PROFILAXIA PRÉ-EXPOSIÇÃO PREP

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Ensaios clínicos

- IPrEX
- FEM PrEP
- TDF2
- Parters PrEP
- VOICE
- Ipergay

Estudos abertos

- IPrEX OLE
- PROUD

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Table 1: Summary of Guidance for PrEP Use

	Men Who Have Sex with Men	Heterosexual Women and Men	Injection Drug Users
Detecting substantial risk of acquiring HIV infection	HIV-positive sexual partner Recent bacterial STI High number of sex partners History of inconsistent or no condom use Commercial sex work	HIV-positive sexual partner Recent bacterial STI High number of sex partners History of inconsistent or no condom use Commercial sex work In high-prevalence area or network	HIV-positive injecting partner Sharing injection equipment Recent drug treatment (but currently injecting)
Clinically eligible	Documented negative HIV test result before prescribing PrEP No signs/symptoms of acute HIV infection Normal renal function; no contraindicated medications Documented hepatitis B virus infection and vaccination status		
Prescription	Daily, continuing, oral doses of TDF/FTC (Truvada), ≤90-day supply		
Other services	Follow-up visits at least every 3 months to provide the following: HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment At 3 months and every 6 months thereafter, assess renal function Every 6 months, test for bacterial STIs		
	Do oral/rectal STI testing	Assess pregnancy intent Pregnancy test every 3 months	Access to clean needles/syringes and drug treatment services

STI: sexually transmitted infection

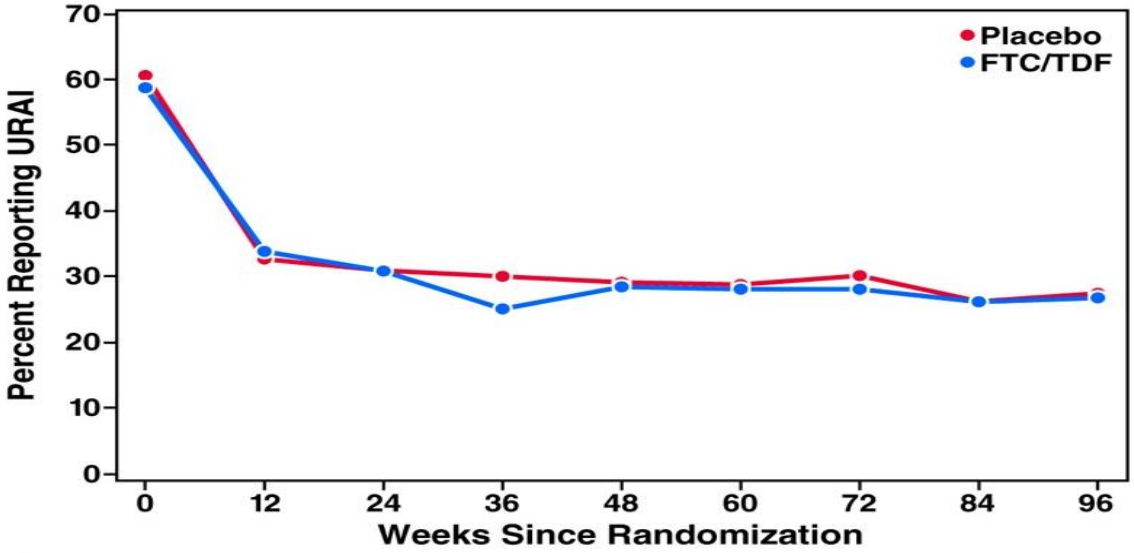
Questões controversas

- Indução de aumento de práticas de risco (compensação de risco)
- Adesão
- Indução de resistência viral
- Segurança
- Custo-efetividade

