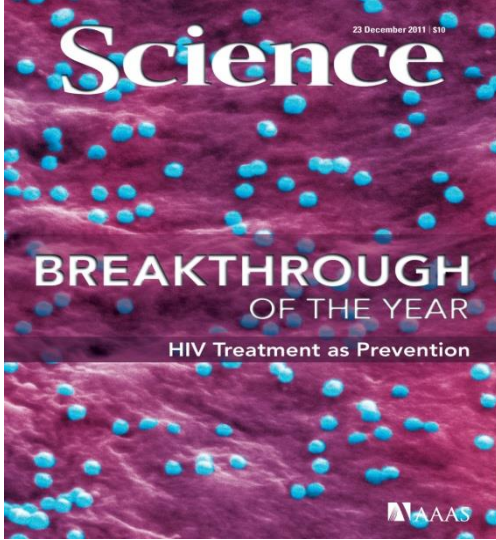




# ***Profilaxia Pré-Exposição Sexual ao HIV***

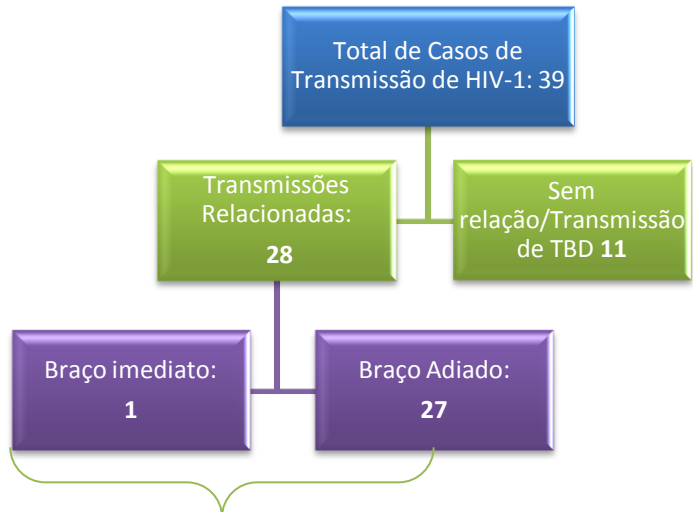
**Valdilea G. Veloso, MD,PhD**

**Fiocruz**



# HPTN 052

## Tratamento Inicial

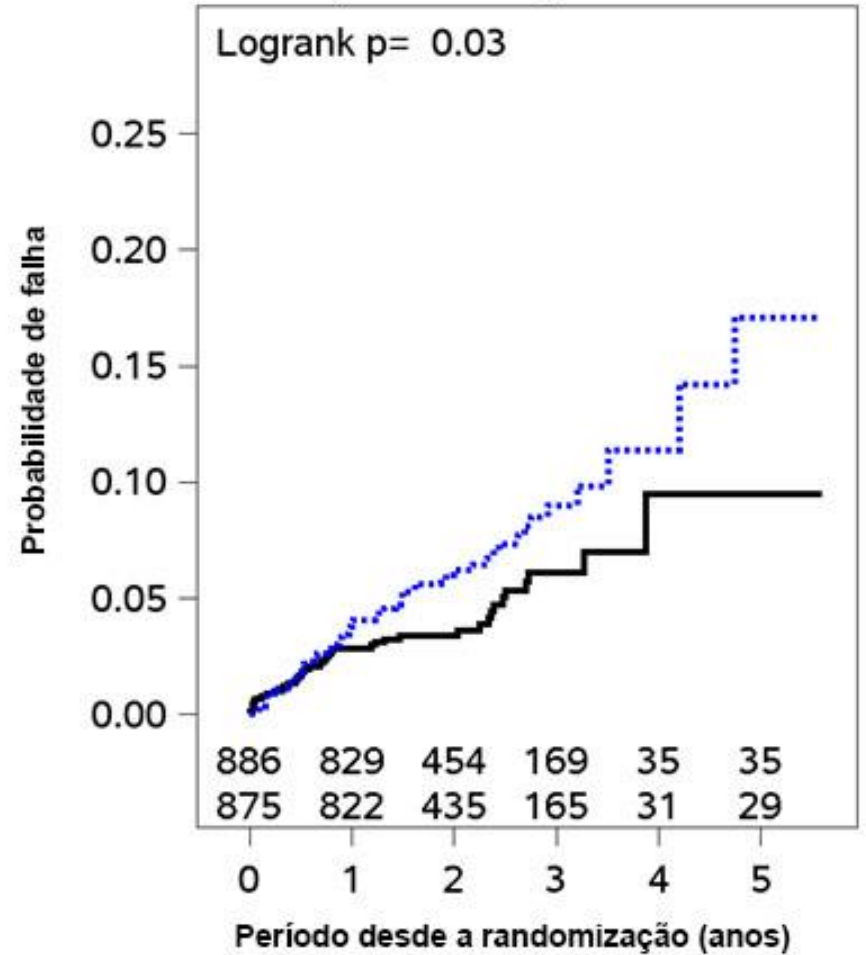


**96% de redução na transmissão**  
**p < 0,001**

Cohen et al. NEJM 2011

