconverions/1,000 persons)
- At least 40 of the 48 seroconversions likely resulted from ongoing risk behavior after completing PEPSE
  - 35/40 seroconversions occurred ≥ 180 days subsequent to PEPSE initiation and are unlikely to constitute failures
- The remaining 8 seroconverters among 1,535 MSM participants (5.2 seroconverions/1,000 persons) may be classified as potential PEPSE failures
  - This included 1 recipient with an indeterminate HIV test result and isolation of an M184 mutation resistant virus on the last day of his 28-day regimen despite initiating PEPSE ≤ 48 hours after exposure indicating…??
  - 4 patients seroconverted at 91 days, 133 days, 160 days, and 168 days after PEPSE initiation, including 3 who reported completing the 28-day regimen; however, there was no description regarding ongoing sexual risk behaviors after PEPSE completion
  - Among the remaining 3 men who seroconverted after taking PEPSE no information was reported regarding the PEPSE regimen prescribed, adherence to PEPSE, delay in PEPSE initiation or timing of HIV-positive results

# Tenofovir-Emtricitabine (TDF-FTC) plus Raltegravir for PEPSE in MSM

- 100 participants enrolled at Fenway Health
- 98% male, 83% MSM, mean age 33 yrs
- Prescribed TDF-FTC plus raltegravir for PEPSE
- 85/100 had 3-months follow-up
- None were HIV infected
- 57% finished the regimen as prescribed
- Comparable to historic controls (AZT-3TC or TDF-FTC + PI/r)
- Biggest limitation = missed second dose of raltegravir by 27%
- Well tolerated and fewer side effects than historic controls

*Mayer K, et al. J Acquir Immune Defic Syndr. 2012;59(4):354-359.*

# Considerations of PEP

- Adherence
- Side effects
- Dosage
- Missed doses
- Prescribed medication
- Other drugs



# Potential risks of offering PEP

- Toxicity
- Resistance
- Service Provision
- Cost
- Impact on sexual behaviour

# PEPSE and sexual behaviour

- UK nonoPEP Study:
  - 77% reported reduced high-risk activity with casual partners
- Brazil:
  - Baseline: 57% reported high-risk behaviour; 24 months: 40%
- San Francisco:
  - 74% reported reduction in high-risk behaviour; 10% reported an increase

Benn et al, BHIVA 2006; Schecter et al, JAIDS 2004; Roland et al, CID 2005

# BASHH PEPSE Guidelines 2015



Table 4 Situations when post-exposure prophylaxis (PEP) is considered (IV, grade C)

| | Source HIV status | | | |
|---|---|---|---|---|
| | HIV-positive | | Unknown from high prevalence group/area* | Unknown from low prevalence group/area |
| | Viral load detectable | Viral load undetectable | | |
| Receptive anal sex | Recommend | Not recommended | Recommend | Not recommended |
| Insertive anal sex | Recommend | Not recommended | Consider† | Not recommended |
| Receptive vaginal sex | Recommend | Not recommended | Consider† | Not recommended |
| Insertive vaginal sex | Recommend | Not recommended | Consider† | Not recommended |
| Fellatio with ejaculation‡ | Consider | Not recommended | Not recommended | Not recommended |
| Fellatio without ejaculation‡ | Not recommended | Not recommended | Not recommended | Not recommended |
| Splash of semen into eye | Consider | Not recommended | Not recommended | Not recommended |
| Cunnilingus | Not recommended | Not recommended | Not recommended | Not recommended |
| Sharing of injecting equipment | Recommended | Not recommended | Consider | Not recommended |
| Human bite§ | Not recommended | Not recommended | Not recommended | Not recommended |
| Needlestick from a discarded needle in the community | | | Not recommended | Not recommended |

Not recommended

*High prevalence groups within this recommendation are those where there is a significant likelihood of the source individual being HIV-positive. Within the UK at present, this is likely to be men who have sex with men and individuals who have immigrated to the UK from areas of high HIV prevalence (particularly sub-Saharan Africa)
†More detailed knowledge of local prevalence of HIV within communities may change these recommendations from *consider* to *recommended* in areas of particularly high HIV prevalence
‡PEP is not recommended for individuals receiving fellatio i.e. inserting their penis into another's oral cavity
§A bite is assumed to constitute breakage of the skin with passage of blood

factors PEPSE *should not* be prescribed when the exposure is an undetectable plasma viral load.[102] In light of this evidence

# EACS PEP Guidelines


- Rapid testing of the source person for HCV and HIV (if HIV-status unknown) recommended
- If source person HIV-positive on ART, order resistance testing if HIV-VL detectable
- Individualise PEP according to the source's treatment history and previous resistance tests
- **For sexual exposure, if HIV-positive source has documented undetectable HIV-VL, PEP is no longer recommended**
- PEP to be started ideally < 4 hours after the exposure and no later than 48/72 hours
- Duration of PEP: 4 weeks
- PEP regimens: TDF/FTC (alternative: ZDV/3TC) + RAL bid, or + DRV/r qd or + LPV/r bid. TDF/FTC + DTG qd may be also considered as an alternative.

- Full sexual health screen in case of sexual exposure
- Follow-up: HIV serology + HBV and HCV, pregnancy test (women) within 48 hours of exposure
- Re-evaluation of PEP indication by HIV expert within 48-72 hours
- Assess tolerability of PEP regimen
- Transaminases, HCV-PCR and HCV serology at month 1 if source person HCV-positive (observed or suspected)
- Repeat HIV serology after 2 and 4 months, syphilis serology after 1 month if sexual exposure

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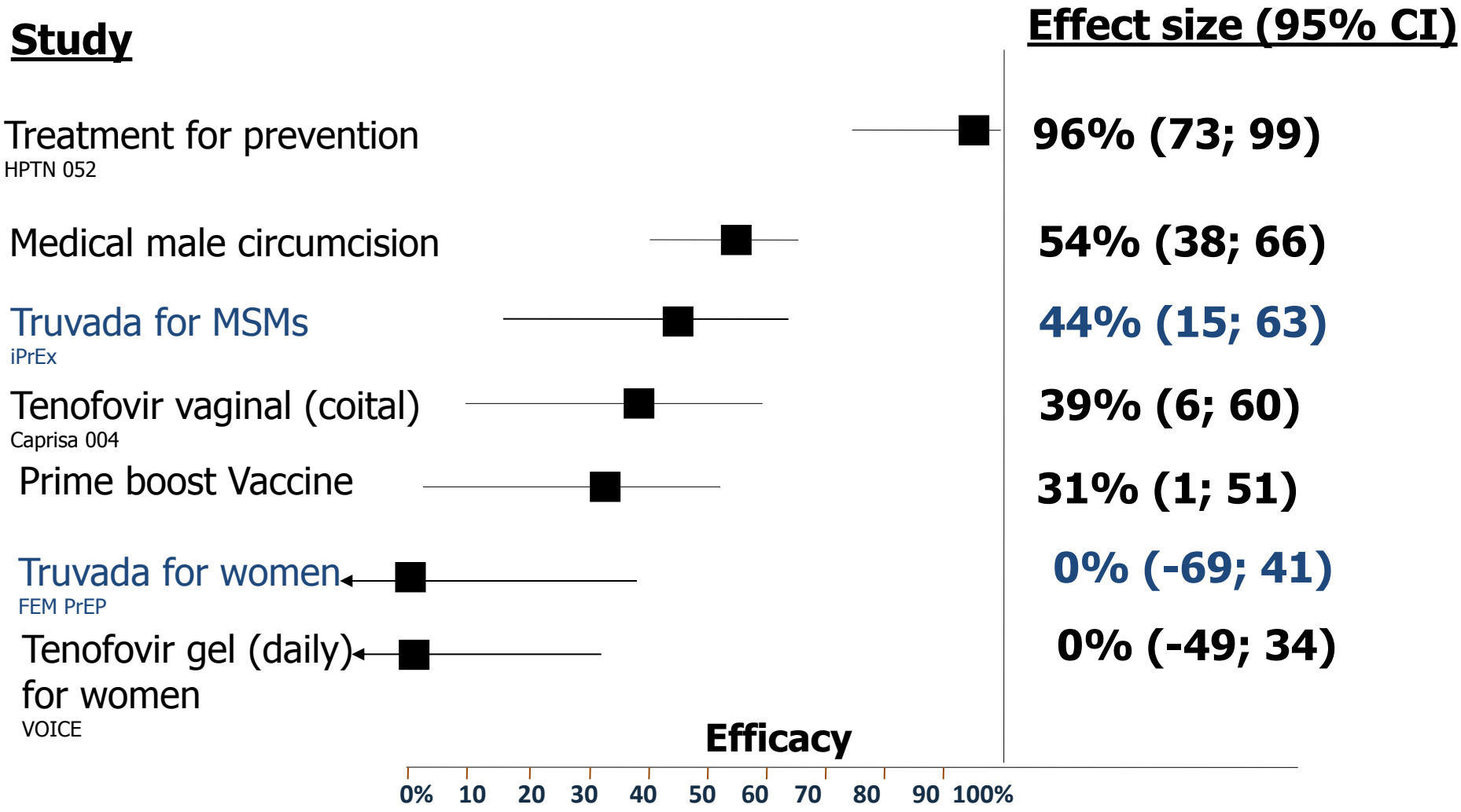
## Assess need for PrEP!

