

Effectiveness of PrEP

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Content

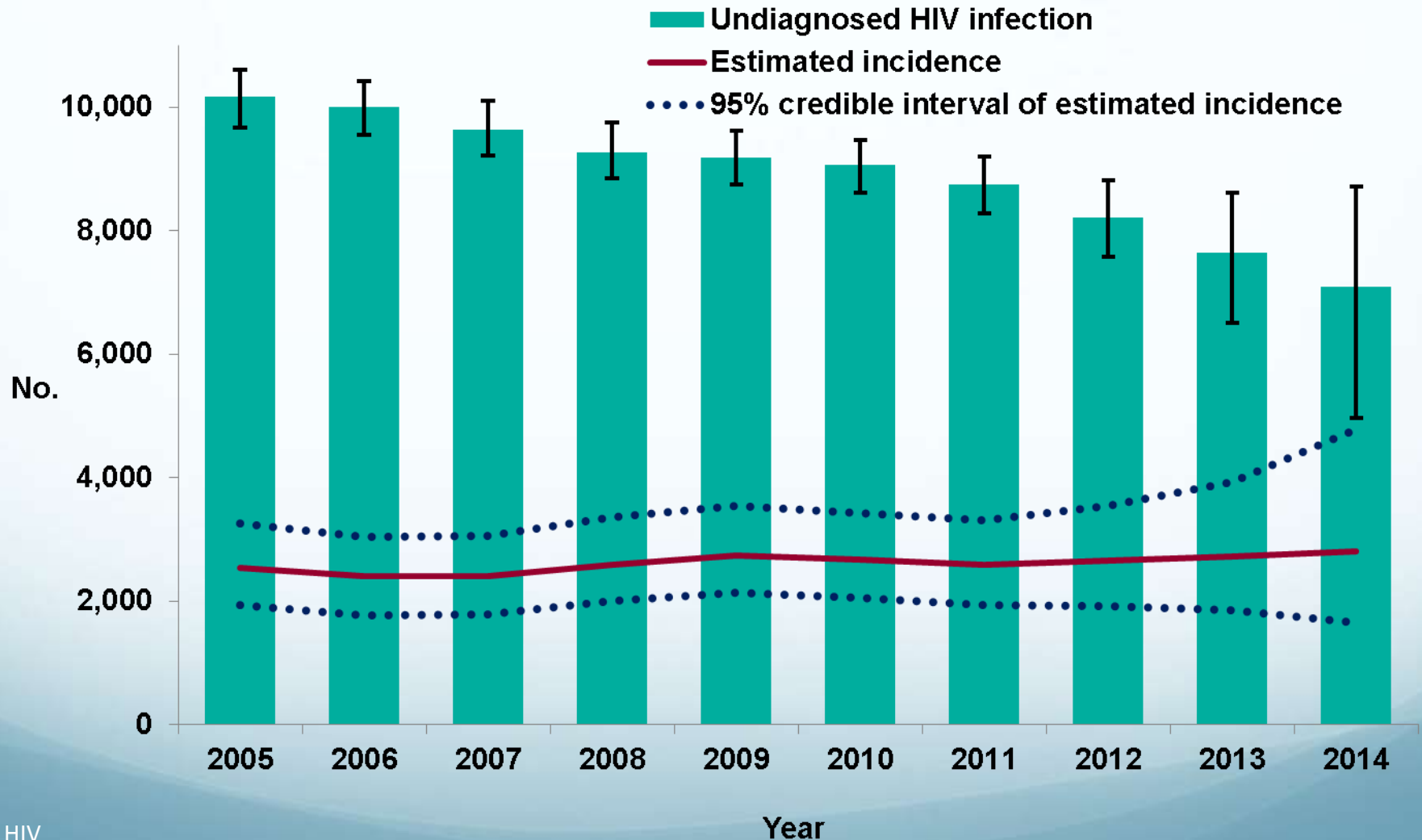
- Evidence for PrEP effectiveness and safety
- Risk compensation and impact on STIs,
- Influence on current clinical practice
- Current and future challenges for PrEP implementation

HIV prevention

- Combination approach to HIV prevention gives us the tools to dramatically reduce HIV transmission
 - Condom use
 - Testing
 - Treatment as Prevention
 - PrEP
- For maximal impact interventions need to be targeted at those most at risk
 - On-going HIV high incidence in MSM
 - Incidence unclear in other ‘at risk’ groups



Back-calculation estimate of HIV incidence and prevalence of undiagnosed infection among men who have sex with men: United Kingdom, 2005 - 2014



HIV incidence

Estimated HIV incidence among sexual health clinic attendees in 2012

Group of attendees	Estimated incidence	95% CI
All	0.15%	0.13% - 0.17%
MSM	1.34%	1.15% - 1.53%
Heterosexuals	0.03%	0.02% - 0.04%
Black African Heterosexuals	0.17%	0.08% - 0.27%

HIV incidence among people who attend sexual health clinics in England in 2012

Sex Transm Infect 2015;91:A2 doi:10.1136/sextrans-2015-052126.4

HIV incidence in HIV negative MSM who re-attended at STI clinics in 2012

Category	HIV incidence (per 100 py)	95% CI
HIV test 42-365 days prior to current attendance	2.4	2.0 – 2.8
Bacterial STI in previous year and/or at current attendance	3.3	2.8 – 4.0
Rectal bacterial STI in previous year and/or at current attendance	5.2	3.7 – 6.7
PEP in previous year	3.3	1.7 – 6.3

Source: GUMCAD, PHE, HIV incidence analyses 2012

The journey to PrEP implementation



Research findings
PROUD study



Policy
Politics
Commissioning



Community activism
Campaigning



Clinical service
support

Effectiveness: MSM

iPREX
(TDF/FTC)

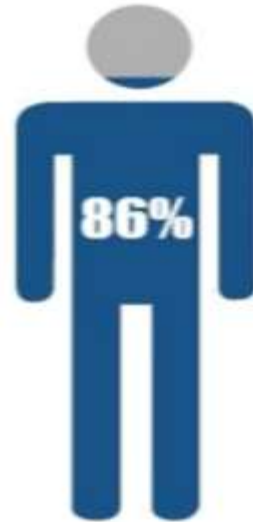
44%

CI: 15 - 63

- Sth America, US, SA
- 2499 MSM/TGW
- Daily TDF/FTC or placebo
- 2499: MSM (88%) and TGW (12%)
- Adherence 50%

Grant et al, NEJM, 2010

PROUD
(TDF/FTC)