Compensação de risco

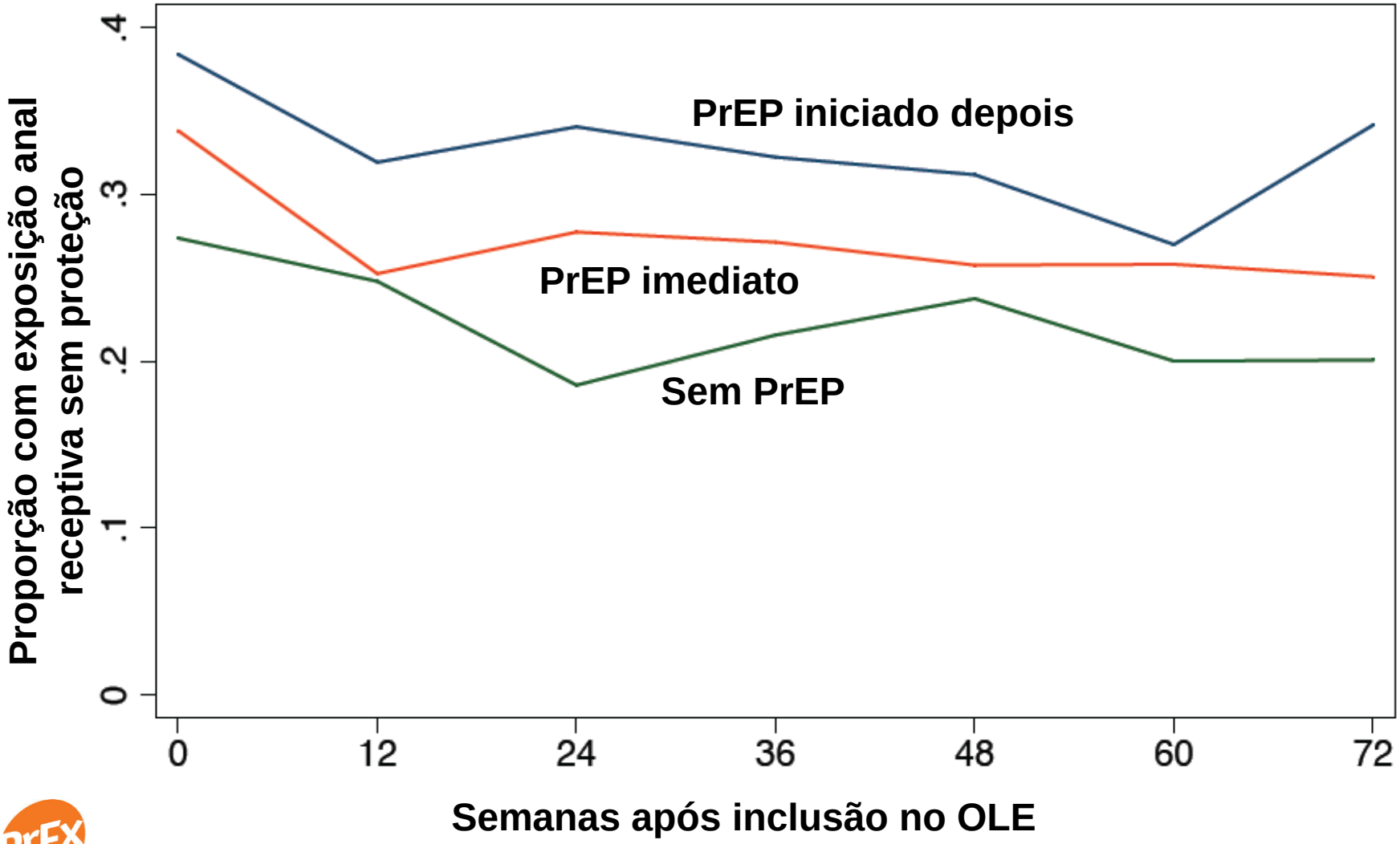
Compensação de risco

- Ausência de compensação de risco em ensaios clínicos cegos
  - Eficácia desconhecida + possibilidade de alocação para grupo placebo