# Pre Exposure Prophylaxis
# PrEP

# Previous Prevention Trials



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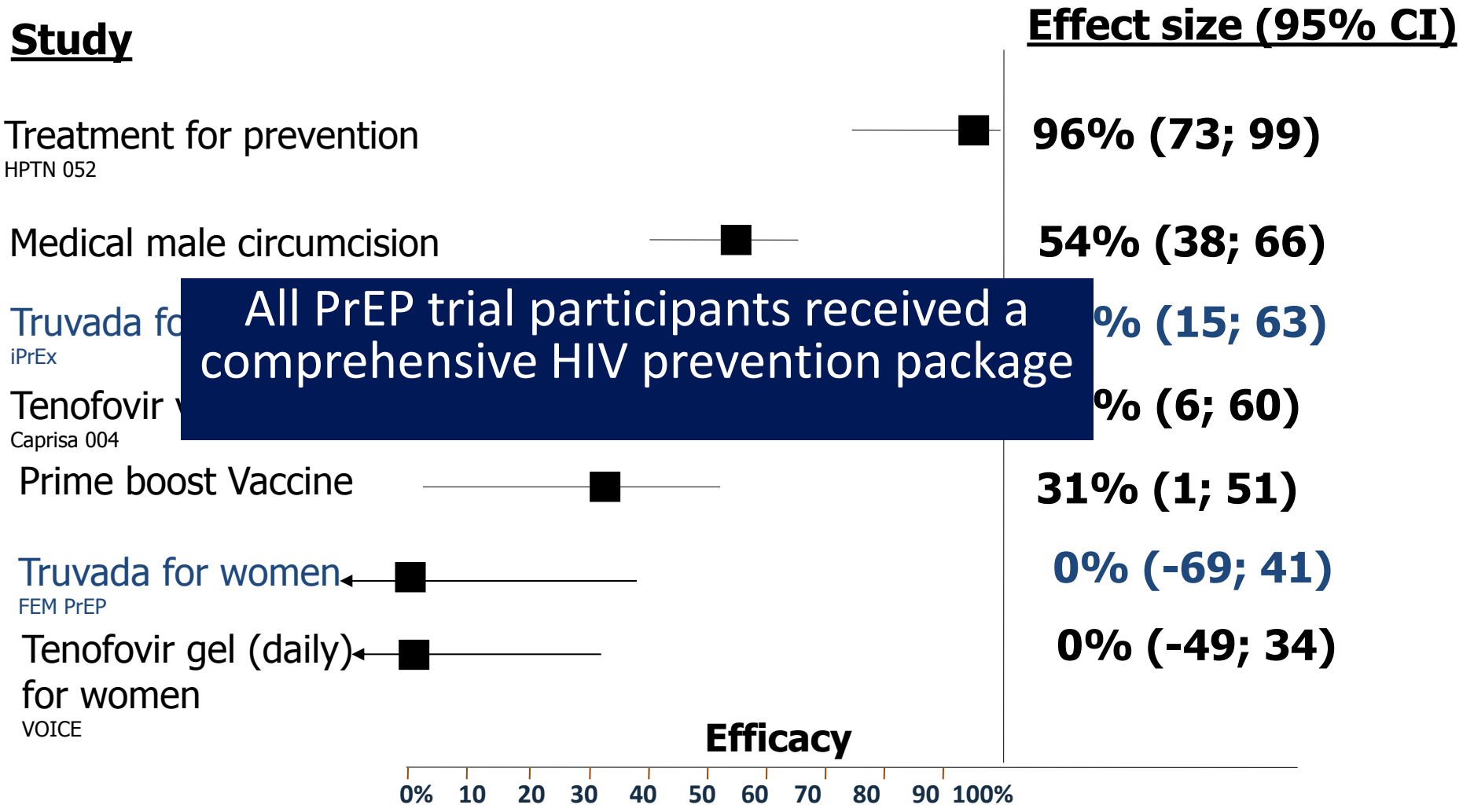

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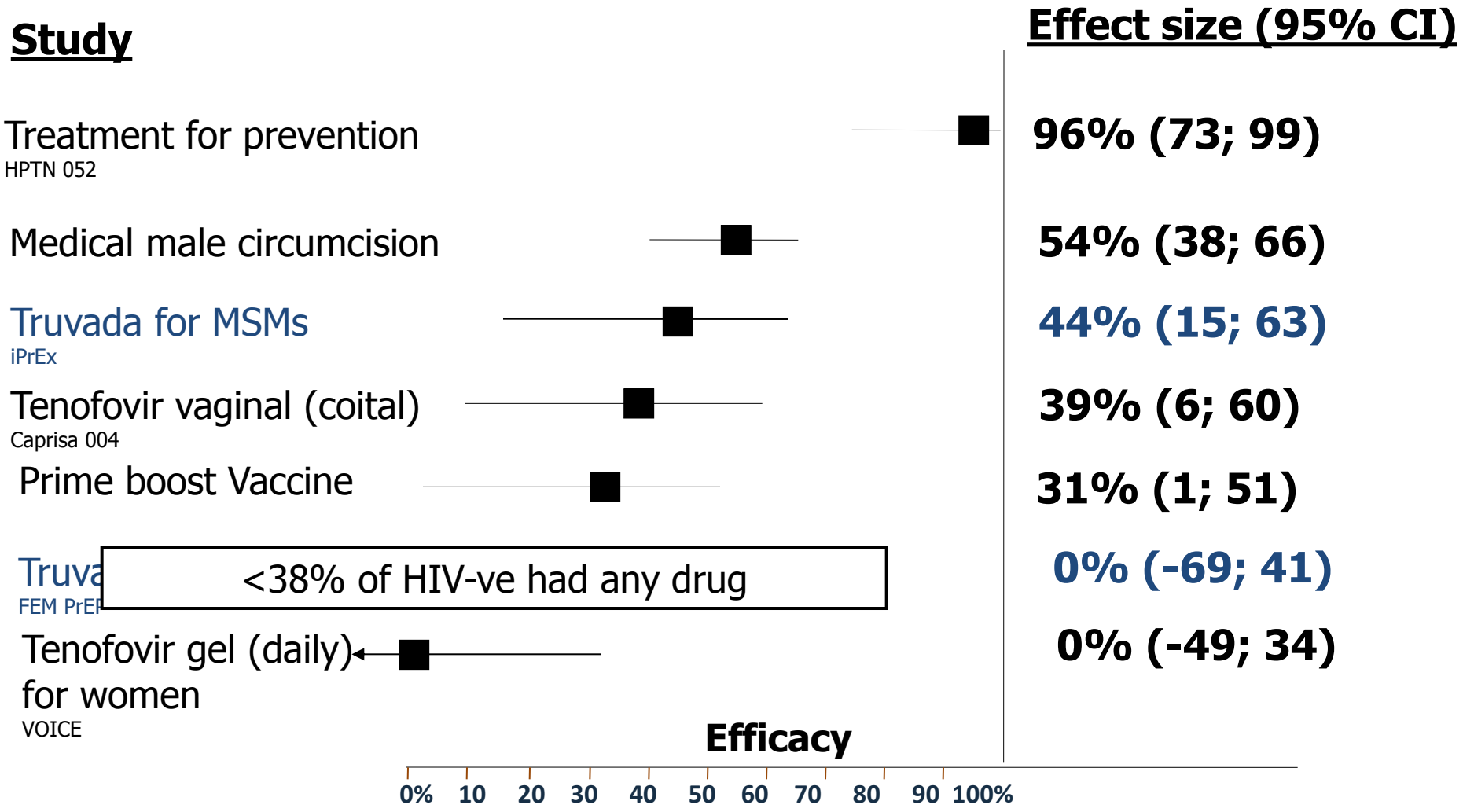
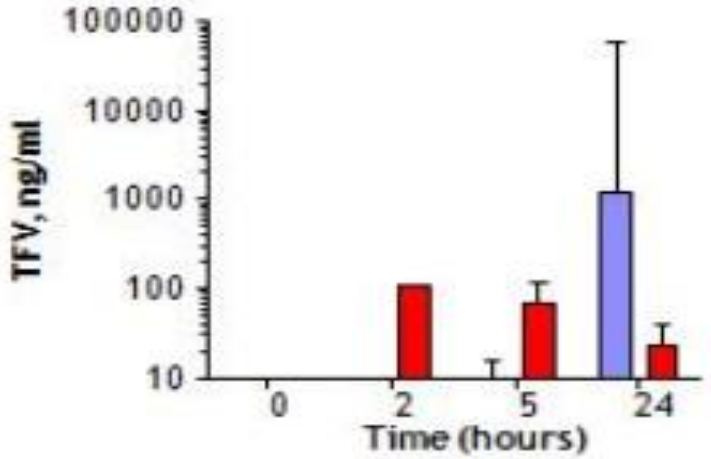


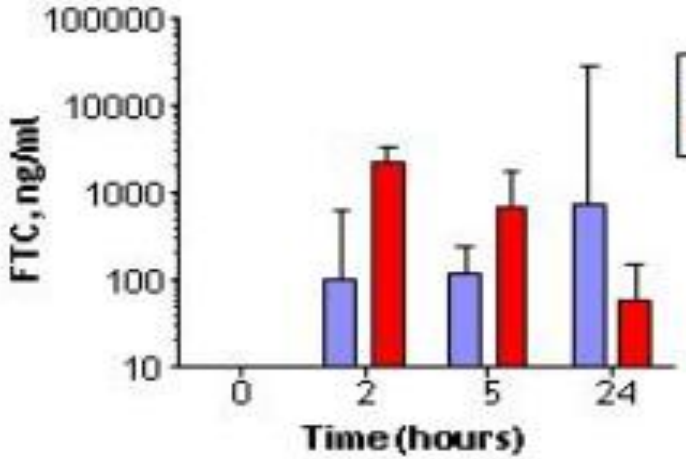
# How do we know oral PrEP is effective?