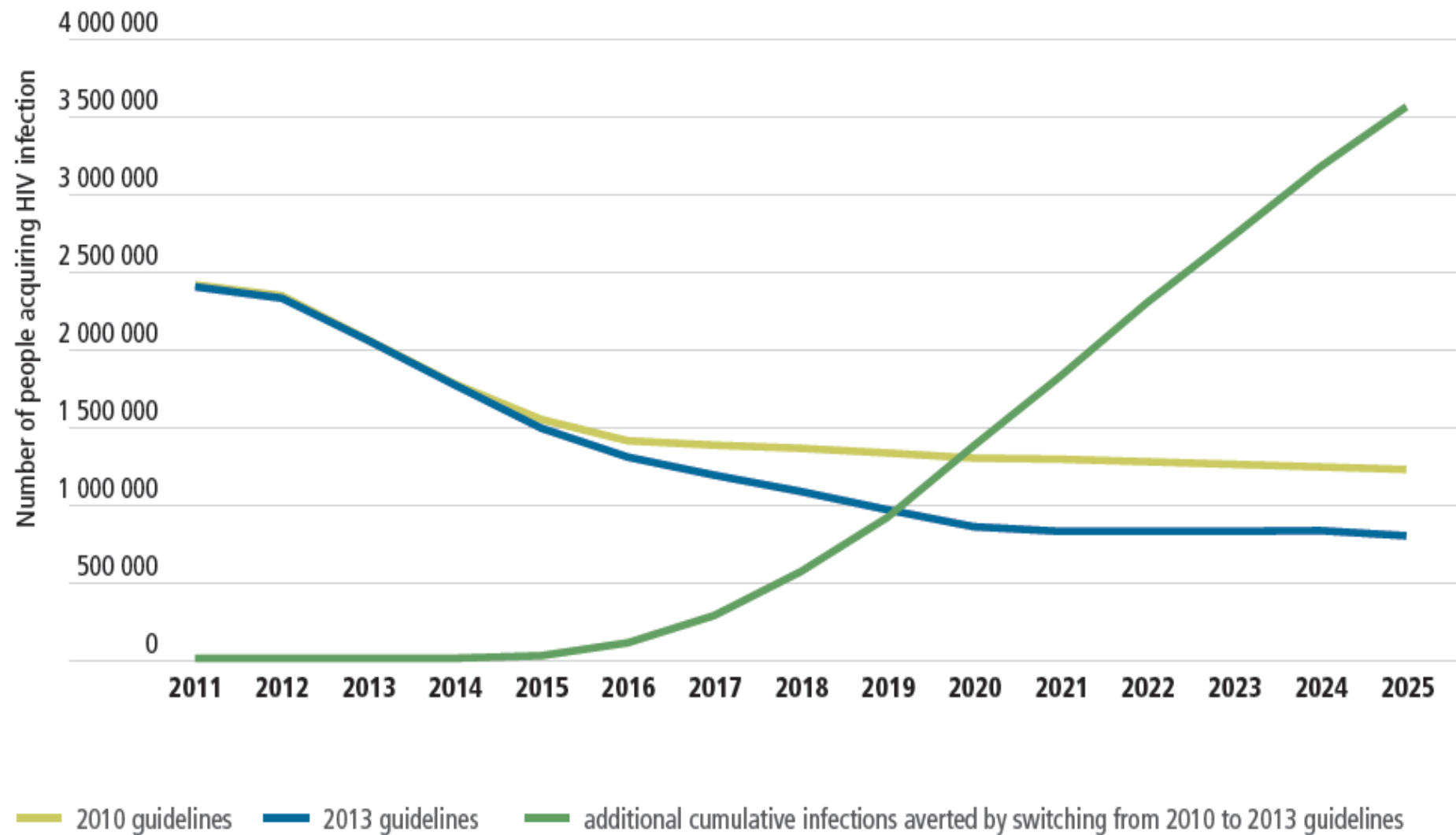
Grinsztejn et al. Lancet ID 2014

Período da primeira doença definidora da AIDS



# Incidência do HIV e as Recomendações de Tratamento da WHO de 2010 e 2013

(Futures Group, 2013)



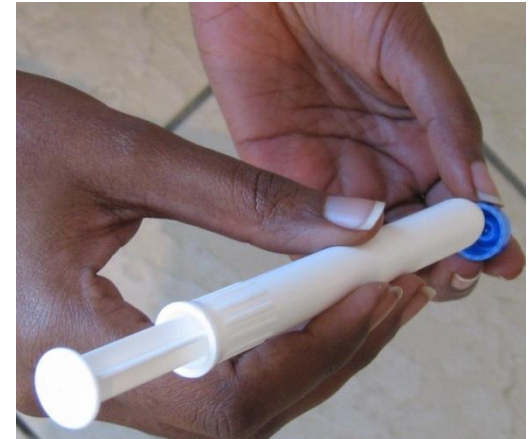
# Avaliação pré-clínica do tenofovir (TDF) + entricitabina (FTC)