Marcus Plos One 2013

Compensação de risco



Grant et al., *Lancet Infect Dis*, 2014

Partners PrEP fase aberta

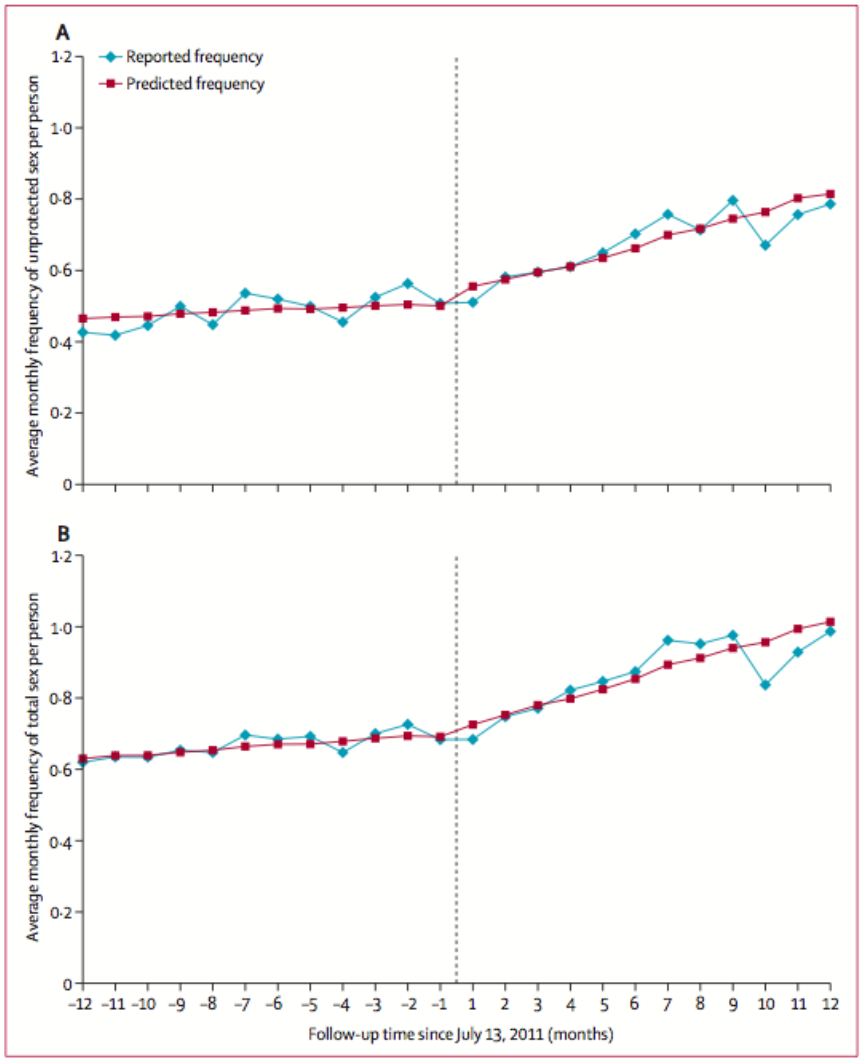


Figure 3: Trend of monthly frequency of sex acts with outside partners

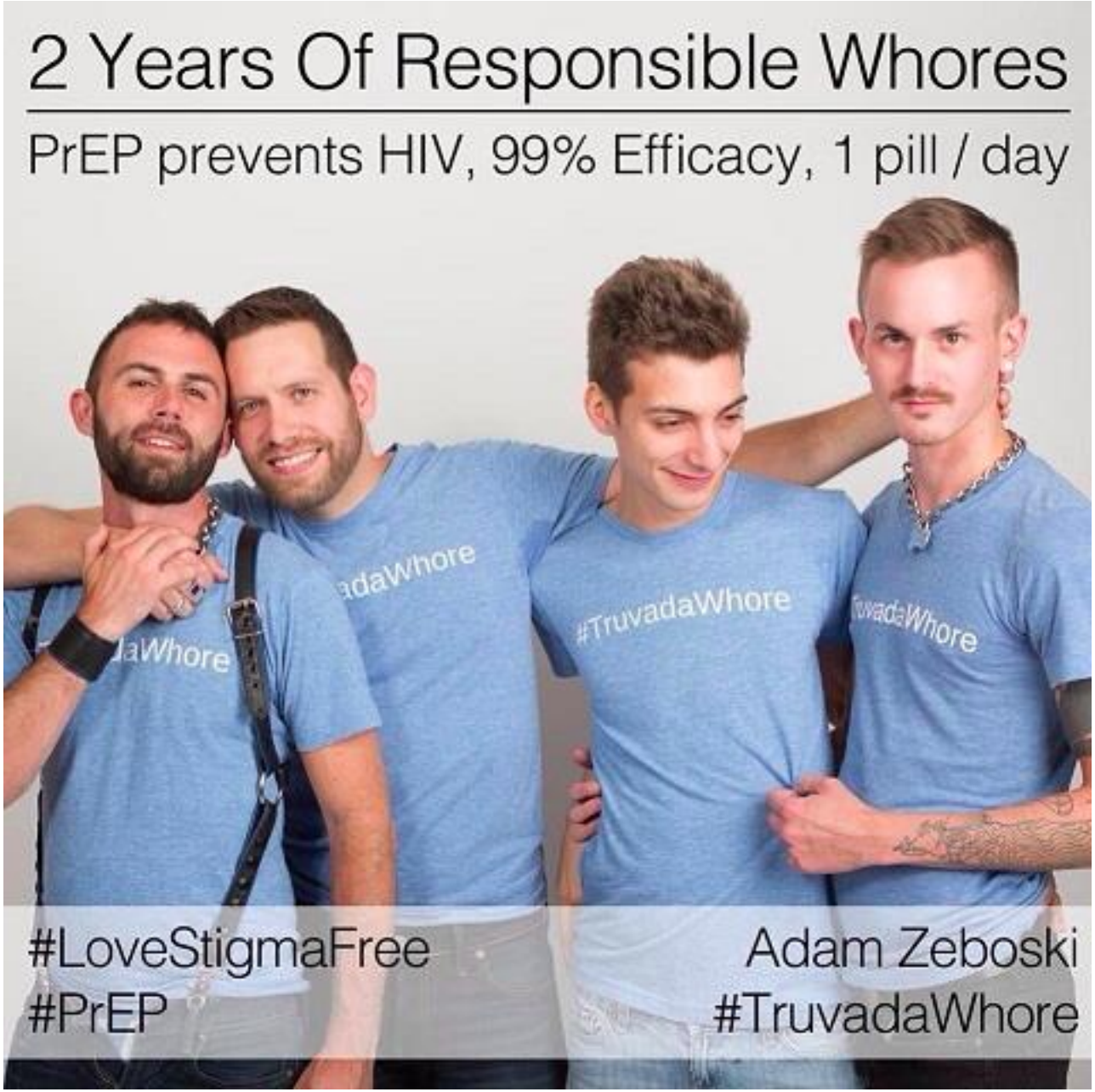
- Sem modificação em práticas de risco com o parceiro HIV+
- Pequeno incremento em práticas de risco com outros parceiros (p=0,04)

Mugwanya Lancet Infect Dis 2013

Compensação de risco

- Evidência indireta de possível efeito negativo de PrEP sobre uso de preservativos de barreira
- Evidência direta - Estudos demonstrativos:
  - Redução do “medo” de contrair HIV levando a práticas anteriormente evitadas
  - Uso diário da medicação e testagem frequente atuando como reforço do desenho de se manter HIV negativo
- Apesar da evidência inconsistente, importante impacto sobre atitude de médicos e usuários

Ryan B, AIDSMEDS, 2014.
Hojilla JC et al., AIDS Behav. 2015;