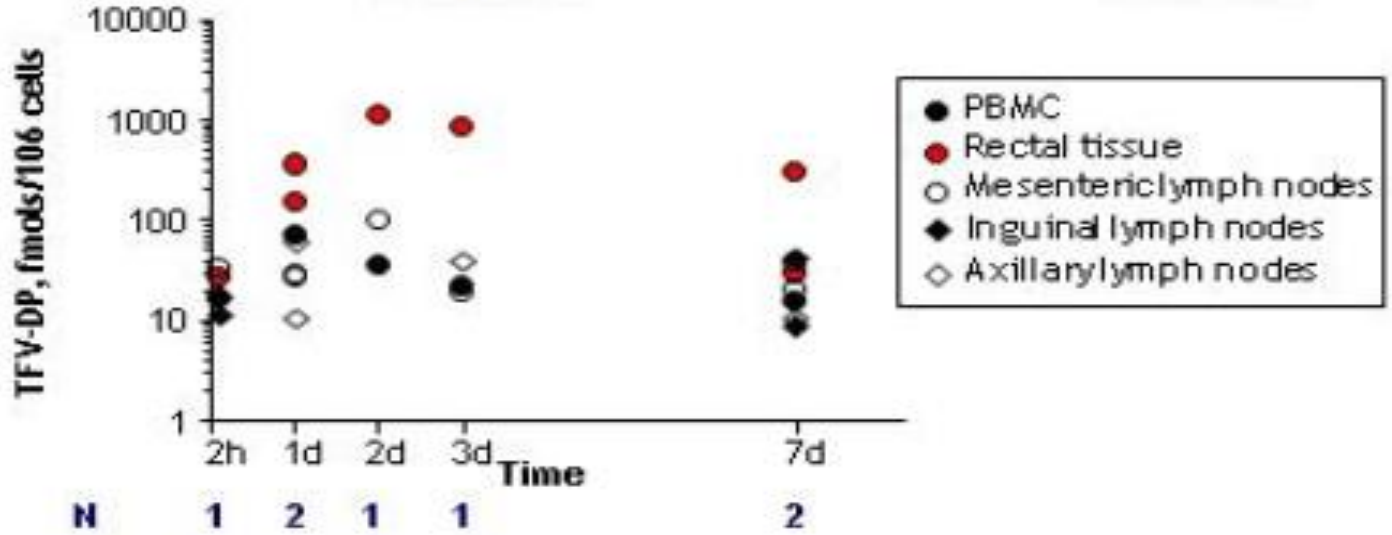
1. Animal studies
2. Major PrEP trials
   - iPrEx
   - PROUD
   - Ipergay

# 1. Animal Studies

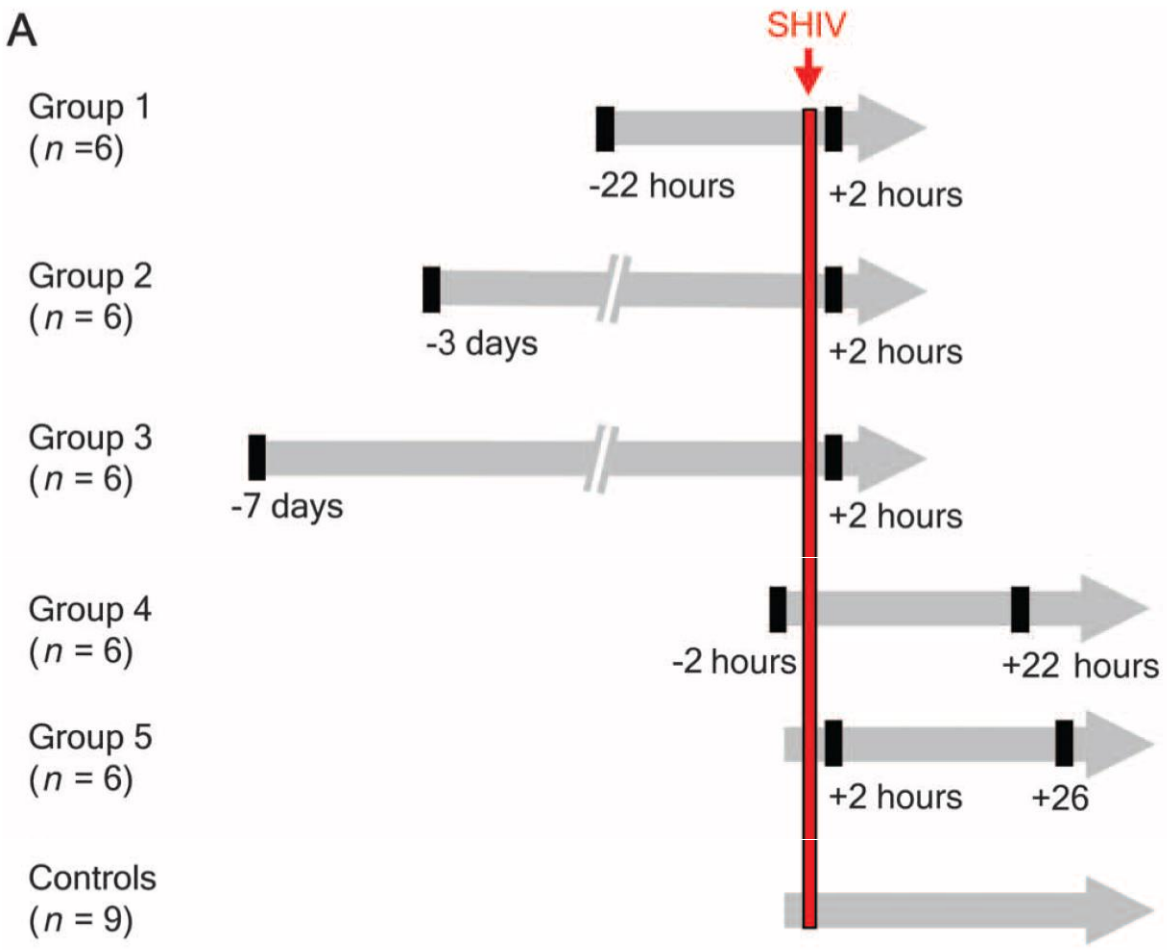
## Local and systemic drug concentrations after oral administration of Truvada



# Efficacy of intermittent PrEP with Truvada in the repeat low-dose macaque model: design




Slides courtesy of Gerardo Garcia-Lerma*1 CROI 2010 Paper # 83

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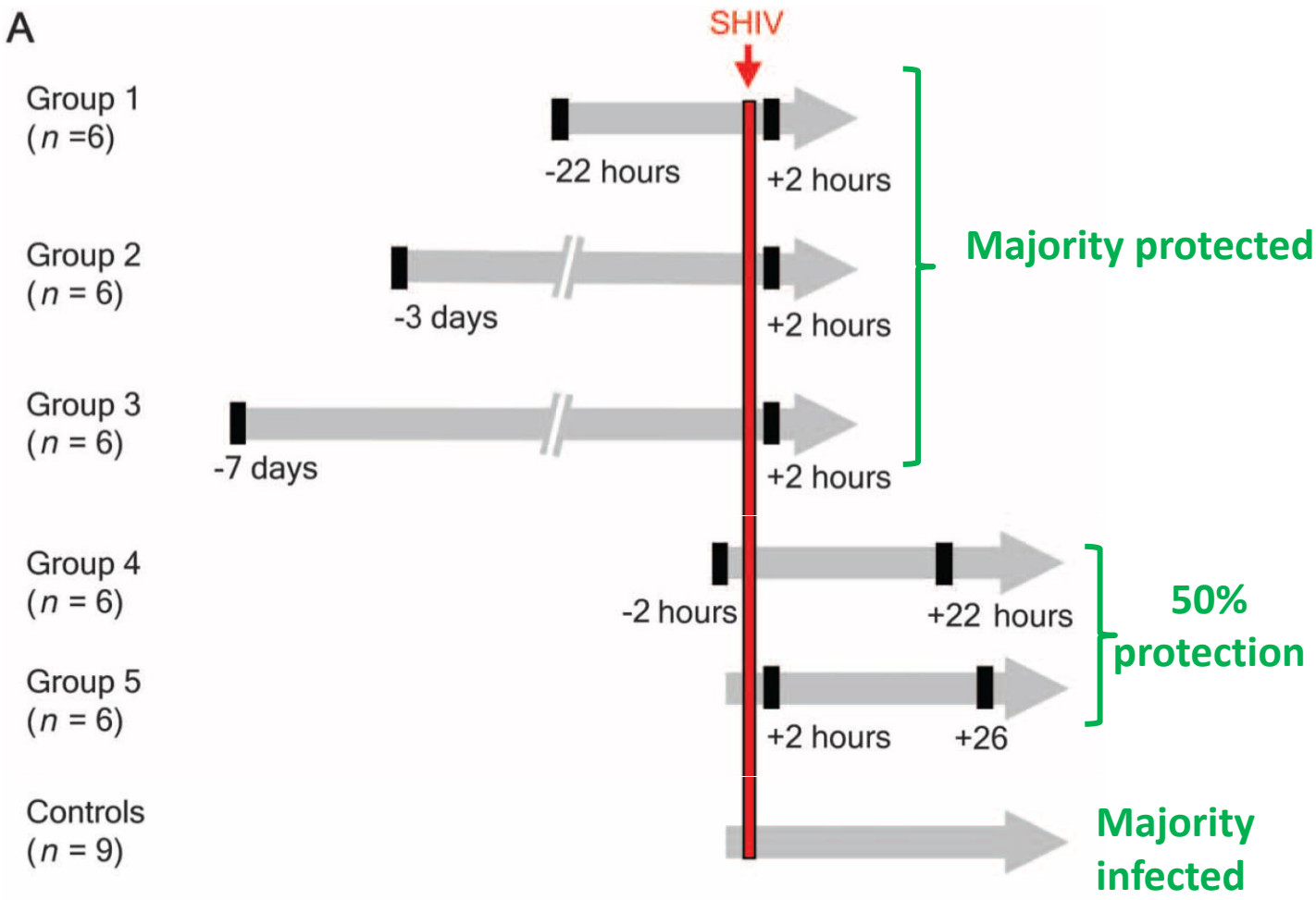