CI: 64 - 96

- UK
- 544 MSM, 1 TGW
- Immediate vs def daily TDF/FTC
- Adherence 88%

McCormack et al, The Lancet, 2015

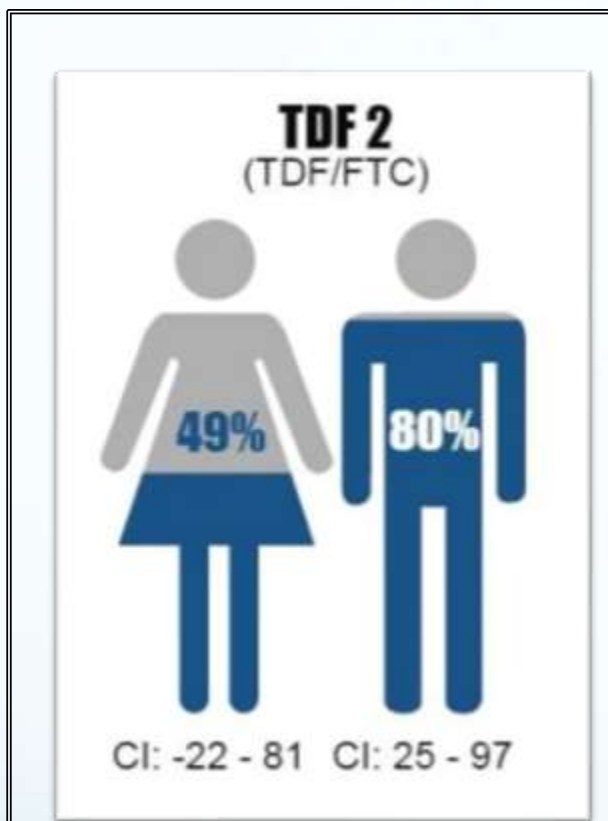
IPERGAY
(on demand TDF/FTC)



CI: 40 - 98

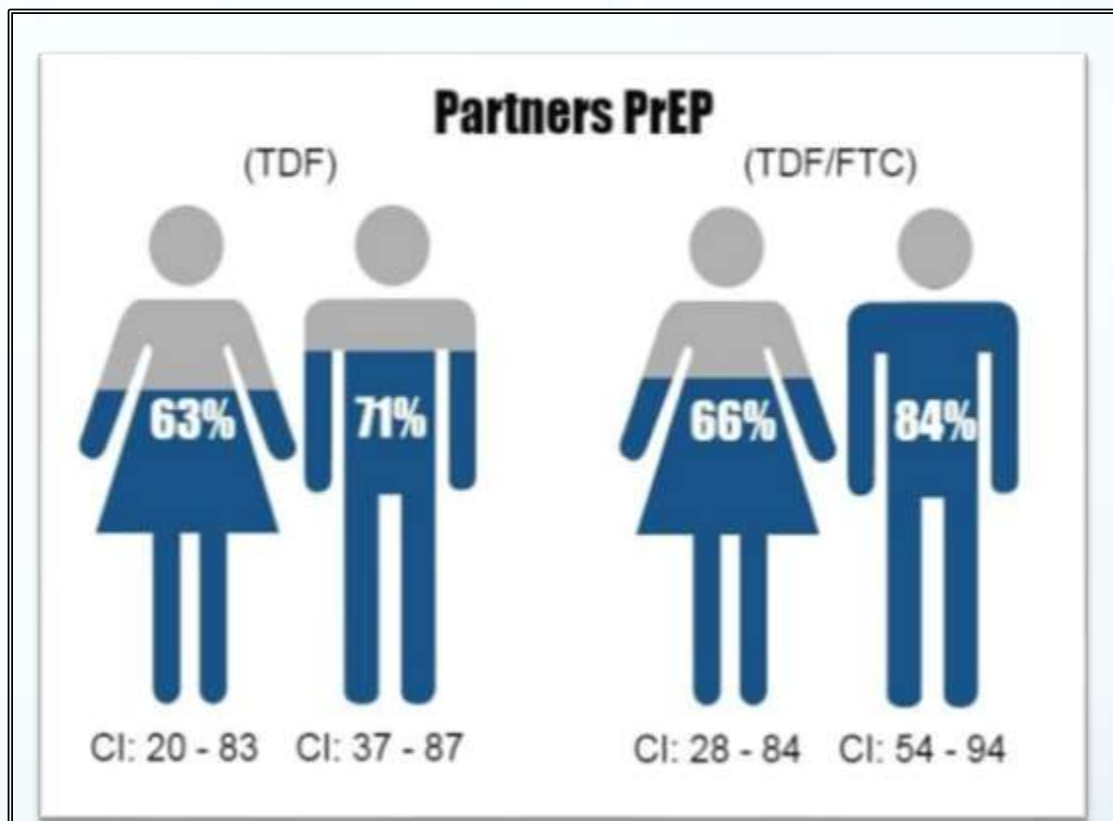
- France, 414 MSM
- On demand FTC/TDF or placebo
- Adherence 86% (TDF in blood)

Effectiveness: Heterosexuals



TDF2

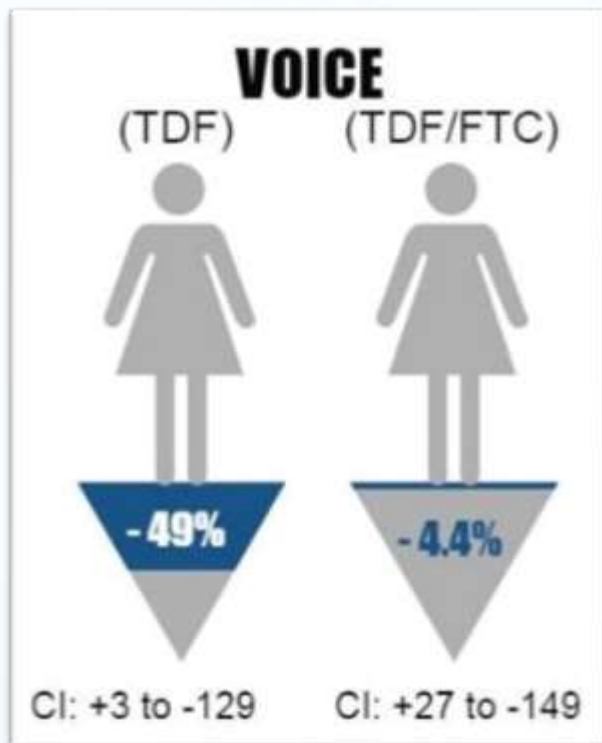
- Botswana. HT men and women (1219)
- Randomised to TDF/FTC or placebo
- Adherence: 84%



Partners PrEP study

- Kenya and Uganda
- HT men and women randomised to placebo (1586) or TDF (1589) or TDF/FTC (1583)
- Adherence: 92%

Effectiveness: Heterosexuals



VOICE

- South Africa, Uganda, Zimbabwe
- 5029 women, randomised to oral TDF, oral TDF/FTC, vaginal TFV gel, placebo
- Zero evidence effectiveness
- Adherence: 25-30%



FEM-PrEP

- South Africa, Kenya, Tanzania
- 2120 women, randomised 1:1 to TDF/FTC or placebo
- No evidence effectiveness
- Adherence <40%

Other at risk groups: Trans women, trans men and people who inject drugs

- Subgroup analysis iPrEx trial¹: 339 TGW
 - 11 infections PrEP arm (none had detectable TDF/FTC in blood) and 10 in placebo (HR: 1.1, 95% CI: 0.5–2.7)
- No PrEP studies in Trans women which are specifically designed for and focussed on trans women and trans issues,
- No data at all in TGM
- The Bangkok Tenofovir Study²: 1:1 male and female PWID randomized to TDF or placebo.
 - 48.9% reduction incidence (95% CI 9.6-72.2)
 - Adherence 83%

1. Deutsch MB et al. HIV pre-exposure prophylaxis in transgender women: a subgroup analysis of the iPrEx trial. *The Lancet* (2015)

2. Choopanya et al. Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study). *The Lancet* (2013)

Effectiveness in open label extension studies - MSM

iPrEx-OLE¹

- 76% of 1603 iPrEX participants, MSM/TGW
- No seroconversions if drug levels compatible with \geq four pills/week