2 Years Of Responsible Whores
PrEP prevents HIV, 99% Efficacy, 1 pill / day
#TruvadaWhore
#LoveStigmaFree
#PrEP
Adam Zeboski
#TruvadaWhore

How Stigma Surrounding the Use of HIV Preexposure Prophylaxis Undermines Prevention and Pleasure: A Call to Destigmatize "Truvada Whores"

American Journal of Public Health | October 2015

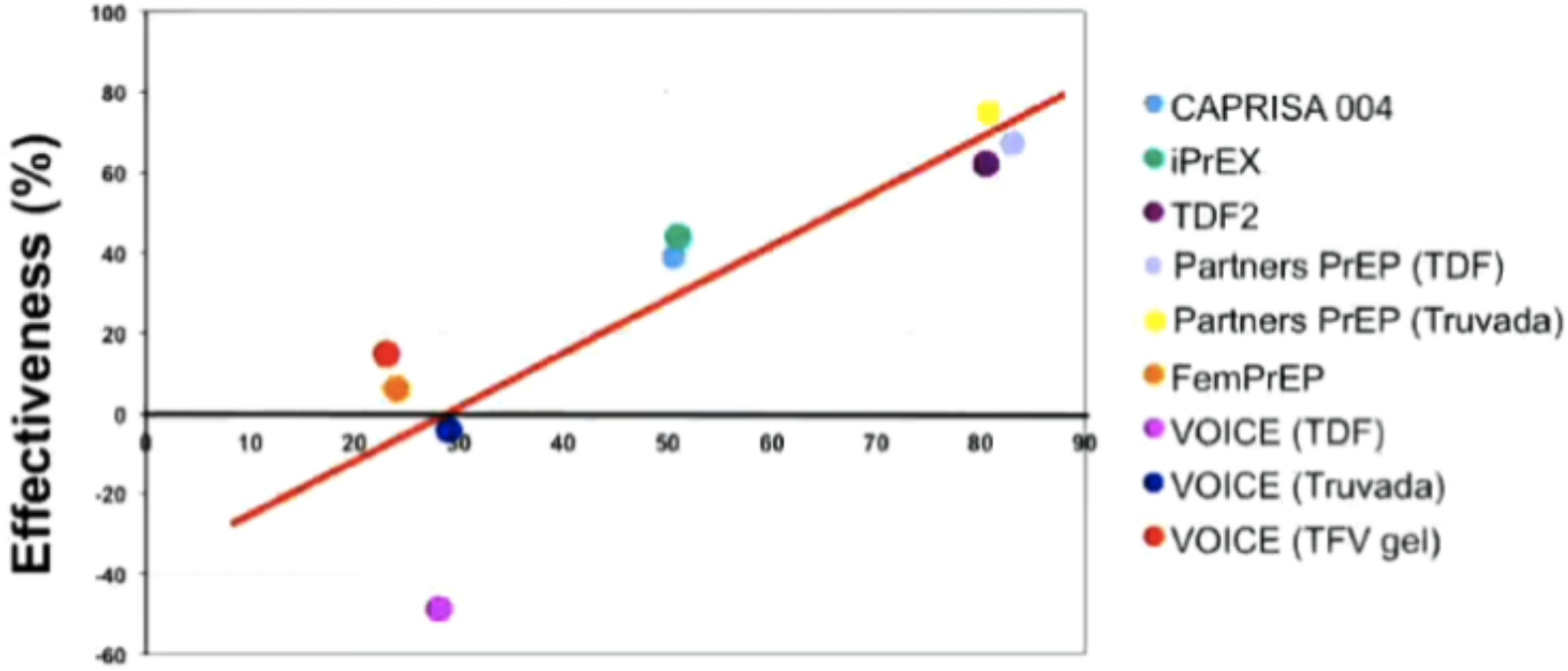
Sarah K. Calabrese, PhD, and Kristen Underhill, JD, DPhil

- "high degree of protection provided by PrEP when taken as prescribed likely outweighs the increased risk of HIV acquisition resulting from increased risk taking"
- "impeding access to PrEP could prevent a net reduction in HIV risk even for individuals who increase their sexual risk behavior"