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# 2. iPrEx


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 30, 2010 VOL. 363 NO. 27

## Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

Robert M. Grant, M.D., M.P.H., Javier R. Lama, M.D., M.P.H., Peter L. Anderson, Pharm.D., Vanessa McMahan, B.S., Albert Y. Liu, M.D., M.P.H., Lorena Vargas, Pedro Goicochea, M.Sc., Martín Casapía, M.D., M.P.H., Juan Vicente Guanira-Carranza, M.D., M.P.H., Maria E. Ramirez-Cardich, M.D., Orlando Montoya-Herrera, M.Sc., Telmo Fernández, M.D., Valdilea G. Veloso, M.D., Ph.D., Susan P. Buchbinder, M.D., Suwat Chariyalertsak, M.D., Dr.P.H., Mauro Schechter, M.D., Ph.D., Linda-Gail Bekker, M.B., Ch.B., Ph.D., Kenneth H. Mayer, M.D., Esper Georges Kallás, M.D., Ph.D., K. Rivet Amico, Ph.D., Kathleen Mulligan, Ph.D., Lane R. Bushman, B.Chem., Robert J. Hance, A.A., Carmela Ganoza, M.D., Patricia Defechereux, Ph.D., Brian Postle, B.S., Furong Wang, M.D., J. Jeff McConnell, M.A., Jia-Hua Zheng, Ph.D., Jeanny Lee, B.S., James F. Rooney, M.D., Howard S. Jaffe, M.D., Ana I. Martinez, R.Ph., David N. Burns, M.D., M.P.H., and David V. Glidden, Ph.D., for the iPrEx Study Team*

2007-2011 NIH interventional double-blind, placebo controlled trial

TRUVADA PREP in sexually active MSM & TG

The study enrolled 2,499 HIV uninfected participants in six countries

# iPrEx Results

| Prevention of HIV acquisition from PREP | |
|---|---|
| | TRUVADA |
| All participants | 44% |
| Took 4/7 days | 96% |
| Took 7/7 days | 99% |

Daily TRUVADA prevents HIV infection in MSM/TGW who take it

Could be used as part of broader prevention strategy for HIV in high risk groups

Public Health England

PROUD

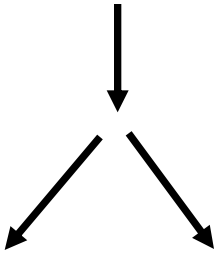
MRC Clinical Trials Unit

# 2. Pragmatic Open-Label Randomised Trial of Pre-Exposure Prophylaxis: the PROUD study

- **To determine whether PrEP worked as well as iPrEx in this setting (44% reduction in HIV)**
- **Possibility that effectiveness might be less in real world**