- FTC ou TDF foram protetores
  - De 70% até 100% efetivos
- Entricitabina + Tenofovir
  - A combinação foi 100% efetiva
  - Mesmo após exposições retais repetidas (14)
  - Mesmo se administrado por uma vez previamente à exposição e por uma vez após
- Essa proteção provavelmente é um reflexo da
  - Alta concentração nos tecidos e fluidos genitais
  - Meia-vida intracelular longa
  - Atividade nos macrófagos

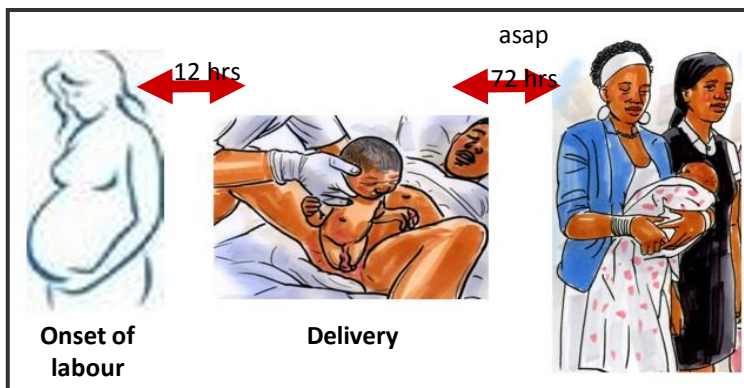


# O CAPRISA 004 avaliou a segurança e a eficácia do gel com tenofovir a 1%

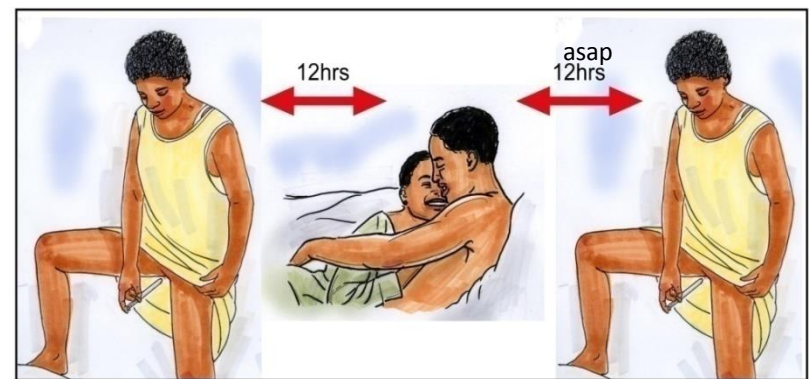
- BAT 24 uso do gel relacionado com o ato sexual
  - Inserir 1 gel até 12 h **A**ntes do sexo,
  - Inserir 1 gel o mais rápido possível em até 12 horas **D**e depois do sexo,
  - Não exceder **D**uas doses em **24** horas