Adesão

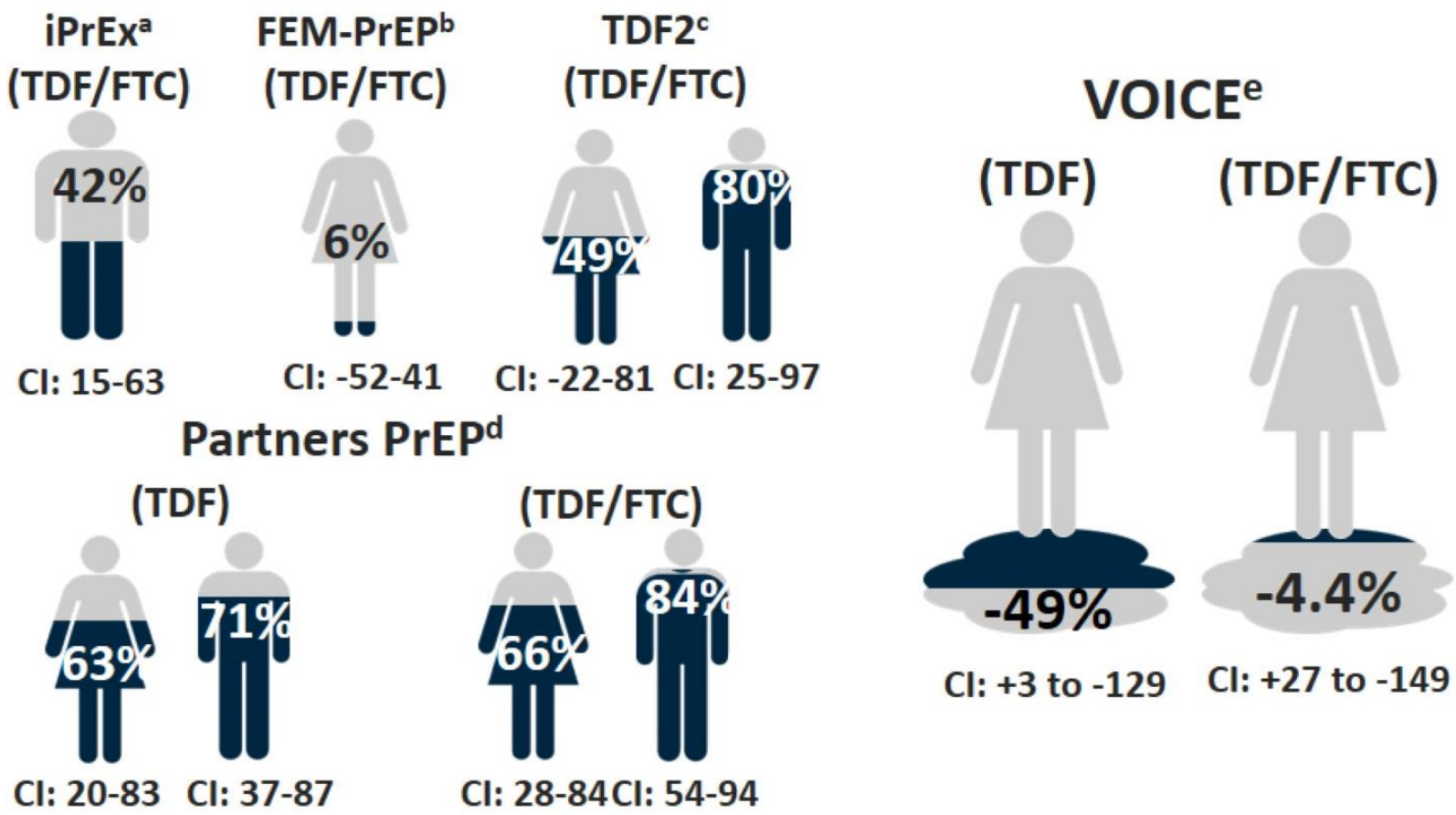
Adesão e eficácia

- Adesão e eficácia diretamente correlacionadas



Percentage of Participants' Samples with detectable drug levels
(Analysis based on a subset of total trail participants, Pearson correlation = 0.86, p=0.003)

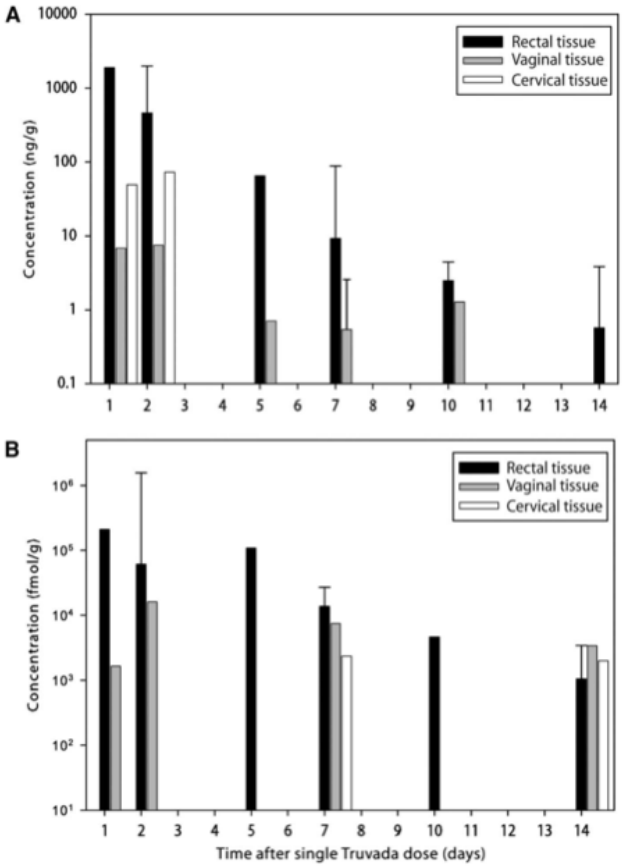
SS Abdool Karim, personal communication


iPrEx[a]
(TDF/FTC)
42%
CI: 15-63
FEM-PrEP[b]
(TDF/FTC)
6%
CI: -52-41
TDF2[c]
(TDF/FTC)
49%
80%
CI: -22-81
CI: 25-97
Partners PrEP[d]
(TDF)
63%
71%
CI: 20-83
CI: 37-87
(TDF/FTC)
66%
84%
CI: 28-84
CI: 54-94
VOICE[e]
(TDF)
-49%
CI: +3 to -129
(TDF/FTC)
-4.4%
CI: +27 to -149

Sci Transl Med. 2011 December 7; 3(112): 112re4. doi:10.1126/scitranslmed.3003174.