IPERGAY-OLE²

- 362 MSM
- 97% reduction in risk compared to the placebo arm of the IPERGAY randomised phase

1. Grant RM et al. Uptake of PrEP, sexual practices, and HIV incidence in men and transgender women who have sex with men. *The Lancet Infectious Diseases* (2014)

2. Molina et al. Efficacy of "On Demand" PrEP in the ANRS IPERGAY Open-Label Extension Study. IAS, Durban (2016)

Effectiveness in open label extension studies – Heterosexual

Partners PrEP OLE¹

- 89% of 1418 heterosexual men and women
- Efficacy of TDF (67%) & FTC/TDF (75%)

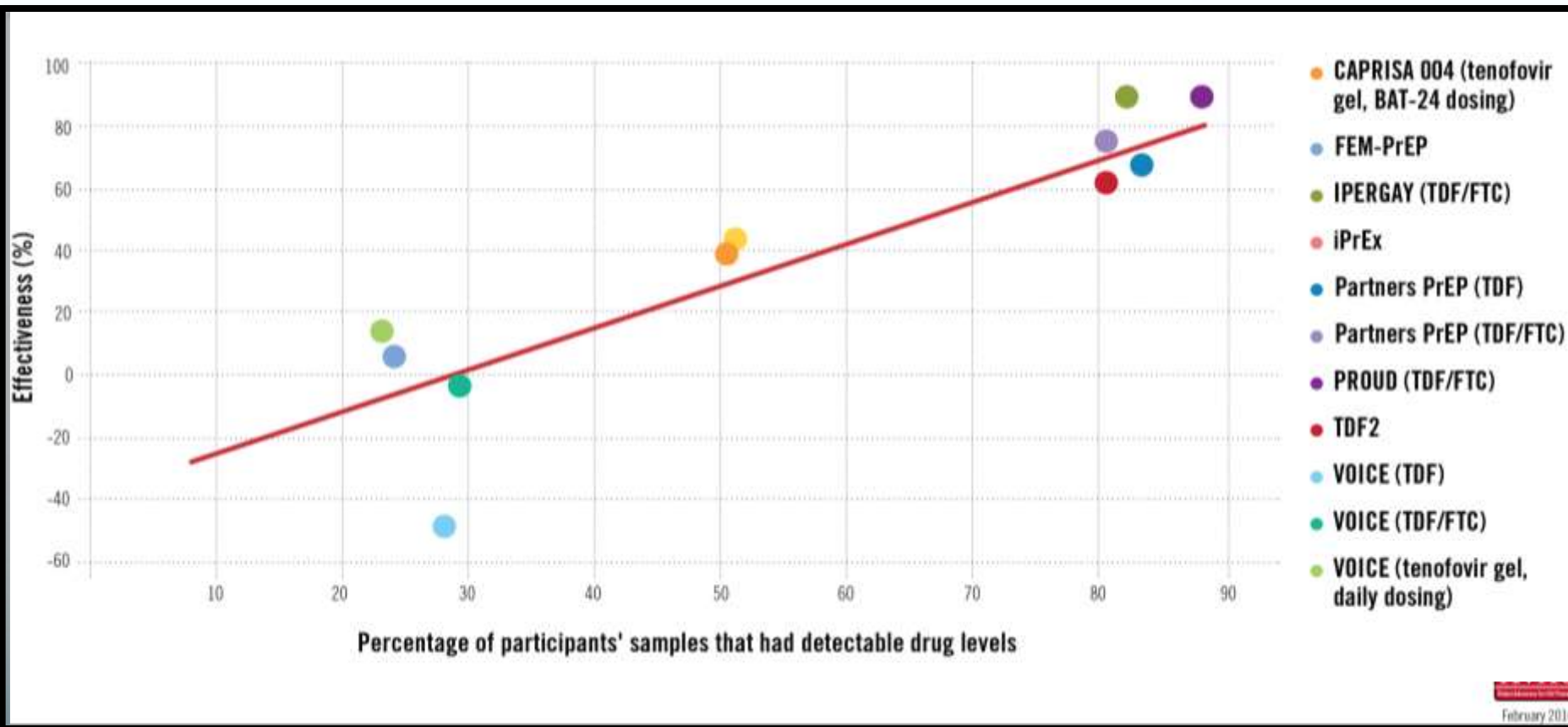
TDF2 OLE²

- 229 men and women, 33% did not complete follow up
- No new HIV infections during the 12 month F/U
- 87% women and 96% men had detectable drug levels at visits

1. Ndase P et al. Successful discontinuation of the placebo arm and provision of an effective HIV prevention product: the partners PrEP study experience. JAIDS. 2014