HIVNET 012 esquema com nevirapina



CAPRISA 004 esquema com gel de TDF





<b>Centros</b>	<b>11</b>
<b>Participantes</b>	<b>2,499</b>

**São Francisco**

**Boston**

**Iquitos**

**Guaiaquil**

**Lima**

**São Paulo**

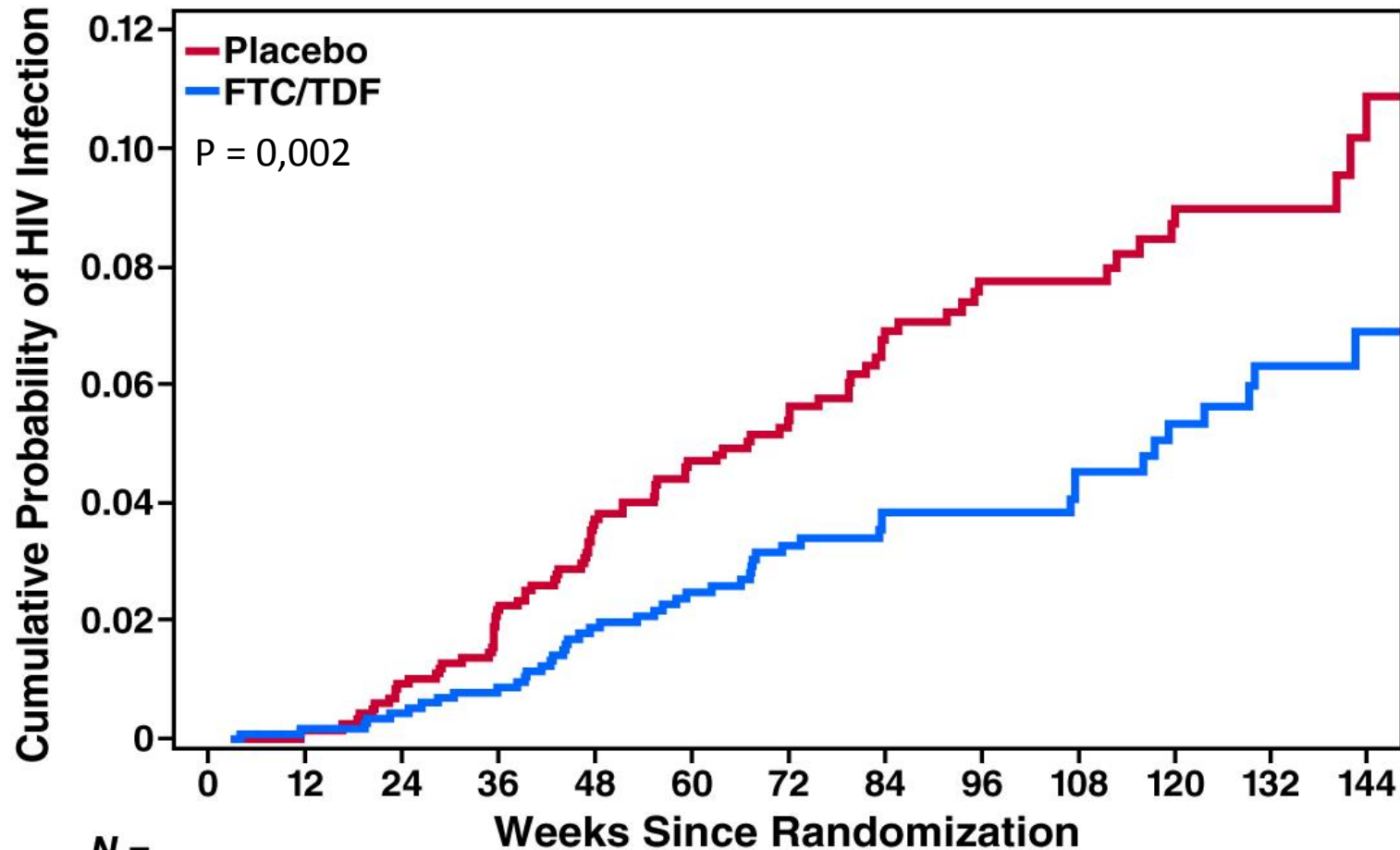
**Rio de Janeiro**

**Cidade do Cabo**

**Chiang Mai**



**Eficácia: (MITT) 42% (18-60%) até o fim do estudo**  
**Número de infecções: 83 - 48 = 35 evitadas**



N =

Placebo:	1248	1198	1157	1119	1030	932	786	638	528	433	344	239	106
FTC/TDF:	1251	1190	1149	1109	1034	939	808	651	523	419	345	253	116