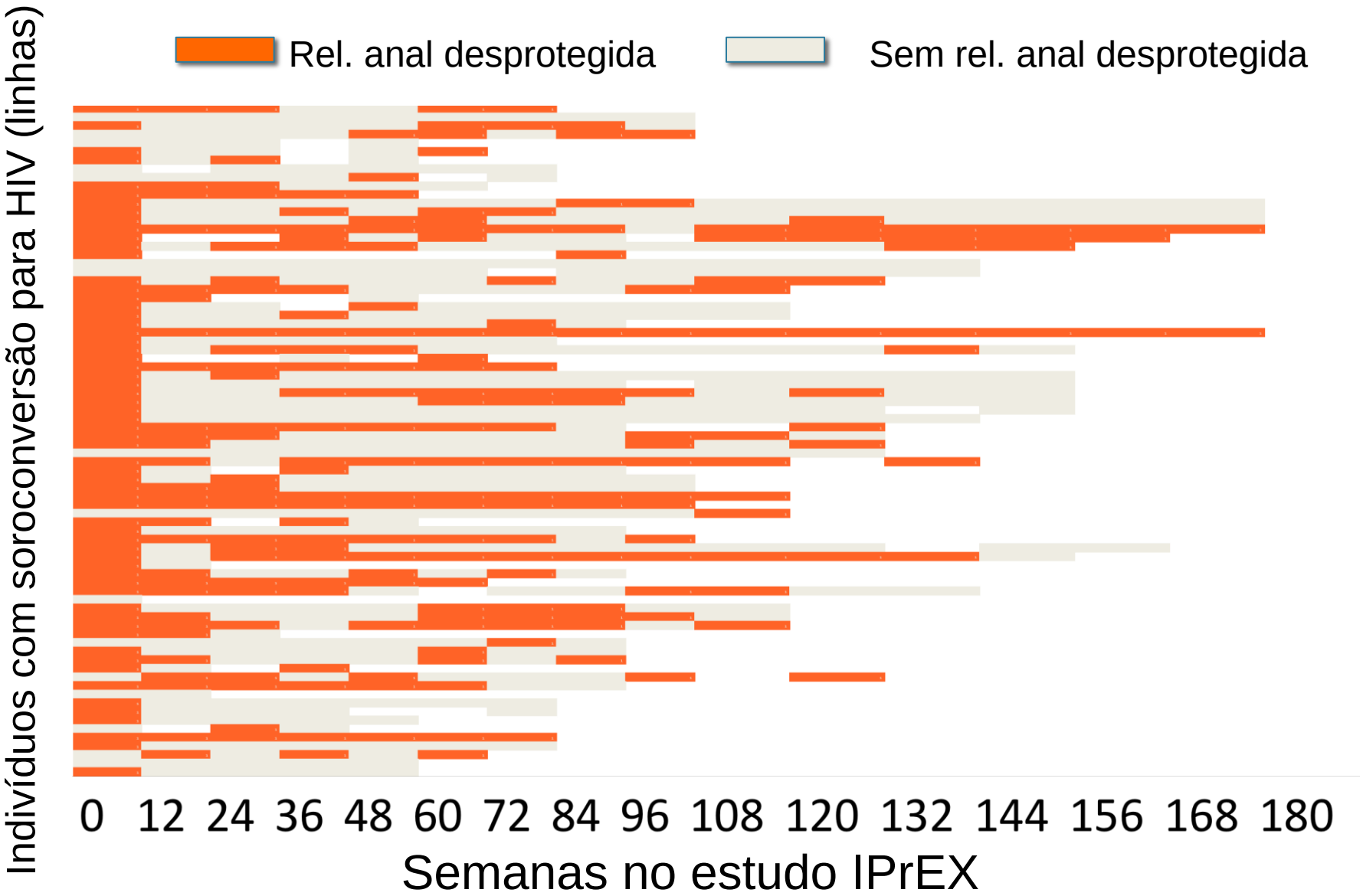
Penetration of Tenofovir and Emtricitabine in Mucosal Tissues: Implications for Prevention of HIV-1 Transmission

Kristine B. Patterson[1], **Heather A. Prince**[1], **Eric Kraft**[2,*], **Amanda J. Jenkins**[2,†], **Nicholas J. Shaheen**[1], **James F. Rooney**[3], **Myron S. Cohen**[1], and **Angela D. M. Kashuba**[2,‡]



