



World Aids Conference 2016 PrEP – was gibt es Neues?

Viviane Bremer
Berlin, 16. August 2016

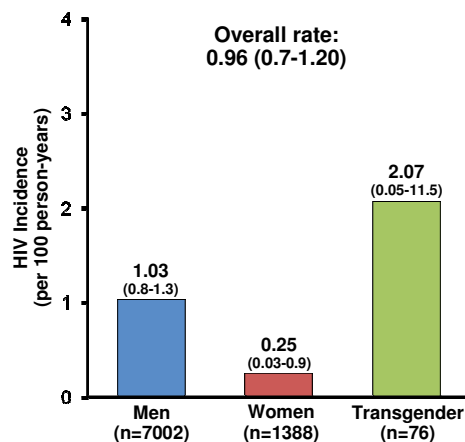


Kenneth H. Mayer
PrEP: A work in progress

International PrEP Demonstration Projects With Emtricitabine/Tenofovir DF (2011-2015)

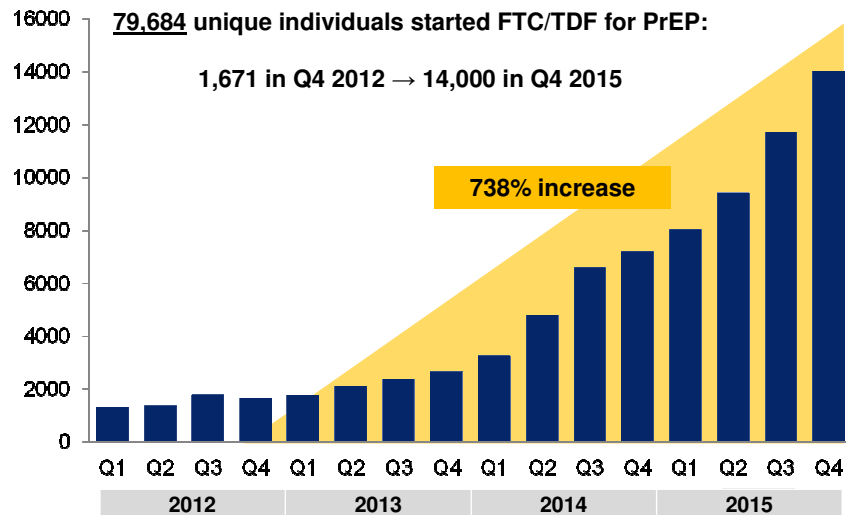
- Individual PrEP demonstration projects with emtricitabine/tenofovir DF n=32 projects in 16 countries
 - 8478 participants with 7061 cumulative years exposure
- 0 HIV seroconversion rate
 - 17 projects with 2467 participants
 - Follow-up: 1315 person-years exposure
- Total HIV seroconversions (n=67)
 - Highest rates in MSM 18 to 25 years of age (7.7/100 person-years)
 - Available intracellular data showed undetectable or very low TFV-DP levels (<2 tablets/ week) in nearly all of those with seroconversion

HIV Seroconversion Rates



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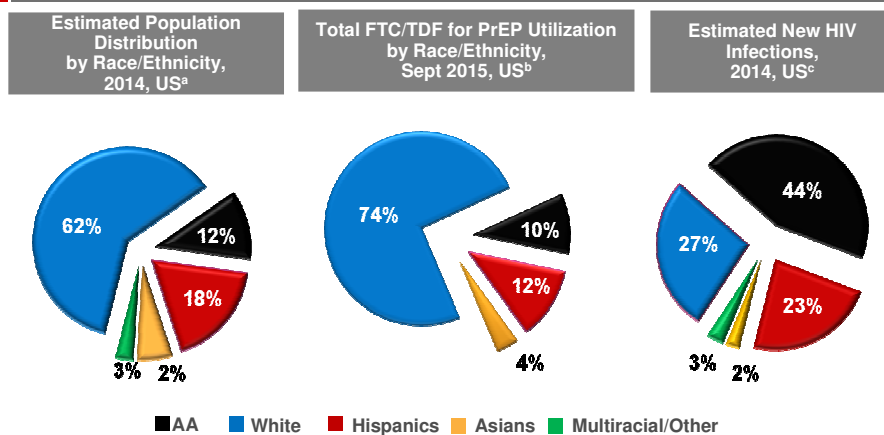
Unique Individuals Starting FTC/TDF for PrEP in US, 2012 to 2015 (by quarter)