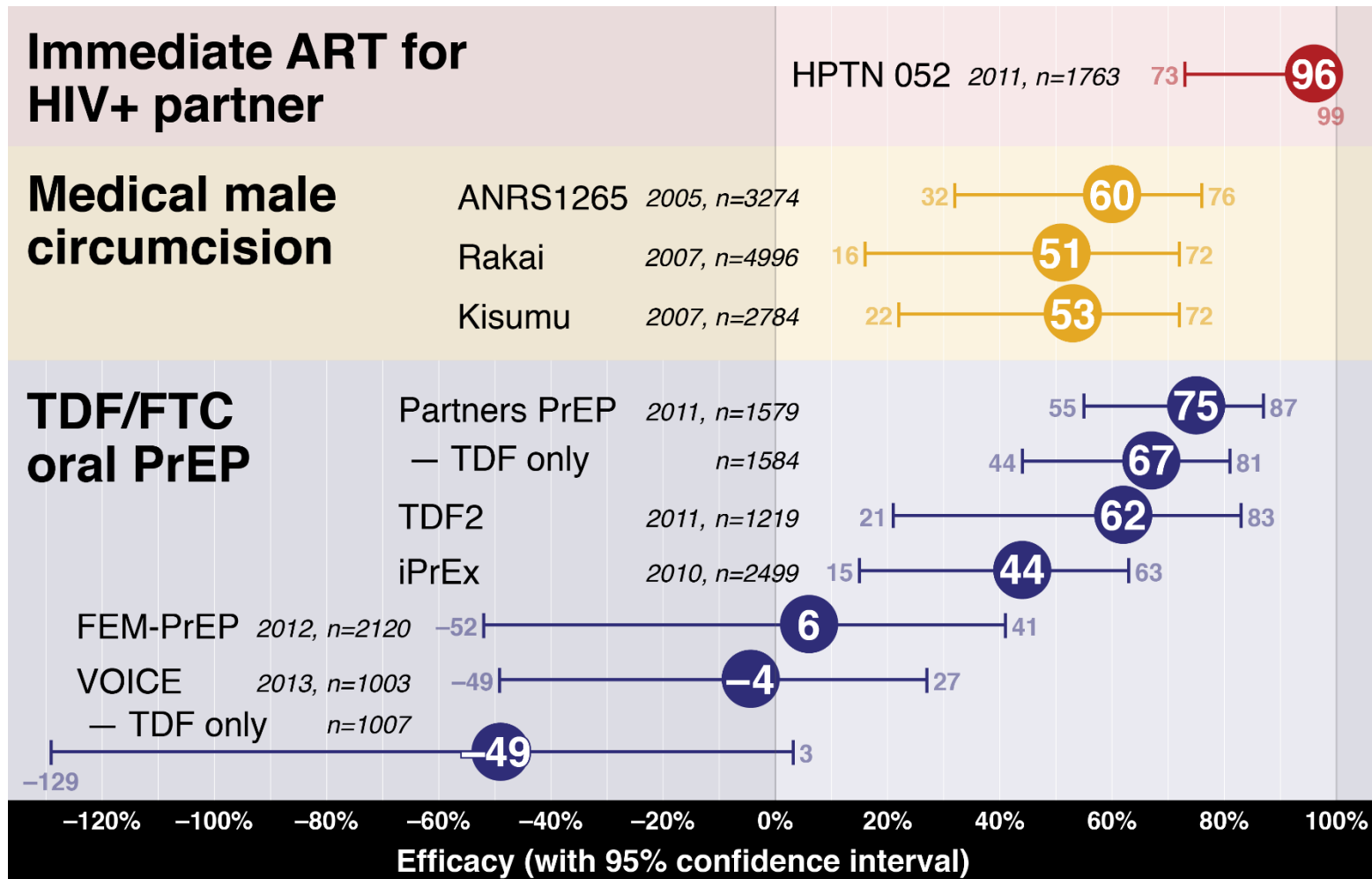
# Eficácia da PrEP com FTC/TDF diário

Estudo	Pop,	Eficácia	IC de 95%
iPrEx	MSM	42%	18 a 60%
Partners PrEP	Homens	83%	49 a 94%
	Mulheres	62%	19 a 82%
TDF2	Homens	80%	25 a 97%
	Mulheres	49%	-22 a 81%
FemPREP	Mulheres	*	

\*DSMB recommended discontinuation for fertility; drug level testing is in progress,



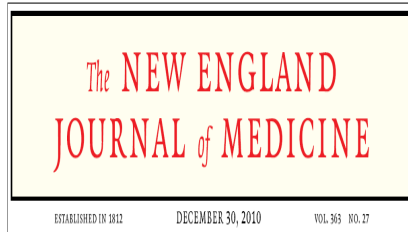
# Eficacia de Intervenciones Biomedicas para prevenir la adquisici3n del HIV



# 16/Julho/2012 FDA Aprova o uso do Truvada para Prevenção

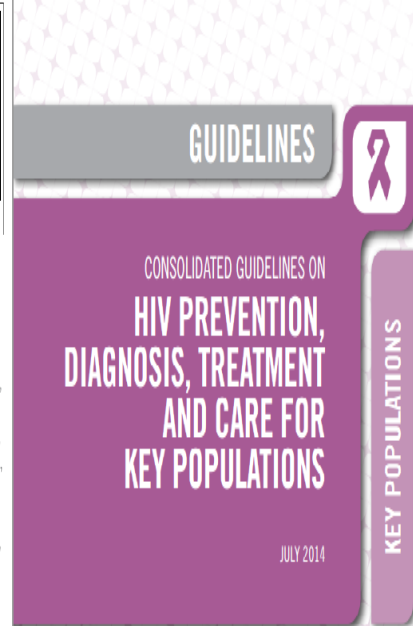


# Profilaxia Pré-Exposição (PrEP)



## 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 McMahon, B.S., Albert Y. Liu, M.D., M.P.H., Lorena Vargas, Pedro Goicochea, M.Sc., Martin Casapia, 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 Fernandez, M.D., Valdeia G. Veloso, M.D., Ph.D., Susan P. Buchbinder, M.D., Suwat Charinyalertsak, 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 Delcheux, 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\*



## THE LANCET Infectious Diseases

Jul 22, 2014

Comment

### Moving HIV PrEP from research into practice

Raphael J Landovitz, Thomas J Coates

Articles

Jul 22, 2014

### Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: a cohort study

Robert M Grant, Peter L Anderson, Vanessa McMahan, Albert Liu, K Rivet Amico, Megha Mehrotra, Sybil Hosek, Carlos Mosquera, Martin Casapia, Orlando Montoya, Susan Buchbinder, Valdeia G Veloso, Kenneth Mayer, Suwat Charinyalertsak, Linda-Gail Bekker, Esper G Kallas, Mauro Schechter, Juan Guanira, Lane Bushman, David N Burns, James F Rooney, David V Glidden