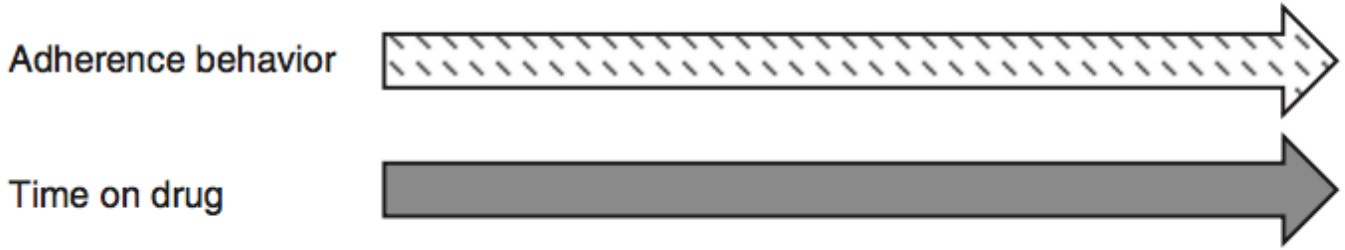
- Dose única oral deTDF/FTC
- No tecido retal, concentrações da droga permaneceram detectáveis por 14 dias e foram 100 vezes maiores que as concentrações em tecido vaginal e cervical

O Risco não é homogêneo ao longo do tempo



Defining success with HIV pre-exposure prophylaxis: a prevention-effective adherence paradigm

(a) Paradigm for ART and clinical trials: Success is achieved through 100% adherence.



(b) Prevention-effective adherence paradigm: Success is achieved because PrEP is used during all episodes of HIV exposure. Adherence to PrEP may be periodic and mapped to periods of risk.

Haberer et.al., AIDS 2015

Indução de resistência viral

Resistência viral

- Rara em todos os ensaios clínicos de PrEP– 9/243 soroconversões identificadas após início de PrEP (3.7%)
- Maioria entre participantes que estavam no período de janela à inclusão
- Mais comum nos ensaios que usaram TDF-FTC que TDF isolado,devido à mutação M184V

Lehman JID 2015
Liegler JID 2014

Segurança

Segurança

- TDF-FTC: bem tolerado em todos os estudos
- Náusea/dispepsia nas primeiras semanas de uso
- Nefrotoxicidade: rara e reversível
  - Elevação grau 2-4 de creatinina: 0,2% dos
- Densidade mineral óssea:
  - Redução média de 0,91% (IC 95%-1,44 a -0.38%) até 6m de uso da PrEP; estabilização após
  - Sem associação com maior risco de fraturas
- VHB: ausência de flares em 6 participantes após interrupção da PrEP
- Limitações: adesão imperfeita, tempo de seguimento, ausência de estudos em subgrupos específicos