# PROUD Pilot

MSM reporting UAI last/next 90 days



Truvada **NOW**

**N= 267**

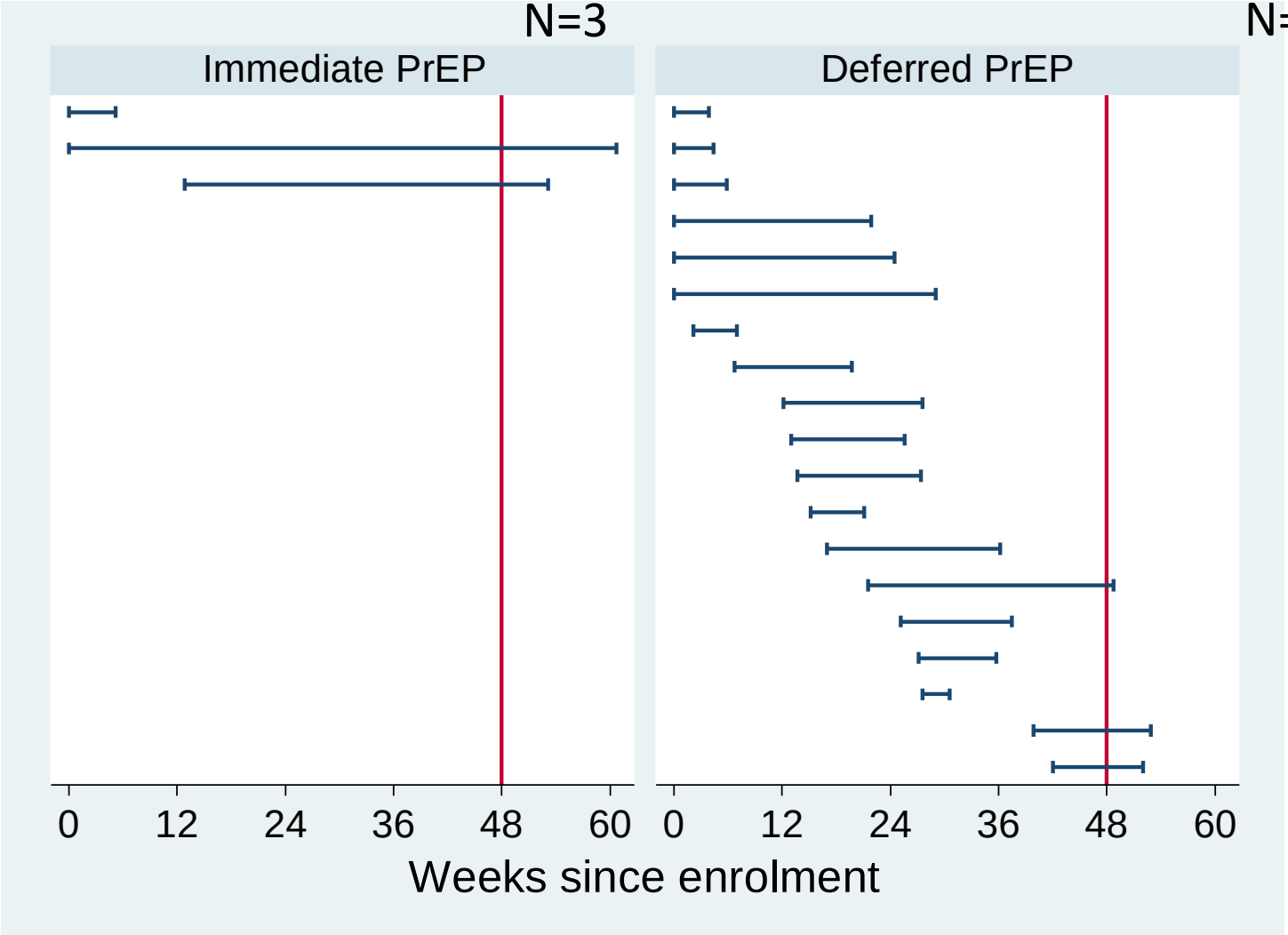
Truvada **AFTER 12M**

**N=256**

Follow **3 monthly** for up to 24 months

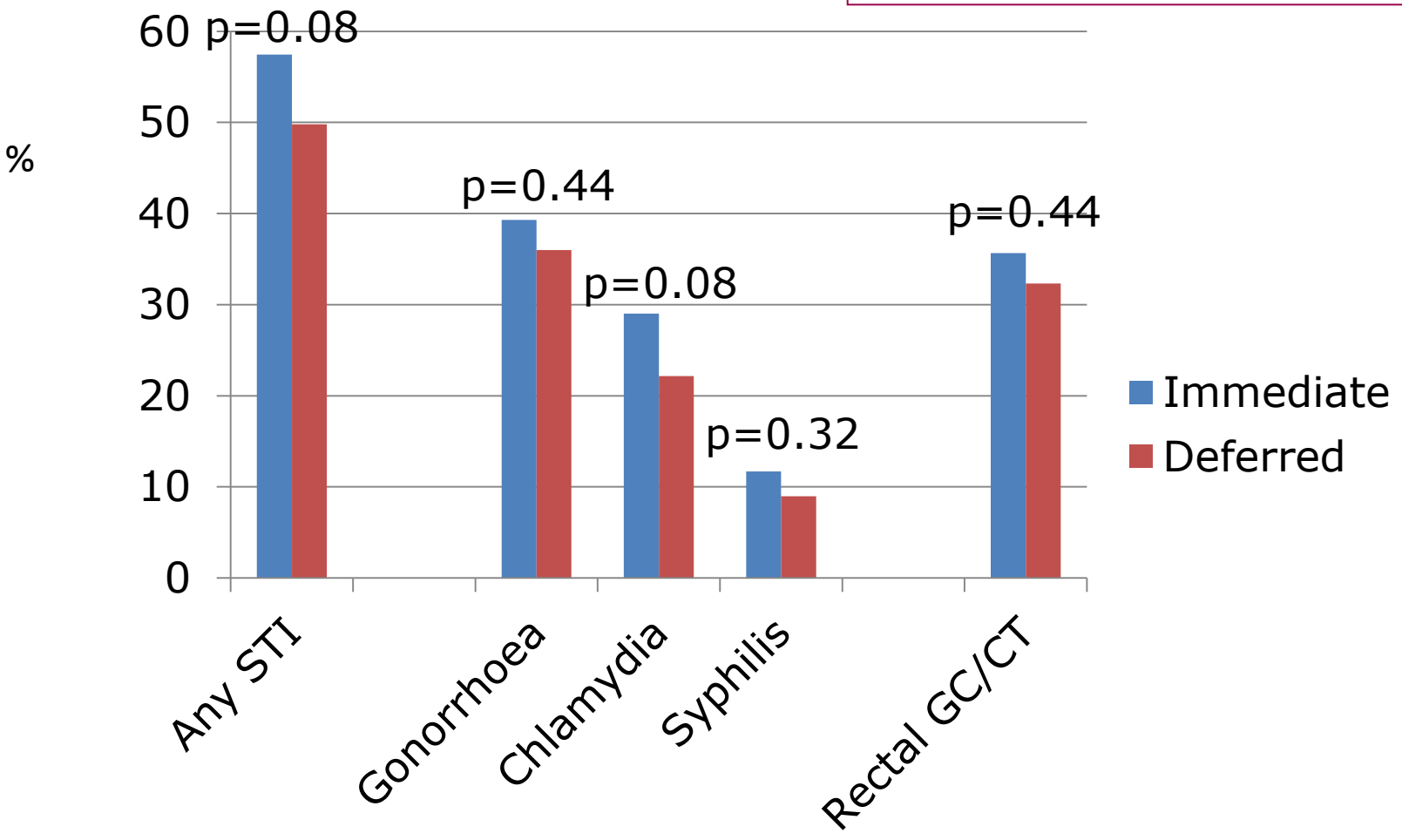
Main endpoints in Pilot: HIV infection in first 12 months

# PROUD: new HIV infections



# PROUD: STIs

**Caveat**
Number of screens differed between the groups:
e.g. Rectal gonorrhoea/chlamydia 974 in the IMM group and 749 in the DEF



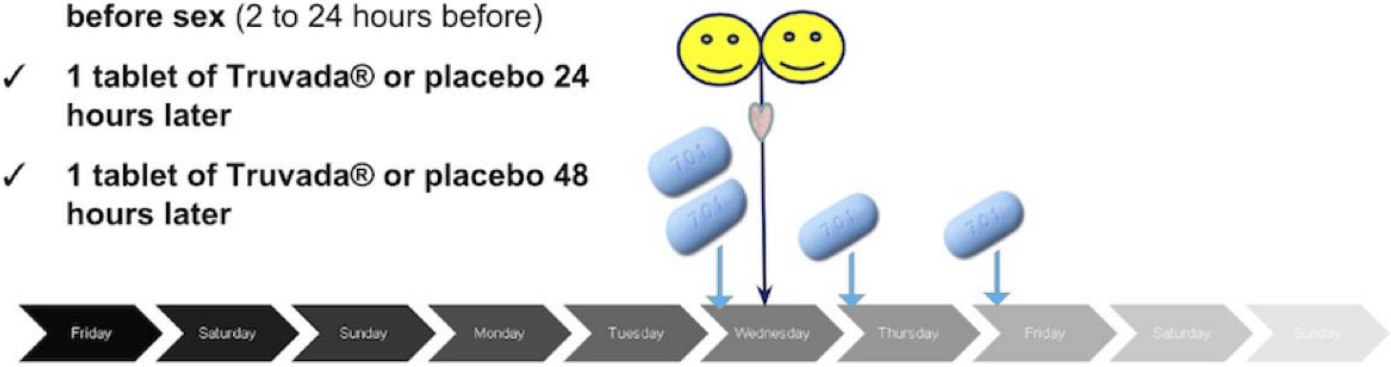
# PROUD: conclusions

- Daily PrEP with Truvada was highly effective in preventing HIV infection – 86% reduction
- HIV incidence was much higher than predicted in the deferred arm
  - despite extensive use of PEP in the deferred period
- Concerns about PrEP being less effective in the real world unfounded
- There was no difference in STIs, which were common in both groups

# 3. Ipergay

## Ipergay : Event-Driven iPrEP

- ✓ **2 tablets of Truvada® or placebo before sex** (2 to 24 hours before)
- ✓ **1 tablet of Truvada® or placebo 24 hours later**
- ✓ **1 tablet of Truvada® or placebo 48 hours later**




anrs France Recherche Nord & sud Sida-hiv Hépatites
Agence autonome de l'Inserm

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de l'Exposition aux Risques
avec et pour les Gays

www.ipergay.fr

# Study Design

**Double-Blinded Randomized Placebo-Controlled Trial**

- HIV negative high risk MSM
- Condomless anal sex with ≥ 2 partners within 6 m

→ **TDF/FTC before and after sex**
**N=199**

→ **Placebo before and after sex**
**N=201**

- Follow-up visits: month 1, 2 and every two months thereafter

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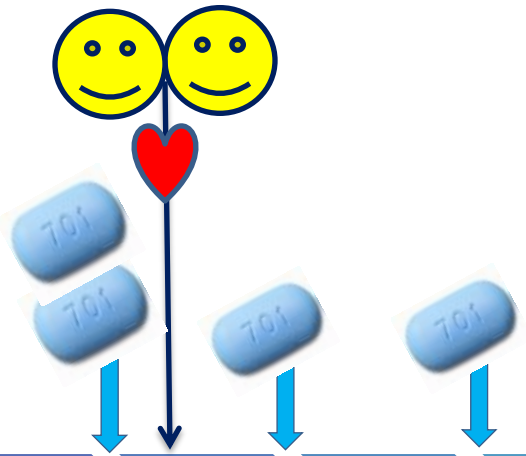
# Ipergay : Event-Driven iPrEP

- ✓ 2 tablets (TDF/FTC or placebo) 2-24 hours before sex
- ✓ 1 tablet (TDF/FTC or placebo) 24 hours later
- ✓ 1 tablet (TDF/FTC or placebo) 48 hours after first intake



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# Ipergay clinical trial results

- 400 participants with a mean follow-up of 13 months

- 16 subjects infected
  **14 in placebo arm** (incidence: 6.6 per 100 PY),
- **2 in TDF/FTC arm** (incidence: 0.91 per 100 PY)

- **86% relative reduction in the incidence of HIV-1 (95% CI: 40-98, p=0.002)**

- NNT for one year to prevent one infection : 18
- 133 STIs diagnosed in the TDF/FTC arm

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# Conclusions

- "On Demand" oral PrEP with TDF/FTC was very effective with a 86% (95% CI: 40-99) reduction in HIV-incidence
- Adherence was good
- Safety of "on demand" TDF/FTC was overall similar to placebo except for gastrointestinal AEs
- Intermittent PrEP may reduce longer term toxicity

# Regimens

- PROUD
  - Daily TRUVADA
  - Takes 14 days to reach steady state
  - Missing 5 doses makes PrEP less effective
- IPERGAY
  - ON DEMAND TRUVADA
  - 2 doses between 2-24 hours before sex
  - 1 dose at 24 hours
  - 1 dose at 48 hours

# Missed Doses

**PROUD**

- Take as soon as remember if within 12 hours. May mean 2 doses in 1 day
- Remind if misses 5 days drug levels fall to concerning level
- Discuss resistance

**IPERGAY**

- If not taken double dose before sex, as soon as possible: should take within 12 hours of sex
- If they missed the second dose/third dose they should take TRUVADA if they are within 3 days of the missed dose

# Case Report: Multiclass Resistant HIV Infection Despite High Adherence to PrEP

- 43-yr-old MSM acquired multiclass resistant HIV-1 infection following 24 mos of oral once-daily TDF/FTC PrEP
- Pharmacy records, blood concentration analyses, and clinical history support recent and long-term adherence to PrEP
- PrEP failure likely result of exposure to PrEP-resistant, multiclass resistant HIV-1 strain

| Drug Class | Mutations Detected on Day 7 Following p24-Positive Test | Estimated Fold-Change in $IC_{50}$ or Change in Response (Drug) |
|---|---|---|
| NRTI | 41L, 67G, 69D, 70R, 184V, 215E | 1.9x (ABC), 61x (3TC), 38x (FTC), 1.3x (TDF) |
| NNRTI | 181C | 43x (NVP) |
| PI | 10I | No relevant change |
| INSTI | 51Y, 92Q | Reduced (RAL), resistant (EVG), reduced (DTG) |

Knox DC, et al. CROI 2016. Abstract 169aLB.