2. Chirwa LI et al. Enrollment into open-label phase of TDF2 PrEP Study. 20th IAC; 2014; Melbourne, Australia.

Differences in efficacy largely explained by adherence



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

<http://www.proud.mrc.ac.uk/>

PROUD Study



MSM and TGW reporting unprotected anal sex in last

**86% reduction in HIV
Transmission**

Truv

**No increased rates of other
STIs**

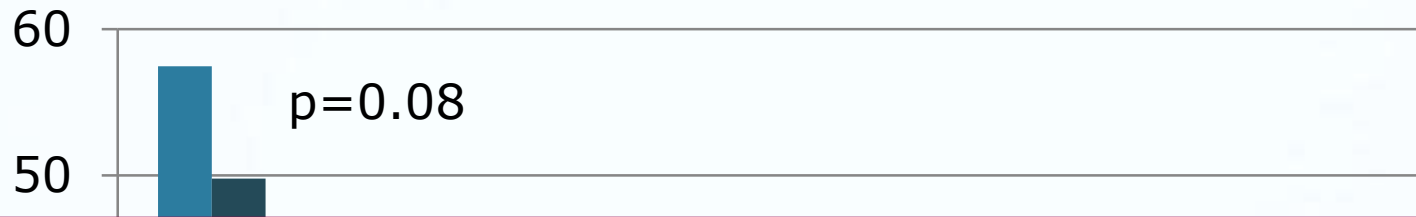
ER 12M

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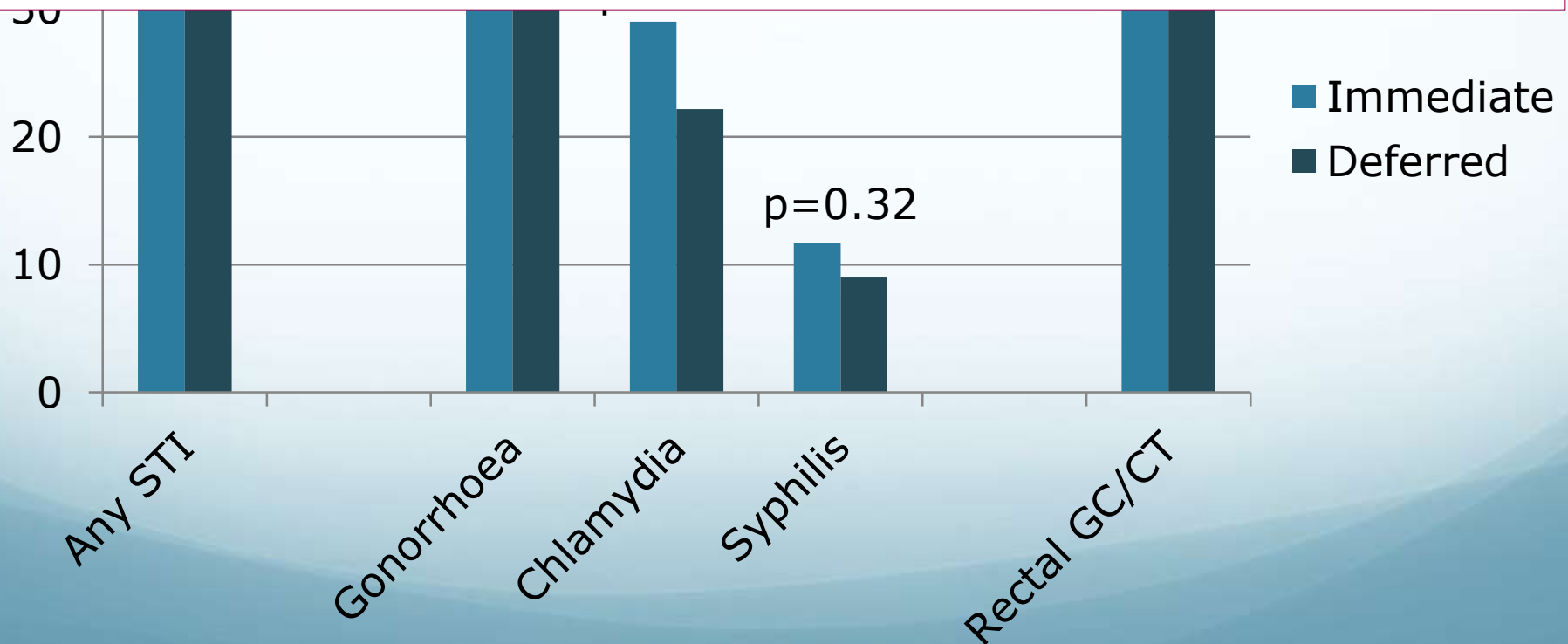
Main endpoints in Pilot: recruitment and retention
From April 2014: HIV infection in first 12 months

STIs



Caveat

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



PrEP interruptions for medical event

- **PrEP interrupted** by 28 participants (**both groups**) but only **13** had events considered related to drug:
 - nausea alone or with diarrhoea/abdominal pain/aches and fatigue (n=5)
 - decline in creatinine clearance (n=2)
 - headache (n=2)
 - joint pain, with fatigue in one case (n=2)
 - sleep disturbance (n=1)
 - flu-like illness (n=1)
- **PrEP re-started** by 11 of 13 participants above

Double-Blinded Randomised Placebo-Controlled Trial

- HIV negative high risk MSM
- Condomless anal sex with ≥ 2 partners within 6 m
- eGFR > 60 mL/mn

Full prevention services*
TDF/FTC before and after sex

Full prevention services*
Placebo before and after sex

* Counseling, condoms, testing and treatment for STIs, vaccination for HBV and HAV, PEP

- End-point driven study : with 64 HIV-1 infections, 80% power to detect a 50% relative decrease in HIV-1 incidence with TDF/FTC (expected incidence: 3/100 PY with placebo)
- Follow-up visits: month 1, 2 and every two months thereafter

- ✓ 2 tablets (TD) 2-24 hours
- ✓ 1 tablet (TD) 24 hours la
- ✓ 1 tablet (TD) 48 hours a

**86% reduction in HIV
Transmission**

**No increased rates of other
STIs**

Friday

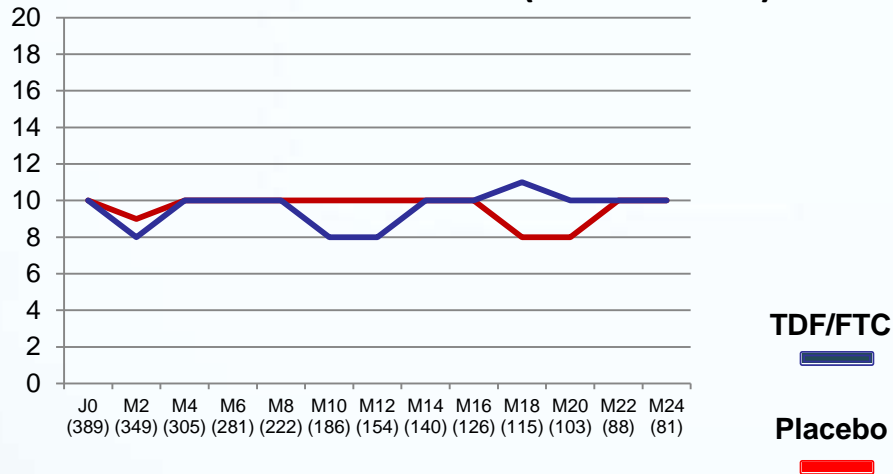
Saturday

Saturday

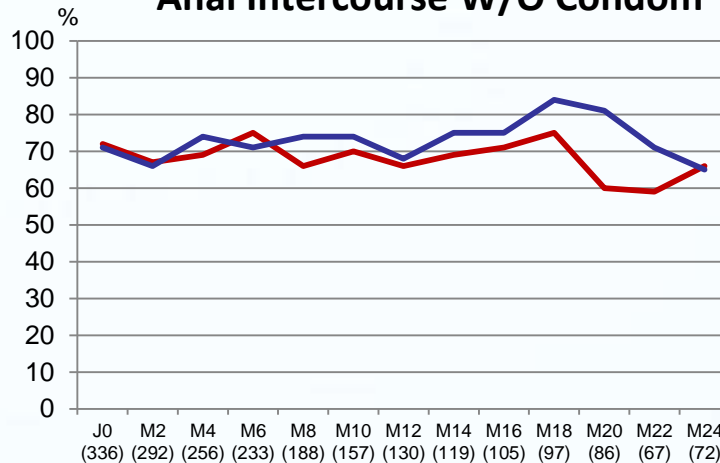
Sunday



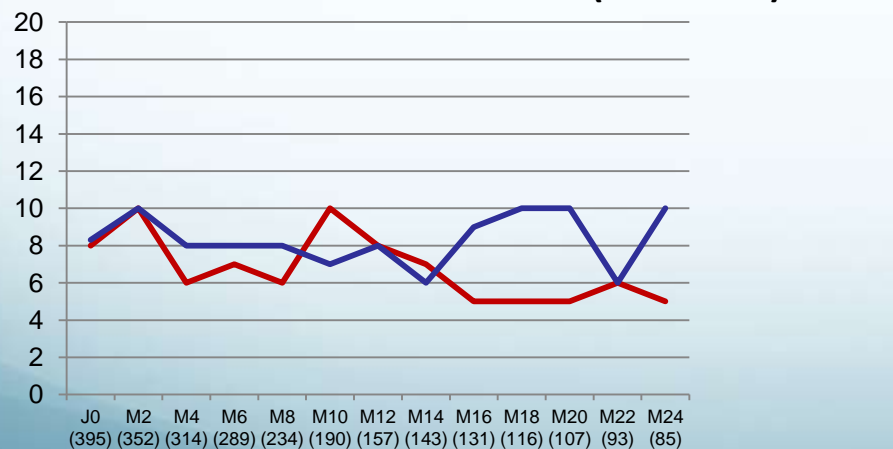
Median Nb of Sexual Acts (last 4 weeks)