Mulligan CID 2015
Solomon JAIDS 2015

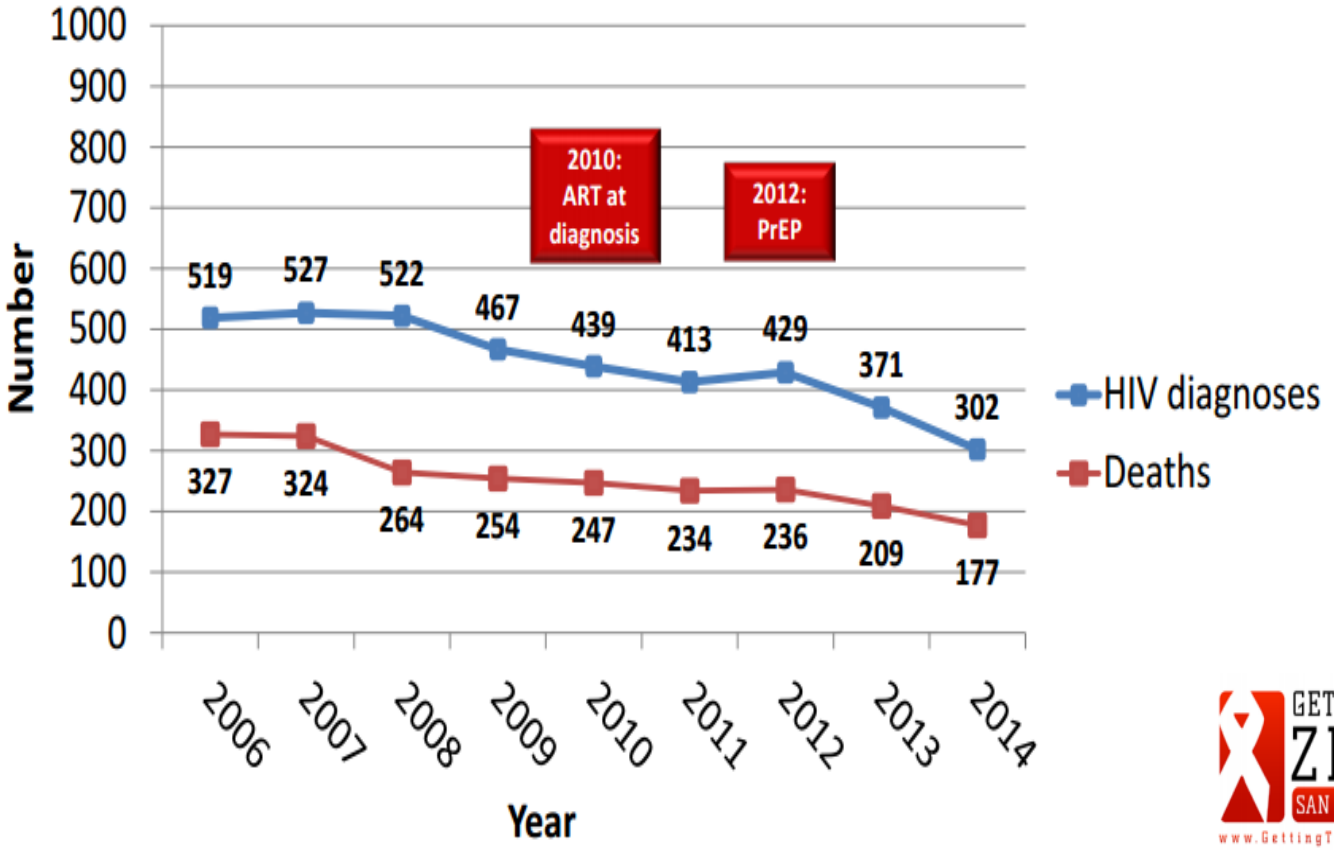
Custo-efetividade

Custo-efetividade de PrEP

Outcome to Prevent	Intervention	Number Needed to Treat
Death from colorectal cancer	Annual fecal occult blood testing colorectal screen[a]	4551
Stroke in women with no previous CV disease	Aspirin 81 mg daily[b]	411
Myocardial infarction in individuals with hypertension and average cholesterol	Atorvastatin 10 mg daily[c]	100
HIV infection in MSM	TDF/FTC 1 pill daily[d]	13

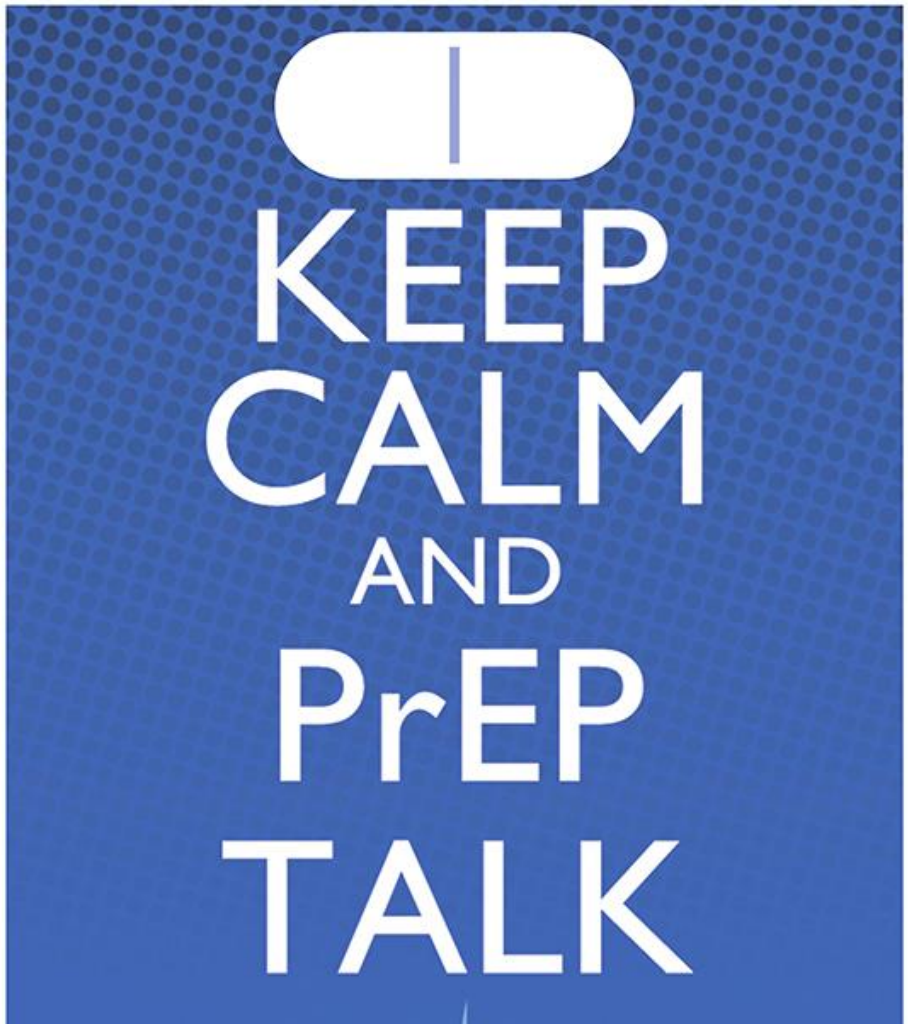
a. Mandel JS, et al. *N Engl J Med*. 1993;328:1365-71[12]; b. Berger JS, et al. *JAMA*. 2006;295:306-13[11]; c. Sever PS, et al. *Lancet.* 2003;361:1149-58[10]; d. McCormack S, et al. CROI 2015. Abstract 22LB.[9]

Número de infecções e mortes ligadas a HIV/AIDS, San Francisco, EUA



GETTING TO ZERO SAN FRANCISCO
www.GettingToZeroSF.org

San Francisco Examiner, July 2015


KEEP
CALM
AND
PrEP
TALK