### Southern African guidelines for the safe use of pre-exposure prophylaxis in men who have sex with men who are at risk for HIV infection

Southern African HIV Clinicians Society Consensus Committee

US Public Health Service

## PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES - 2014

A CLINICAL PRACTICE GUIDELINE



### Special Communication

### HIV Prevention in Clinical Care Settings: 2014 Recommendations of the International Antiviral Society–USA Panel

FREE



Jeanne M. Marrazzo, MD, MPH; Carlos del Rio, MD; David R. Holtgrave, PhD; Myron S. Cohen, MD; Seth C. Kalichman, PhD; Kenneth H. Mayer, MD; Julio S. G. Montaner, MD; Darrell P. Wheeler, PhD, MPH; Robert M. Grant, MD, MPH; Beatriz Grinsztejn, MD, PhD; N. Kumarasamy, MD, PhD; Steven Shoptaw, PhD; Rochelle P. Walensky, MD, MPH; Francois Dabis, MD, PhD; Jeremy Sugarman, MD, MPH; Constance A. Benson, MD

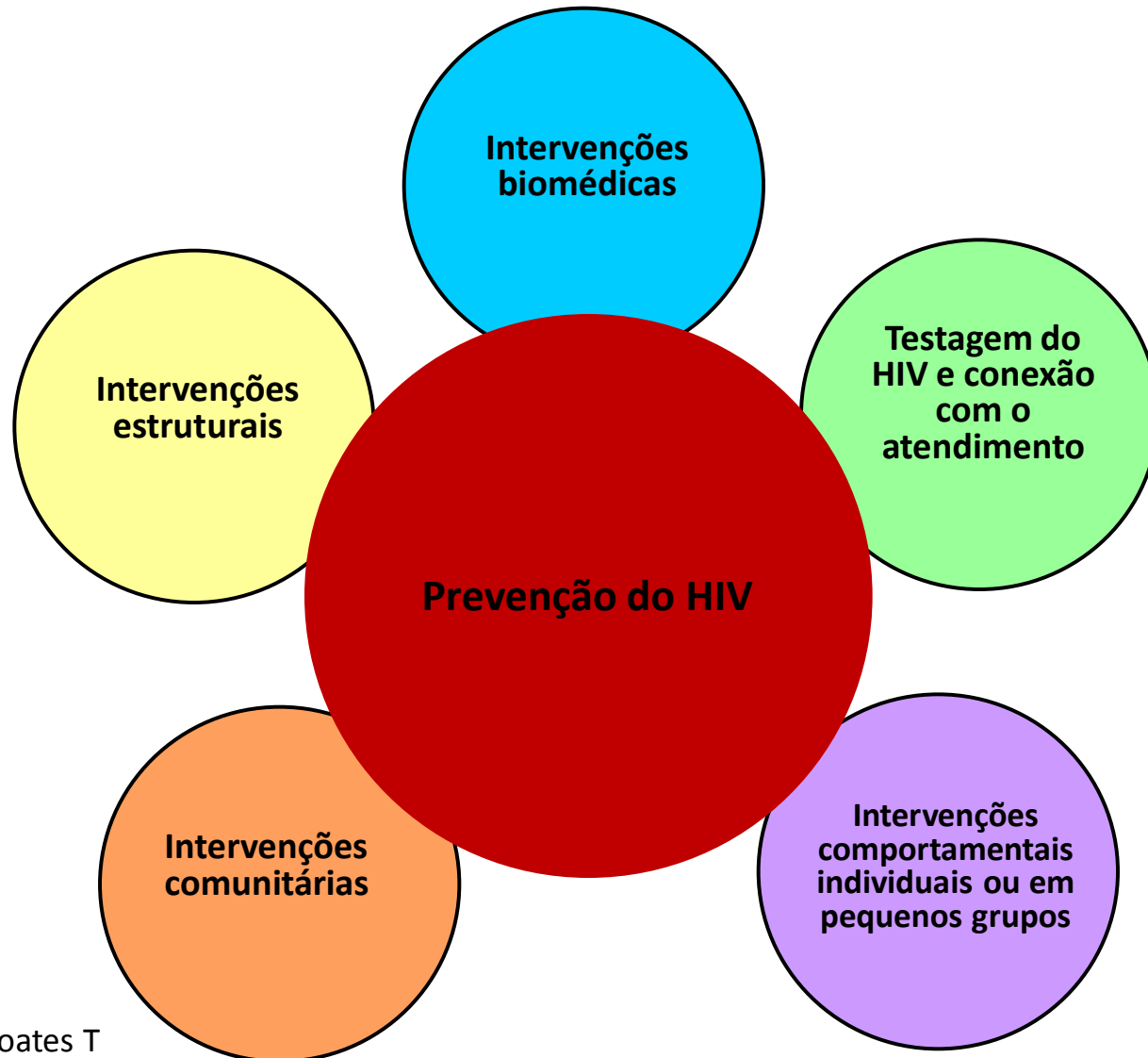
# Sumário das Recomendações da OMS para as populações chave