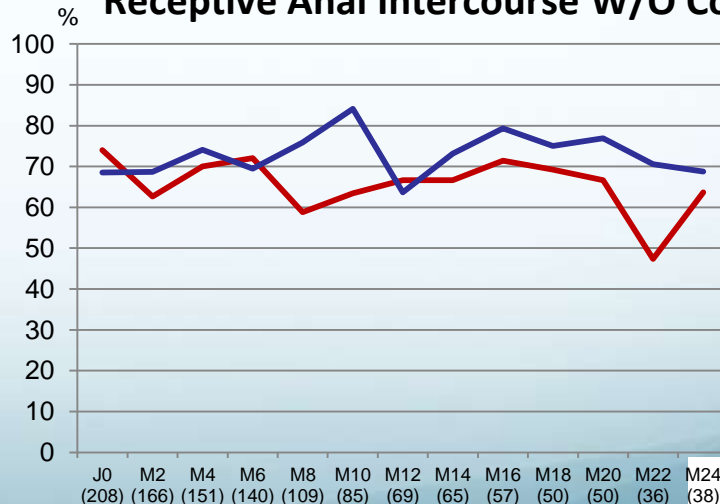
Anal Intercourse W/O Condom



Median Nb of Sexual Partners (2 months)



Receptive Anal Intercourse W/O Condom

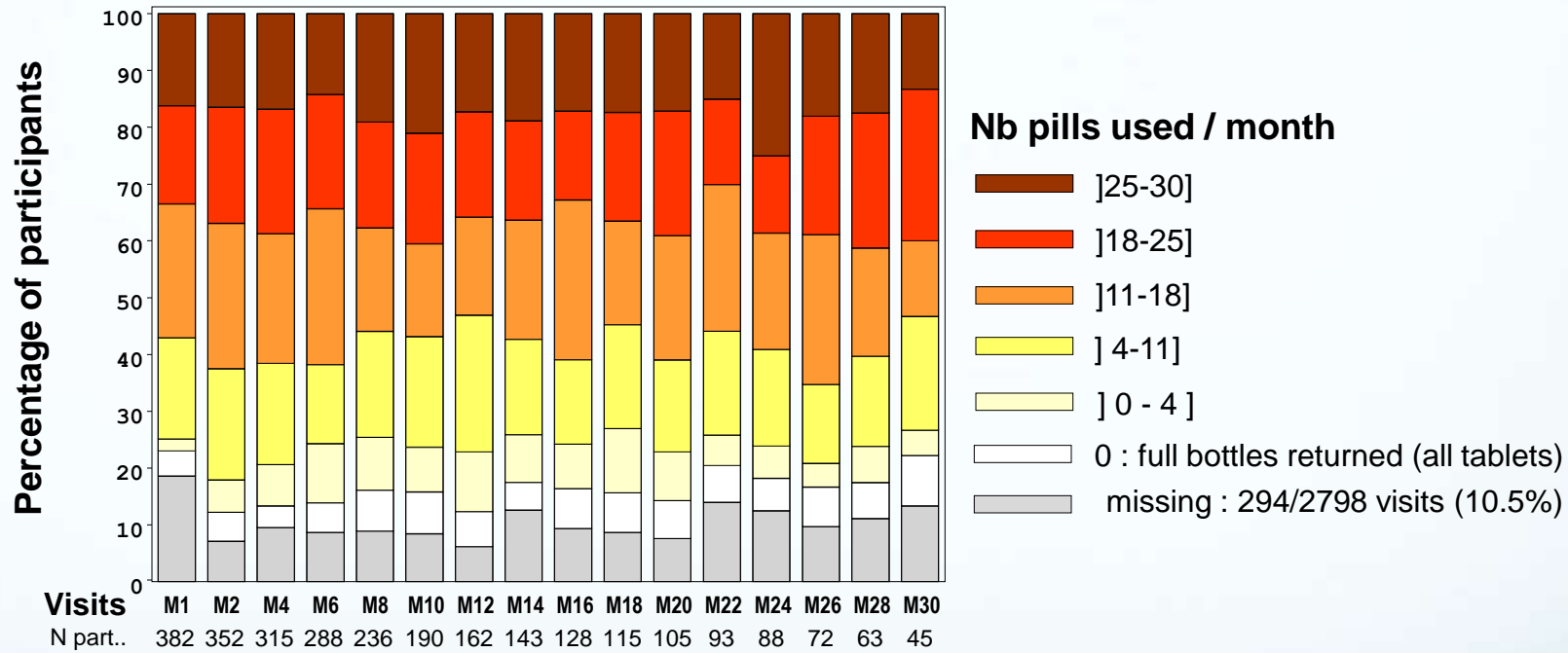


Sexually Transmitted Infections

- 276 STIs were diagnosed in 141 participants

	TDF/FTC n=199		Placebo n=201		P value
	Nb Pt (%)	Nb Events	Nb Pt (%)	Nb Events	
Chlamydia	43 (22)	61	34 (17)	48	0.23
Gonorrhoea	38 (19)	50	45 (22)	67	0.42
Syphilis	19 (10)	19	19 (10)	25	0.98
HCV	3 (<2)	3	3 (<2)	3	1.00
Any STI	76 (38)	133	65 (32)	143	0.22

Adherence by Pill Count



- **Median number of pills/month (IQR):** 16 pills (10-23) in the placebo arm and 16 pills (12-24) in the TDF/FTC arm (p=0.84)
- **48 participants (12%) received PEP**
25 (13%) in the TDF/FTC arm and 23 (11%) in the placebo arm (p=0.73)

Adverse Events

Nb of Participants (%)	TDF/FTC n=199	Placebo n=201	P value
Any AE	184 (92)	178 (89)	0.18
Any Serious AE	18 (9)	16 (8)	0.70
Any Grade 3 or 4 AE	17 (9)	14 (7)	0.56
Treatment D/C due to AE	1*	0	
Drug-Related GI AEs	25 (13)	11 (6)	0.013
Nausea/vomiting	15	2	
Abdominal pain	11	4	
Diarrhea	7	5	

* deep veinous thrombosis with suspected DDI with dabigatran

Risk compensation

- In the iPrEx study, there was no evidence of risk compensation.
- In the iPrEx-OLE study, both groups reported decreases in reported condomless receptive anal intercourse
- In the PROUD study, there was no difference in the total number of sexual partners at 1 year or in the frequency of bacterial STIs
- However, a greater proportion of the immediate group reported condomless receptive anal sex with 10+ partners at 1 year compared to the deferred group (21% vs 12%, $p=0.03$).
-

Risk compensation

- In IPERGAY, there were no significant differences between Truvada and placebo groups in the proportion of condomless receptive anal sex and incident STIs
- In the open label phase (Ipergay OLE) there was an increase in overall reported condom use over time

Evidence – summary

- PrEP is highly effective – when good adherence is achieved
- HIV incidence in PROUD was much higher than expected
- On demand PrEP was as effective as regular PrEP
- No major safety concerns
- No evidence of ‘risk compensation’ or increase in STIs
- PROUD demonstrated that PrEP was highly effective in a more ‘real world’ setting
- Clinics were able to adapt routine practice to incorporate PrEP (PROUD)