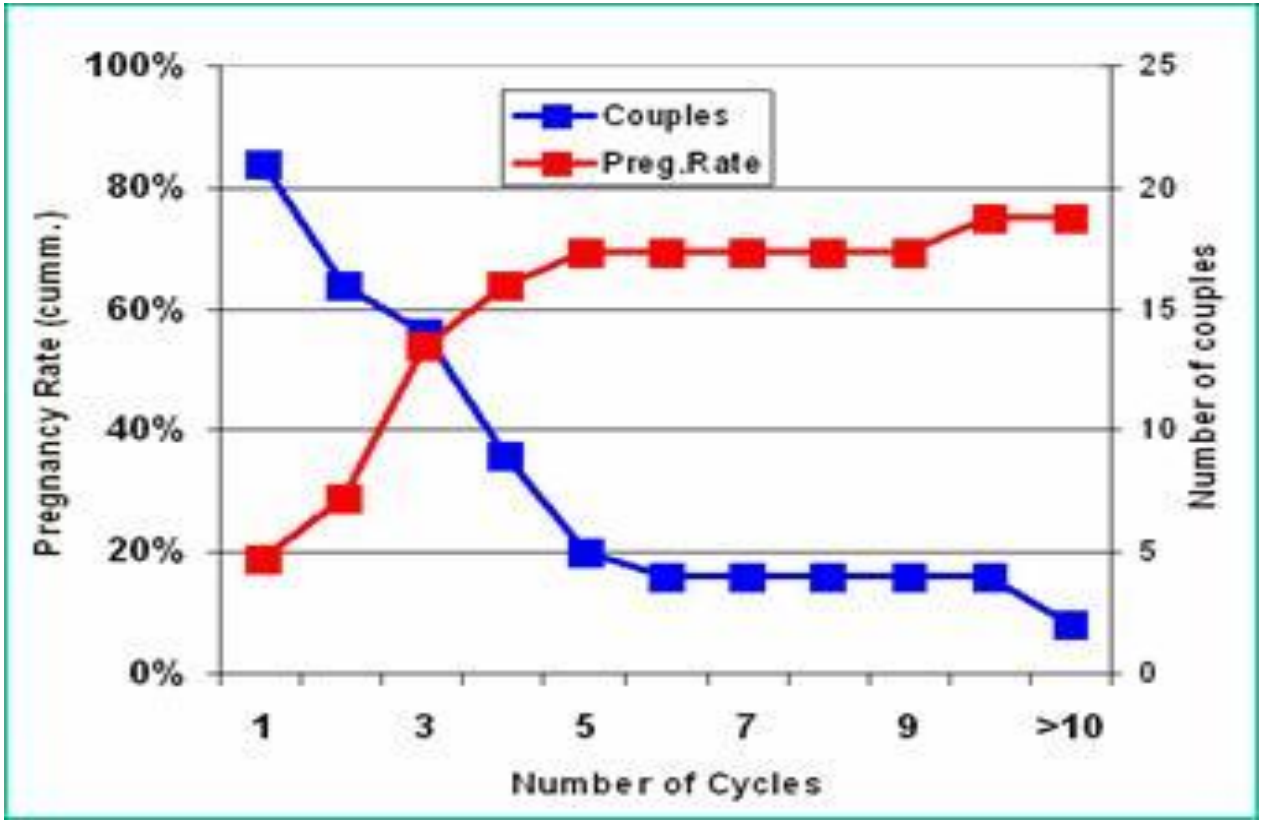
Slide credit: clinicaloptions.com

# PrEP assumptions

- Adherence
- May have periods not requiring PrEP
- Patients need to be aware not protective against STIs (hep C)
- Require regular HIV tests
- Discordant partners of HIV+ on treatment may need (HPTN-052)

- **<u>PrEP is not recommended in</u>**
  - Unable to tolerate TRUVADA
  - Hepatitis B infection

# PrEP-C with Tenofovir
# n=22

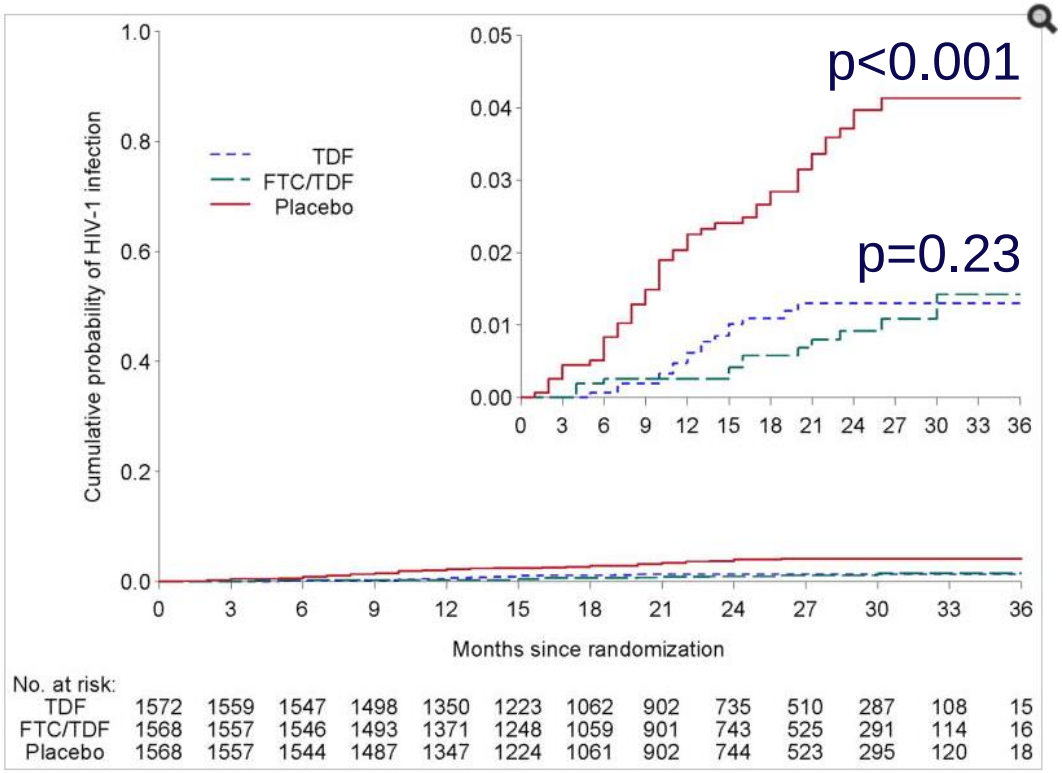



All women HIV negative 3/12 after last exposure
Maximum attempts 12*
Fertility investigations after 6 attempts*

*Vernazza, et al . 4th IAS, 2007*
* Personal communication from P Vernazza

# Efficacy in Partners PrEP[1]

**Table 2: Kaplan-Meier curve for the primary modified ITT analysis**




Heterosexual study in Kenya and Uganda.
N=4758.
38% HIV neg partners were women.