## HEALTH SECTOR INTERVENTIONS

### HIV PREVENTION

<b>1</b>	The correct and consistent use of condoms with <b>condom-compatible lubricants</b> is recommended for all key populations to prevent sexual transmission of HIV and sexually transmitted infections (STIs).
<b>2</b>	Among men who have sex with men, <b>pre-exposure prophylaxis (PrEP)</b> is recommended as an additional HIV prevention choice within a comprehensive HIV prevention package. <b>NEW RECOMMENDATION</b>
<b>3</b>	Where serodiscordant couples can be identified and where additional HIV prevention choices for them are needed, daily oral <b>PrEP</b> (specifically tenofovir or the combination of tenofovir and emtricitabine) may be considered as a possible additional intervention for the uninfected partner.
<b>4</b>	<b>Post-exposure prophylaxis (PEP)</b> should be available to all eligible people from key populations on a voluntary basis after possible exposure to HIV.
<b>5</b>	<b>Voluntary medical male circumcision (VMMC)</b> is recommended as an additional, important strategy for the prevention of heterosexually acquired HIV infection in men, particularly in settings with hyperendemic and generalized HIV epidemics and low prevalence of male circumcision.

# Combinando a prevenção com *abordagens multidisciplinares*



# Principais Questões

- Compensação de Risco
- Resistência
- Adesão
- Como implementar ?