Evidence – summary

- All data for PrEP in heterosexuals is from sub-Saharan Africa
- We have no data to support risk assessment in heterosexuals in the UK
- There are no specifically designed studies in trans women and trans men
- NHSE study will address issues re:
 - Large scale experience
 - Access and eligibility (regular and on-demand PrEP)
 - Ongoing risk and need for PrEP
 - STI and HIV incidence

Clinical implications

- Generics
- Clinical support and service provision

Access to generics

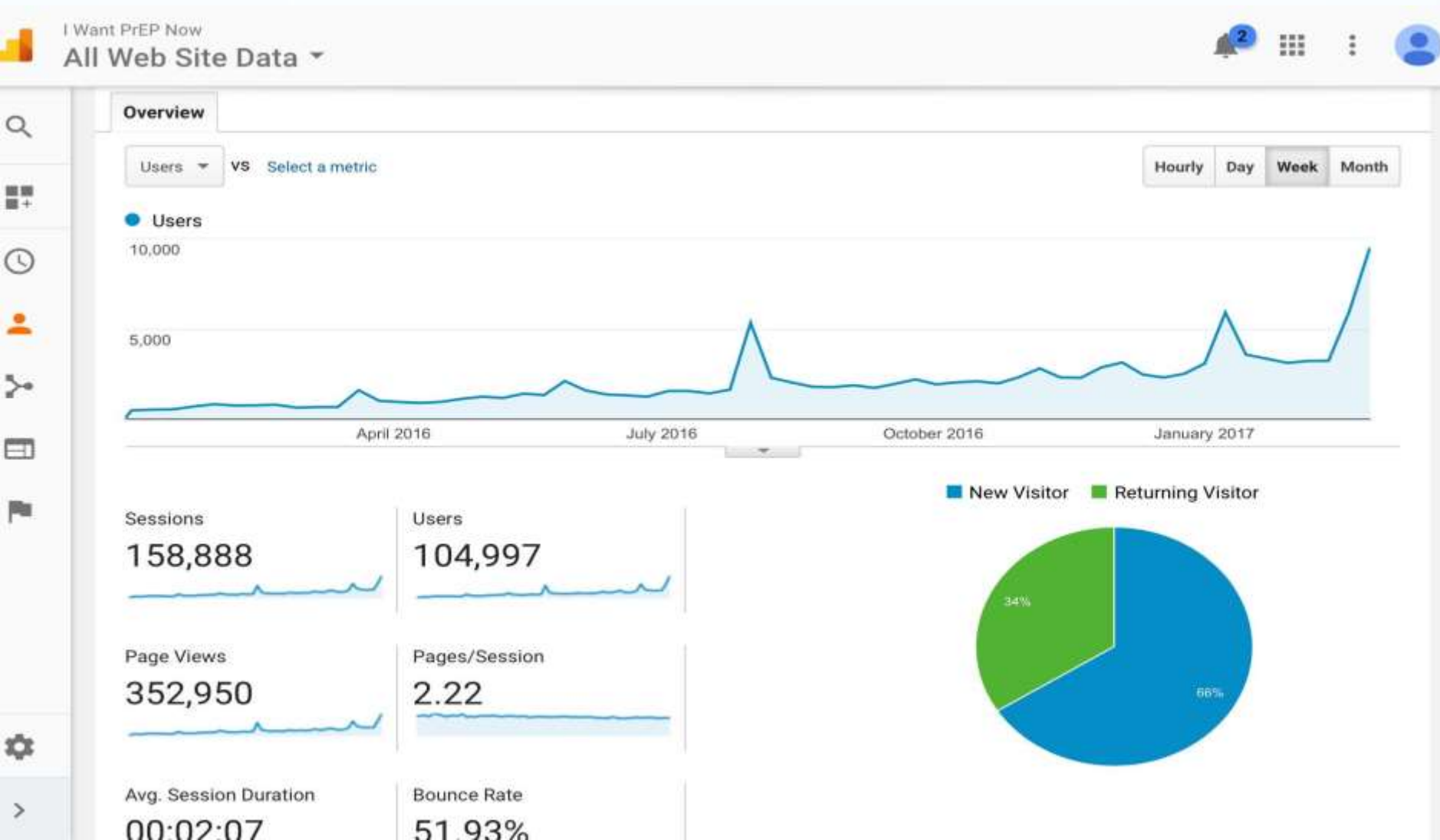
- www.iwantprepnw.co.uk
- **Tenvir-EM (Cipla)**
 - Tavin-EM (Emcure)
 - Ricovir-EM (Mylan)
 - Tencitab (Aspen)