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FTC/TDF for PrEP Utilization Compared With Population and New HIV Infections



FTC/TDF for PrEP use among AA and Hispanics is low relative to the rate of new HIV infections

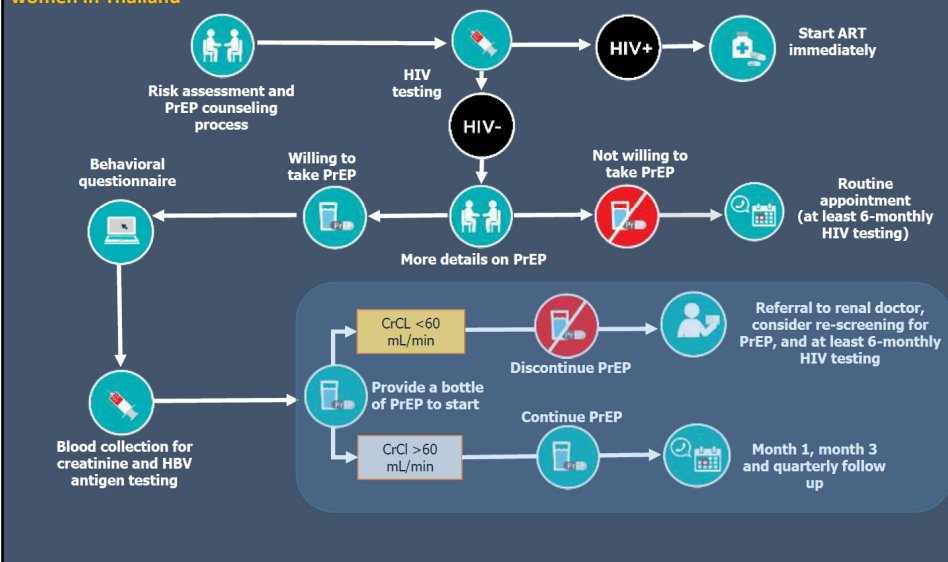
b. These data represent 43.7% (n=21,463) of unique individuals who have started TVD for PrEP from 2012-3Q2015.

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Bush S. et al. ASM/ICAAC 2016, Boston, MA #2651

Nittaya Phanuphak:
Implementing PrEP for
gay men, other men
who have sex with
men, and transgender
women in Thailand

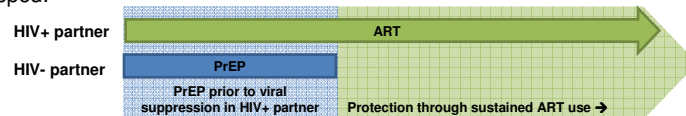
Same-day PrEP clinic flow



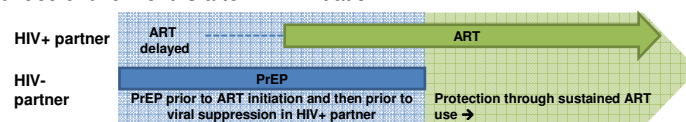
Jared M. Baeten et al.: Integrated delivery of
PrEP and ART results in sustained near
elimination of HIV transmission in African HIV
serodiscordant couples: Final results from the
Partners Demonstration Project

PrEP as a bridge to ART

- For couples initiating ART at enrollment, PrEP was offered through 6 months, then stopped:



- For couples in which the infected partner delayed or declined ART, PrEP was continued until 6 months after ART initiation:



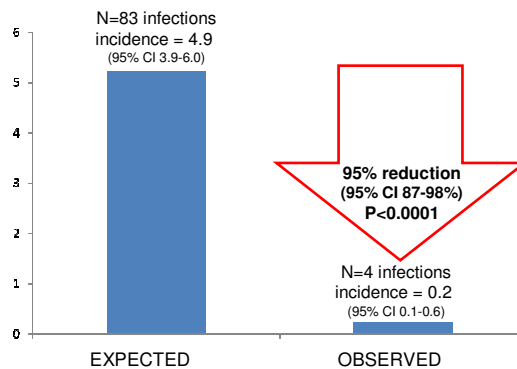
- This strategy is supported by mathematical modeling as potentially highly effective and cost-effective (Hallett et al. PLoS Med 2011; Ying et al. JIAS 2015)