| | HIV+ |
|---|---|
| Placebo | 52 |
| 75% TDF/FTC | 13 |
| 67% TDF | 17 |

31% vs 81% detectable TNF at seroconversion visit in HIV+ vs HIV-

1. Baeten JR et al, NEJM, 2012.

Funding: Bill & Melinda Gates

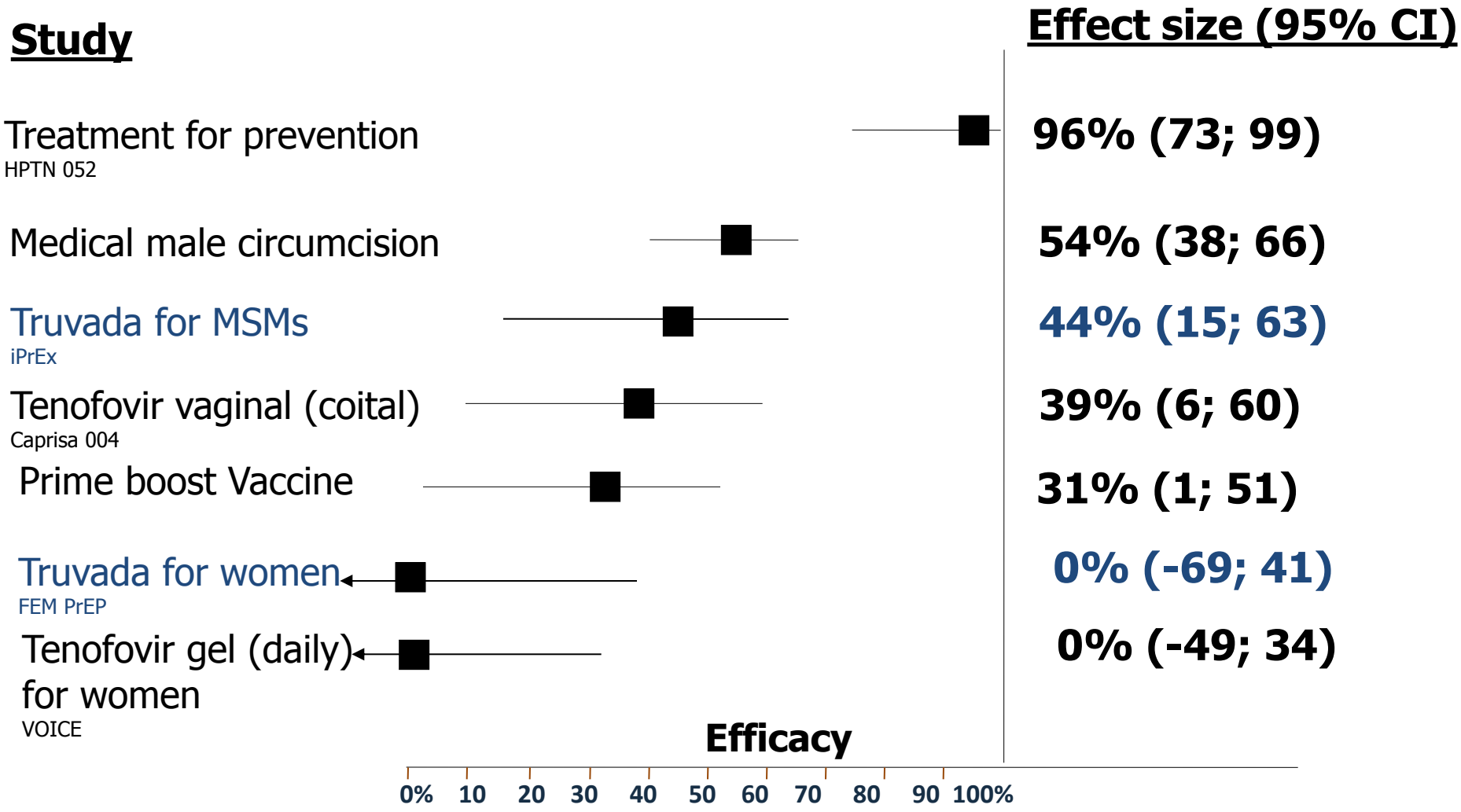
# Safety in Partners PrEP [1]

| | FTC/TDF | TDF | Placebo |
|---|---|---|---|
| Neutropenia | | | |
| Grade 1 or 2 | 15% | 2% | 2% |
| Grade 3 or 4 | 4% | 2% | 2% |
| Serum creatinine | | | NS |
| phosphorus abnormalities | | | NS |
| SAEs | | | NS |
| Deaths | | | NS |

Modest GI and fatigue in active arms during month 1.

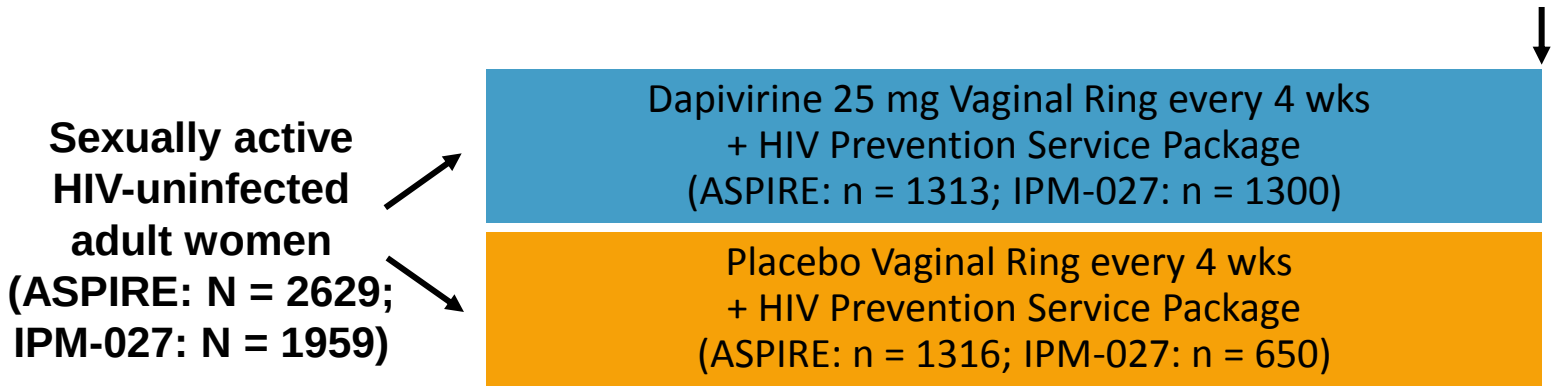
1. Baeten JR et al, NEJM, 2012.

# Previous Prevention Trials



# MTN-020/ASPIRE & IPM-027: Dapivirine Vaginal Ring for HIV Prevention in Women

- Silicone elastomer vaginal matrix ring containing NNRTI dapivirine 25 mg; ring replaced every 4 wks
- Randomized, double-blind phase III trials
  - MTN-020/ASPIRE[1,2]: Malawi, South Africa, Uganda, Zimbabwe
  - IPM-027 (The Ring Study)[3]: South Africa, Uganda
  - Primary endpoints: efficacy and safety




1. Baeten JM, et al. CROI 2016. Abstract 109LB.
2. Baeten JM, et al. N Engl J Med. 2016;[Epub ahead of print].
3. Nel A, et al. CROI 2016. Abstract 110LB.

Slide credit: clinicaloptions.com

# MTN-020/ASPIRE & IPM-027: Efficacy and Safety of Dapivirine Vaginal Ring

- Efficacy for HIV prevention similar in both studies
- No clinically relevant safety differences between arms

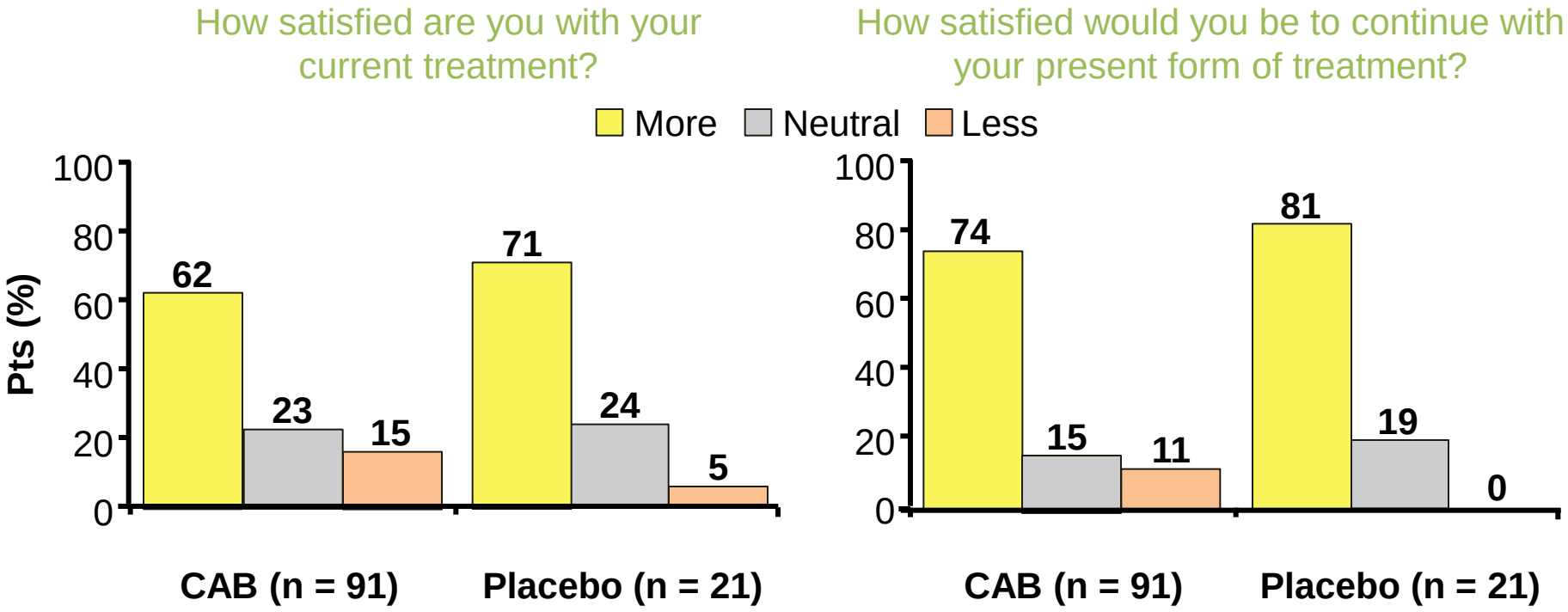
| Outcome | ASPIRE[1,2]: 15 Sites | | ASPIRE[1,2]: 13 Sites* | | The Ring Study[3] | |
|---|---|---|---|---|---|---|
| | Dapivirine (n = 1308) | Placebo (n = 1306) | Dapivirine (n = 1198) | Placebo (n = 1197) | Dapivirine (n = 1300) | Placebo (n = 650) |
| HIV infections, n | 71 | 97 | 54 | 85 | 77 | 56 |
| HIV incidence (per 100 PYs) | 3.3 | 4.5 | 2.8 | 4.4 | 4.1 | 6.1 |
| **HIV protection efficacy, %** | **27 (*P* = .046)** | | **37 (*P* = .007)** | | **31 (*P* = .040)** | |
| ▪ **Among women older than 21 yrs** | - | | **56 (*P* < .001)** | | **37 (*P* = .10)** | |

*Excludes 2 sites with low adherence.