Prepster



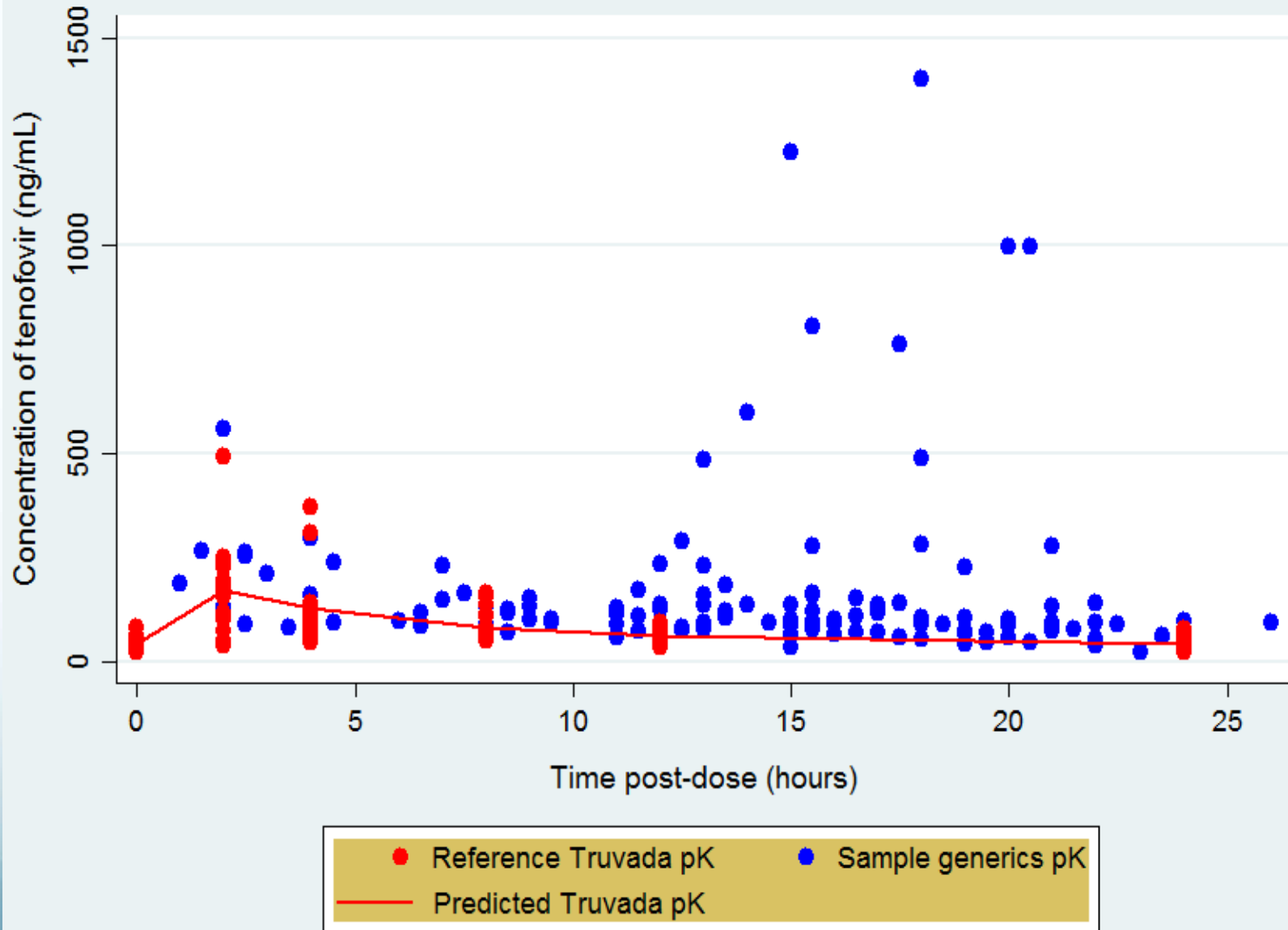
IwantPrEPnow on-line activity



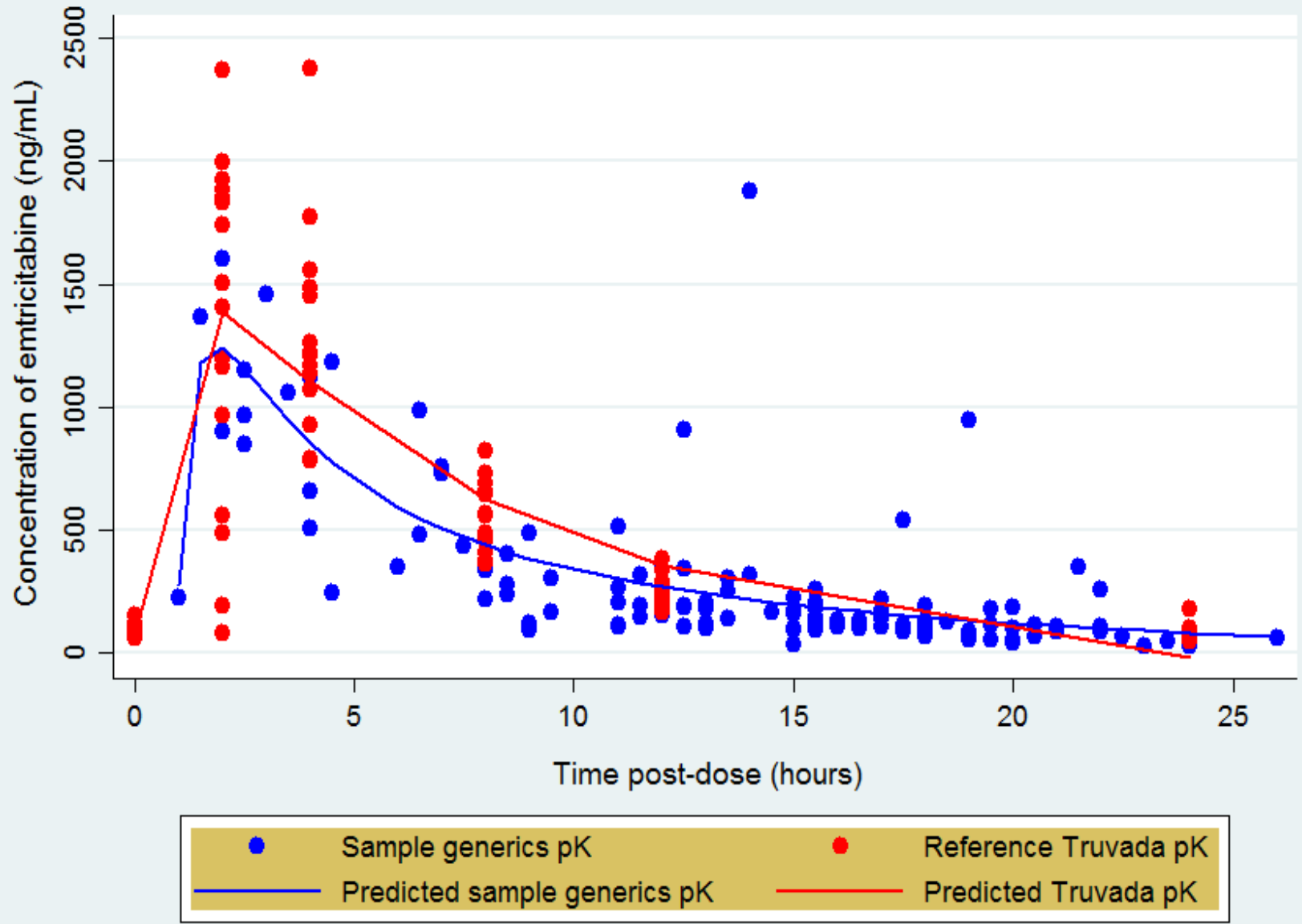
Clinical Service support

- 56 Dean Street opens PrEP clinic in September 2015
 - Private prescriptions of Truvada
 - Support for those buying generic drug
 - STI and HIV testing and renal monitoring
 - Therapeutic drug monitoring for those taking generic TDF/FTC

Time-dependent concentration of plasma tenofovir following generic oral PrEP consumption



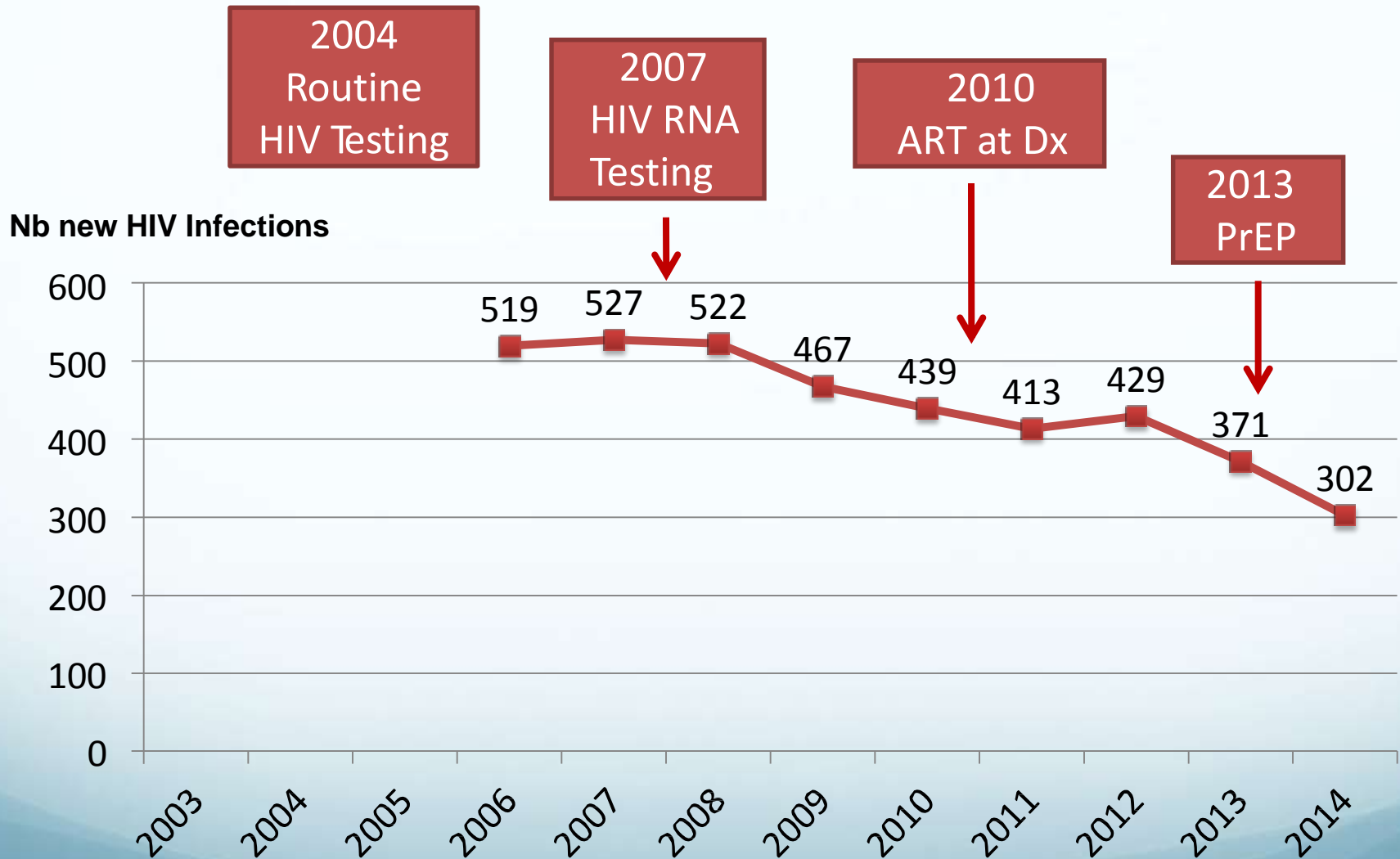
Time-dependent concentration of plasma emtricitabine following generic oral PrEP consumption