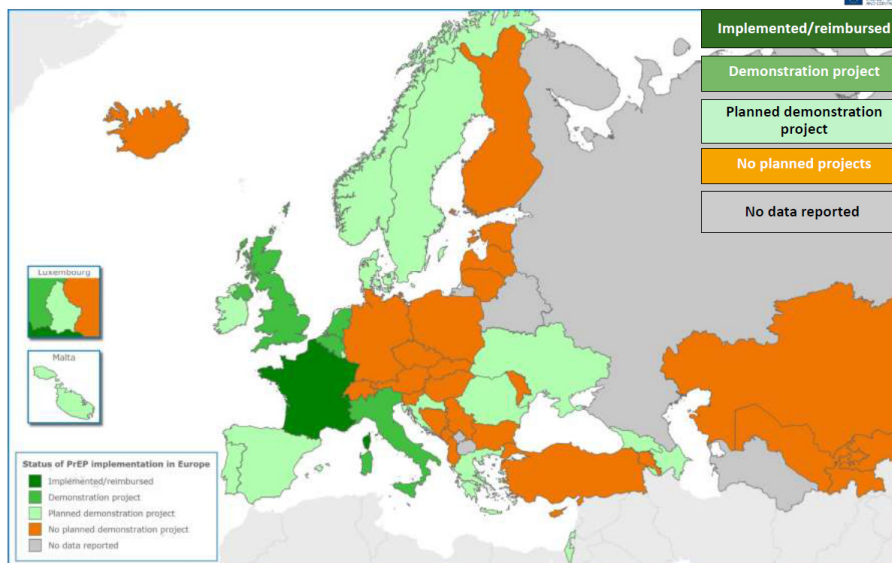
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HIV incidence

- 83 HIV infections predicted, (incidence 4.9/100 person-years)
- 4 incident HIV infections **observed**, (incidence 0.2/100 person-years)
- Similarly high HIV protection:
 - Men (97% $p < 0.0001$)
 - Women (93% $p < 0.0001$)
 - HIV- partner <25 years of age (95% $p < 0.0001$)
 - HIV+ partner with plasma viral load $\geq 50,000$ copies/mL (95% $p < 0.0001$)



Status of PrEP implementation in Europe



Based on reported data from countries of Europe and Central Asia as part of Dublin Declaration monitoring 2016 (preliminary data)



HIV Incidence (mITT Analysis)

Treatment	Follow-Up Pts-years	HIV Incidence per 100 Pts-years (95% CI)
Placebo	212	6.60 (3.60-11.1)
TDF/FTC (double-blind)	219	0.91 (0.11-3.30)
TDF/FTC (open-label)	515	0.19 (0.01-1.08)

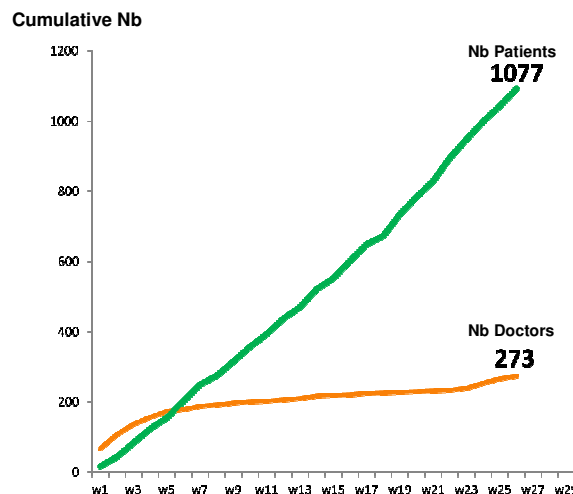
Median Follow-up in Open-Label Phase 18.4 months (17.5-19.1)

97% relative reduction vs. placebo

Molina et al AIDS 2016, July 20, Durban, South Africa

PrEP Implementation in France in 2016

- > 90 PrEP clinics have opened, initially in ANRS Ipergay sites (Paris, Lyon, Nice, Lille, Nantes)
- AIDES Website: <http://www.aides.org/info-sante/prep>
- TDF/FTC can be prescribed by hospital-based HIV specialists and STI clinics since June 2016
- TDF/FTC can be obtained at private and hospital pharmacies