1. Baeten JM, et al. CROI 2016. Abstract 109LB.
2. Baeten JM, et al. N Engl J Med. 2016;[Epub ahead of print].
3. Nel A, et al. CROI 2016. Abstract 110LB.

# ÉCLAIR: Patient Satisfaction With IM Therapy vs Oral Phase

- Pt satisfaction assessed by questionnaire at Wk 18 of IM treatment; asked pts to compare satisfaction of current IM vs past oral therapy[1]




- In separate macaque study, CAB LA conferred 88% protection (21/24 animals) against IV exposure to SIVmac251; results may be relevant to humans who inject drugs[2]

1. Markowitz M, et al. CROI 2016. Abstract 106. 2. Andrews CD, et al. CROI 2016. Abstract 105. Reproduced with permission.

# HPTN-069/A5305: Maraviroc-Based PrEP for MSM 48w

- Randomized, double-blind phase II trial
  - Primary endpoints: safety (grade ≥ 3 AEs), tolerability (rate/time to discontinuation of study drug)


67 grade 3/4 AEs; rates similar across arms

9% discontinued study drug early

Rates of study drug discontinuation (*P* = .6) and time to permanent discontinuation (*P* = .6) similar across arms

5 new HIV infections occurred during study for annual incidence rate of 1.4% (95% CI: 0.8-2.3);

4xMVC, 1xMVC/TDF; all R5 tropic; no transmitted drug resistance

*Gulick R, et al. CROI 2016. Abstract 103.*

# I Want PrEP Now

Home | About PrEP | How To Get PrEP | Buy PrEP Now | PrEP Abroad | News | About Us / Donate

## Buy PrEP Now

### Where to buy PrEP online, now, in the UK

So far we have independently verified 4 different companies who reliably sell PrEP that you can trust. For full details on our independent verification process, click here.


**United Pharmacies UK** (£44 per month) Buy Now

United Pharmacies UK is our personally recommended supplier of PrEP, you do not need to upload a prescription after purchasing and they have some of the cheapest prices on the internet. In addition to independently verifying their product, we also use United Pharmacies to buy PrEP ourselves. The only minor issue is that due to running out of stock, orders occassionally have a delay of around 1 - 2 weeks.

1 months supply = £45.79 per month.
3 months supply = £41.69 per month, (£125.07 in total).
Delivery to the UK costs £6.75 and takes 7 - 14 business days.

**All Day Chemist** (£42 per month) Buy Now

All Day Chemist also does not ask you to upload a prescription to buy PrEP. Their website operates in US dollars but w
converted the prices below to make them easier to compare. We have had many anecdotal reviews of All Day Chemis
are a popular choice for many PrEP users. Again, we have fully verified their sales process and reliability of their drugs
especially with All Day Chemist, see below for information on rare but potential import taxes.

1 month supply = £36.26
3 months supply = £108.78
Delivery to the UK costs £16.45 and takes 7 - 14 days

**In House Pharmacy** (£78 per month) Buy Now

In House Pharmacy does not ask you to upload a prescription for PrEP but their prices are higher than most other selle
the others we have fully verified that they are a reliable supplier of PrEP.

1 month supply = £83.93
3 months supply = £234.63
Delivery to the UK is free and takes 10 - 21 days

**Aids Drugs Online** (£59 per month) Buy Now

We have ourselves made a purchase from Aids Drugs Online with no problems. However they do require you to upload
prescription before they dispatch your order. See here for more info on prescriptions. Their website also operates in US
and they ship from Singapore. ADO have the most paperwork out of any of the sellers listed, which takes 2 - 3 busines
process before they will dispatch your order.

Remember - Aids Drugs Online will not dispatch your order unless you have a prescription!

1 month supply = $104.98 (US dollars) (around £68)
3 month supply = $260.48 (US dollars) (around £168.40)
Delivery costs $15.00 and takes 7 - 14 business days after your prescription has been checked, which takes 2 - 3 bus

### Our Verification Process

Many people including doctors question if you can trust medications that are bought online. If you haven't placed an o
before you may not trust the company or be able to tell if they are operating legitimately. You may also not have the me
testing the drugs you buy from them to make sure that they are genuine and working as they should.

One of the key objectives of this website is to try to assist with the above concerns. All of the PrEP that we list on this w
made by Cipla and has been officially approved by the United States Food and Drug Administration (US FDA). We do
PrEP supplier until we have had a first hand account from someone we know (or even tested personally ourselves) tha
process was smooth, easy and reliable. Then most importantly, the drugs purchased from each website have been tes
customer, by taking a test which detects the levels of active Tenvir-EM / Tenofovir (PrEP protection) in the blood. The 4
buy PrEP listed on this site have gone through and passed this process. These sellers are tried, tested and reliable. W
currently working with a few HIV organisations to establish some offical support and a statement on this.

There are numerous other online pharmacies that sell PrEP. If we have not listed them here then this is for the simple fact that we have not been able to personally verify them yet, not because we have had a negative experience with them.

If you have bought PrEP from any other websites and been able to verify your purchase with a blood test then please let us know on iwantprepnow.co.uk@gmail.com so that we investigate and add other reputable sites to our list for everyone else to use.

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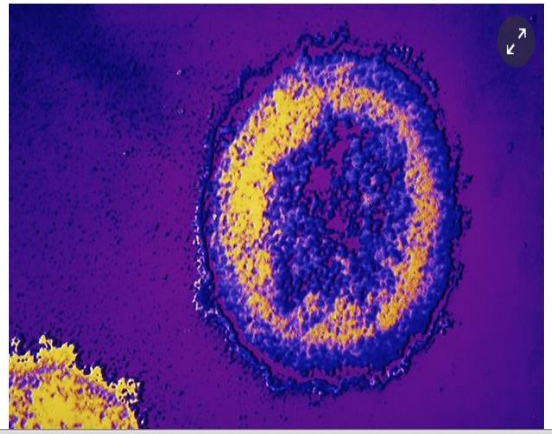
Aids and HIV

# NHS can fund 'game-changing' PrEP HIV drug, court says

NHS England to appeal against judgment ruling it has legal power to fund drugs that are highly effective in preventing HIV



Sarah Boseley Health editor

Tuesday 2 August 2016 11.07 BST

Shares 6,268

Save for later

Most popular

'Someone punched him

AUGUST 19 2016



# HIV prevention drug Truvada won't be subsidised in Australia

Rania Spooner

# EACS PrEP Guidelines


- PrEP can be used in adults at high-risk of acquiring HIV infection.
- Recommended in HIV-negative men who have sex with men (MSM) and transgender individuals who are inconsistent in their use of condoms with casual partners or with HIV-positive partners who are not on treatment
- A recent STD or use of post-exposure prophylaxis may be markers of increased risk for HIV acquisition.
- May be considered in HIV-negative heterosexual women and men who are inconsistent in their use of condoms and likely to have HIV positive partners who are not on treatment
- PrEP is a medical intervention that may not provide full protection against acquiring HIV, does not protect against other STDs and should be used in combination with other preventive interventions, including the use of condoms.
- PrEP should be supervised by a doctor, experienced with sexual health and use of HIV medicines, possibly as part of a shared care arrangement.
- The following procedures are recommended:
- Documented negative fourth generation HIV test prior to starting PrEP.
- During PrEP, this test should be repeated every 3 months, and PrEP should be stopped immediately in case of early clinical signs of HIV seroconversion or a positive HIV diagnostic test and the person referred for evaluation to an HIV unit.

# EACS PrEP Guidelines

- Before PrEP is initiated, HBV serology status should be documented.
- If HBsAg positive see Clinlical Management and Treatment of HBV and HCV Co-infection in HIV-positive Persons.
- Counsel that PrEP does not prevent other types of STD; screen for STD (including HCV) when starting PrEP and regularly during use of PrEP.
- Counsel that PrEP may impact renal and bone health
- Check renal function and bone mineral density according to guidelines on TDF use.
- Counsel that PrEP, like other prevention methods, only works when it is taken. Adherence counselling is recommended.
- Counsel that PrEP can be prescribed long term but that each consecutive PrEP prescription should be for a period of **maximum 3 months (90 tablets) to ensure appropriate monitoring.**
- PrEP regimen
- TDF/FTC 300*/200 mg 1 tablet qd. For MSM with high-risk sexual behavior PrEP may be dosed ‘on demand’ (double dose of drug 2-24 hours before each sexual intercourse, followed by two single doses of drug, 24 and 48 hours after the first drug intake). If dosed ‘on demand’, the total dose per week should not exceed 7 tablets.
- In certain countries TDF is labelled as 245 mg rather than 300 mg to reflect the amount of the prodrug (tenofovir disoproxil) rather than the fumarate salt (tenofovir disoproxil fumarate).

# Summary PEP and PrEP

- Assessment of risk and engagement in care
- Part of risk reduction strategy
- Highly effective
- Regimens well tolerated
- Newer agents/methodologies being assessed for PrEP
- Studies ongoing in heterosexual populations
- Clear guidelines on management and follow-up
- Essential part of HIV and Sexual Health Care