Clinical Service support

- Support and advice about PrEP is being provided by sexual health services (GMC advice)
- PrEP is not commissioned and can't be prescribed
- National guidance recommends 3 month STI and HIV tests for high risk MSM
- Services focus on MSM and providing a range of prevention services:
 - HIV and STI testing,
 - Renal monitoring
 - Drug and alcohol support (chemsex),
 - Behavioural interventions and condom provision

HIV Epidemic Trends in San Francisco



HSHS Homerton SexHealth
 @HomertonSHS

Following

Our new #HIV diagnoses this year in gay/bi men down by a whopping 40%

#EndHIV #SexualHealth #Hackney



BH Sexual Health
 @BHSexHealth

Following

Barts Health Sexual Health have seen a 36% drop in new #HIV diagnoses in MSM in 2016 compared to 2015, similar to other London clinics

RETWEETS 54 LIKES 56

9:04 AM - 28 Dec 2016

3 54 56

NHS Central and North West London
 @MMC_cnwl

Mortimer Market

Following

So, joining @56deanstreet and @HomertonSHS we have also seen big decreases in new HIV diagnoses in 2016. More than 50% drop! Wow!! #EndHIV

56 DEAN STREET
 56 Dean Street
 23 December 2016 at 16:52 · 🌐

Gay Times are spreading the good news. Condoms, PrEP, Early diagnosis, Immediate treatment. We can beat HIV in 2017.

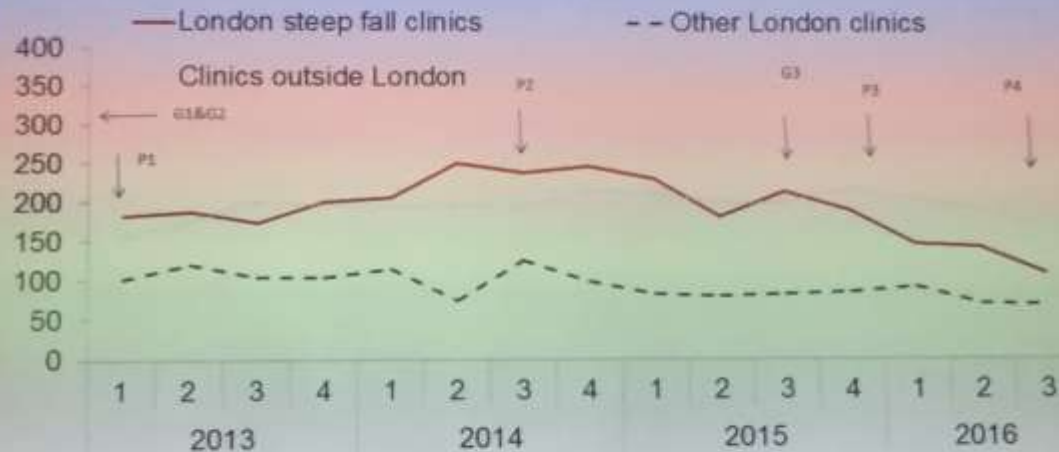


40% drop in new HIV diagnoses at leading London sexual health clinic

56 Dean Street gave 373 new diagnoses of HIV in 2016, compared to 626 in 2015.

Similar reduction in HIV diagnoses in MSM (England)

New HIV diagnoses among gay/bisexual men attending sexual health clinics England 2013-2016



Steep fall Clinics = those with >20% decrease in new HIV diagnoses - Oct 2014-Sep 2015 versus Oct 2013-Sep 2014, and over 40 diagnoses during period.
P1: PROUD Recruitment begins (50% of participants deferred). P2: All deferred participants offered PrEP. P3: Online purchasing of PrEP begins.
G1: In 2013 BHIVA/BASHH (P4a) and Public Health England (November) recommend three-monthly HIV testing for gay men at high risk.
G2: start ART with a CD4 >350 should the patient wish to protect partners.
G3: Treatment for all individuals for purposes of treatment as prevention.

Summary (1)

- Getting closer to PrEP access has required collaborative working between academics, clinicians, activists and community groups
- Community engagement will be key to ensuring awareness, access and efficacy of national PrEP programme
- For maximal impact of PrEP it is essential to target those most at risk
- Strategies are required to engage with the most ‘hard to reach’ groups to ensure equity of access

Summary (2)

- Stigma around HIV remains a potential barrier to implementation and access
- Clinical service delivery has potential for most impact when PrEP is delivered in a combination approach with other HIV prevention and health improvement strategies
- Early experience suggests the impact on HIV transmission can be significant
- Monitoring for impact on other STIs will be important
 - Regular testing may result in earlier diagnosis and treatment



Prepster

Central and North West London **NHS**
NHS Foundation Trust



Kings College Hospital **NHS**
NHS Foundation Trust

**UNITED
4
PrEP**

PositiveEast

POSITIVE 21



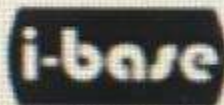
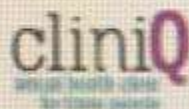
NAZ



#United4PrEP



Barts Health **NHS**
NHS Trust



AFRICA ADVOCACY FOUNDATION



Homerton University Hospital **NHS**
NHS Foundation Trust



HIV JUSTICE NETWORK



Chelsea and Westminster Hospital **NHS**
NHS Foundation Trust



European African Treatment Advocates Network



Imperial College London

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Consultant, HIV and Sexual Health

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