STIs in IPERGAY: Placebo-controlled & open label phases

	Double-Blind Median FU: 9.3 months n=400		Open-Label Median FU: 18.4 months n=362	
	Nb Pt (%)	Nb Cases	Nb Pt (%)	Nb Cases
Chlamydiae	81 (20)	114	122 (34)	158
Gonorrheae	88 (22)	123	117 (32)	175
Syphilis	39 (10)	45	68 (19)	77
HCV	5 (1)	5	5 (1)	5
All STIs	147 (37)	287	210 (58)	415

Incidence rate of first STI:
35.2 vs 40.6 per 100 PY in the double-blinded and OLE
phases

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Slide courtesy of Jean Michel Molina



Clinical Genotypic Drug Resistance (to TDF or FTC) in PrEP Trials

Study	Incident DR Infections PrEP	PrEP arm N	Incident DR Infections Placebo	Placebo arm N
Bangkok TDF	0	1204	0	1209
FEM-PrEP	4	1024	1	1032
iPrEx	0	1251	0	1248
Partners PrEP	0	3155	0	1578
TDF2	0	610	0	606
VOICE	1	1978	0	999
TOTAL	5	9222	1	6672

Overall risk of FTC or tenofovir resistance is 5/9222 (0.05%);

The Number Needed to Harm: NNH = 1844;

The Number Needed to Prevent 1 HIV infection: NNT = 13 to 60.

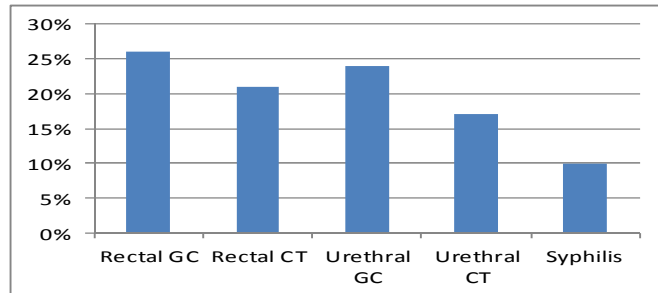


STIs occur for persons using PrEP

PROUD Study, UK

N=544

STIs in the 12 months *prior to enrollment*



But the population who needs PrEP has high STI rates – and STI rates have been rising in countries prior to PrEP (McCormack et al. Lancet 2016)

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Connie Celum: Antiretroviral pre-exposure prophylaxis (PrEP):
Interaction with & impact on STIs

Can PrEP reduce the incidence of STIs?

- Tenofovir has *in vitro* anti-HSV-2 activity; EC_{90} is high so likely need high adherence to see an effect (Andrei Cell Host Microbe 2011)
- Partners PrEP: Daily oral TDF and TDF/FTC PrEP reduced HSV-2 acquisition by 31%
 - 35% efficacy in the subset with known HSV-2+ partners (Celum Annals Int Med 2014)
- iPrEX: No reduction in HSV-2 (Marcus PLoS One 2014)
- Given limited interventions for primary prevention of HSV-2, efficacy against HSV-2 provides additional benefit to oral PrEP

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Are incident STIs useful as a marker of 'risk compensation' among PrEP users?

- No increase in condom-less sex in clinical trials
- Modest increase in condom-less sex in some, but not all, open label PrEP studies
- Incident STIs are an indicator of condom-less sex
- PrEP is reaching a population at high risk of HIV incidence
 - 2.6 fold higher risk of HIV incidence among MSM with syphilis in iPrEX (Solomon CID 2014)

Can PrEP programs reduce STIs through engagement in care, screening & treatment?

- Yes, given quarterly visits for PrEP refills & 3-6 month STI testing
- Opportunity for earlier treatment & STI partner notification
- Need for STI treatment based on diagnostic testing in Africa
 - High STI prevalence in young women
 - Poor performance of syndromic treatment



Summary: STIs & oral PrEP

- No evidence that STIs reduce efficacy of oral PrEP
- Modest reduction in HSV-2 with oral PrEP in heterosexual African HIV serodiscordant couples
 - Adds to substantial HIV protection
- STIs are prevalent in populations who benefit from PrEP
 - Useful for PrEP targeting
 - Incident STIs increase risk of HIV; indicates reaching 'right' population
- STI screening & treatment, ideally based on etiologic testing, are key part of PrEP delivery

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