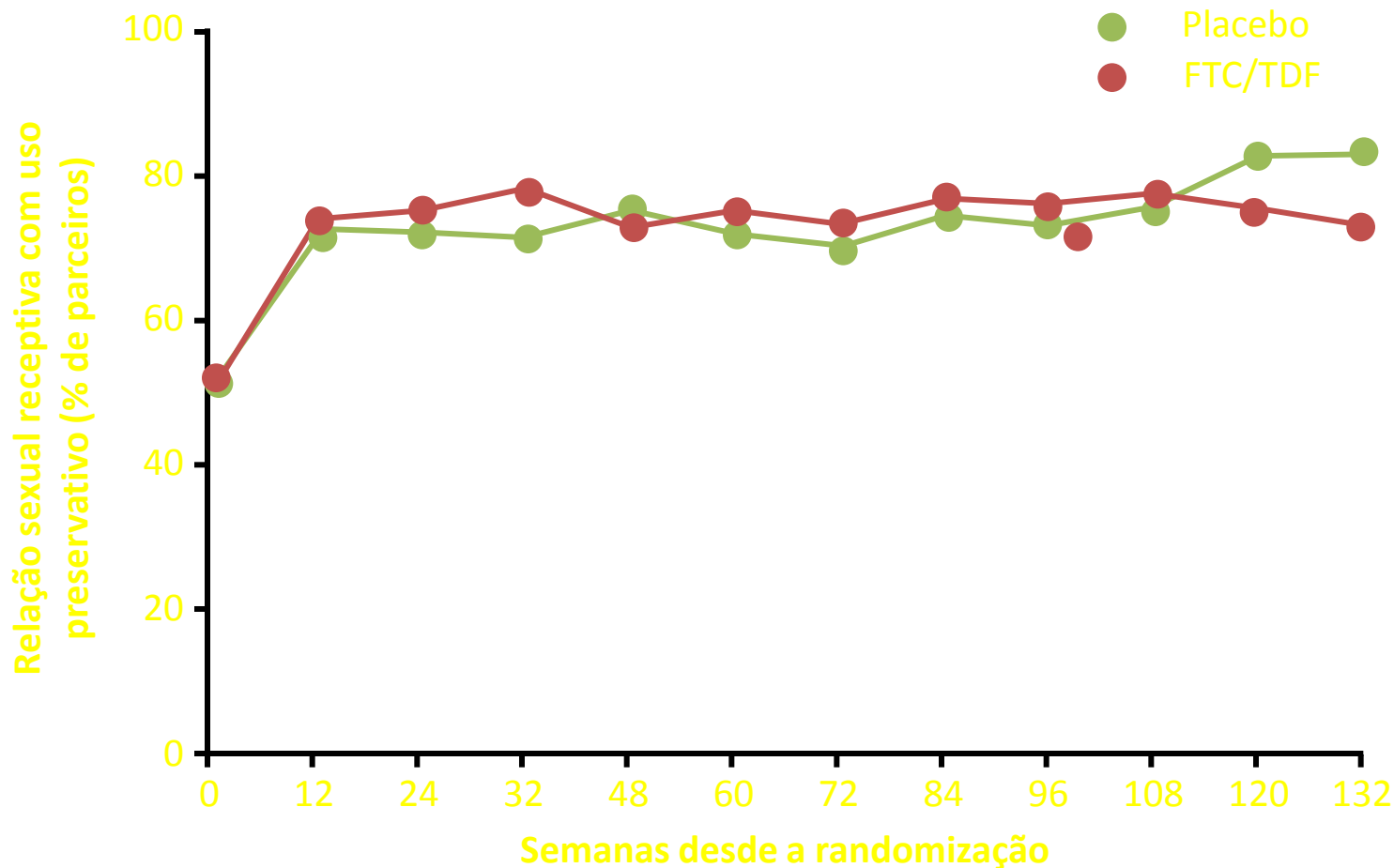
# Compensação de Risco

---

- **Não evidenciada nos Ensaio Clínicos de PrEP**
  - **Nos ensaios clínicos os participantes sabiam que poderiam estar recebendo placebo**
  - **Aconselhamento repetido enfatizando que o medicamento ainda não tinha eficácia comprovada e que o uso dos preservativos deveria ser mantido**



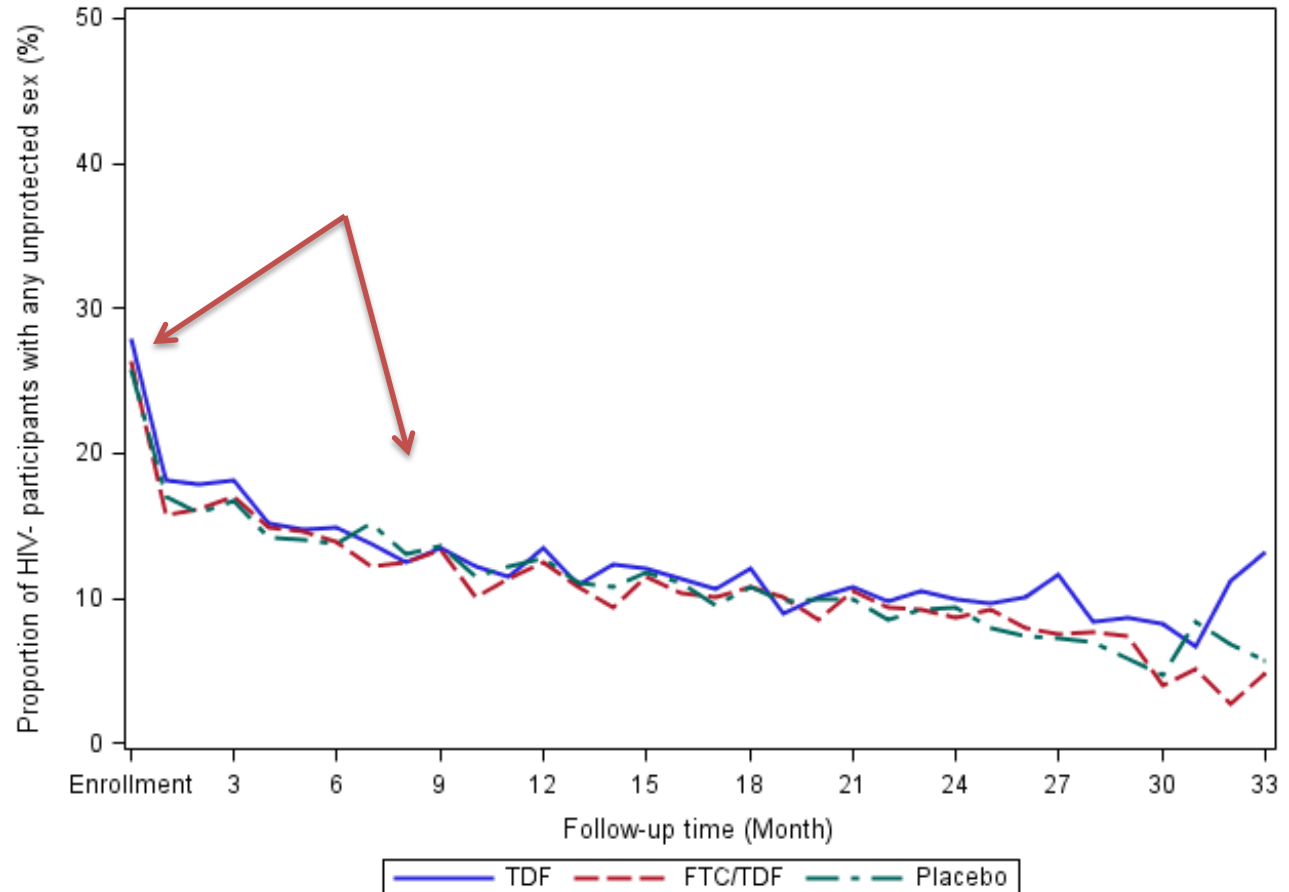
# iPrEx: Uso de preservativos na prática de sexo de alto risco



Grant R, et al, CROI 2011, Abstract 92.

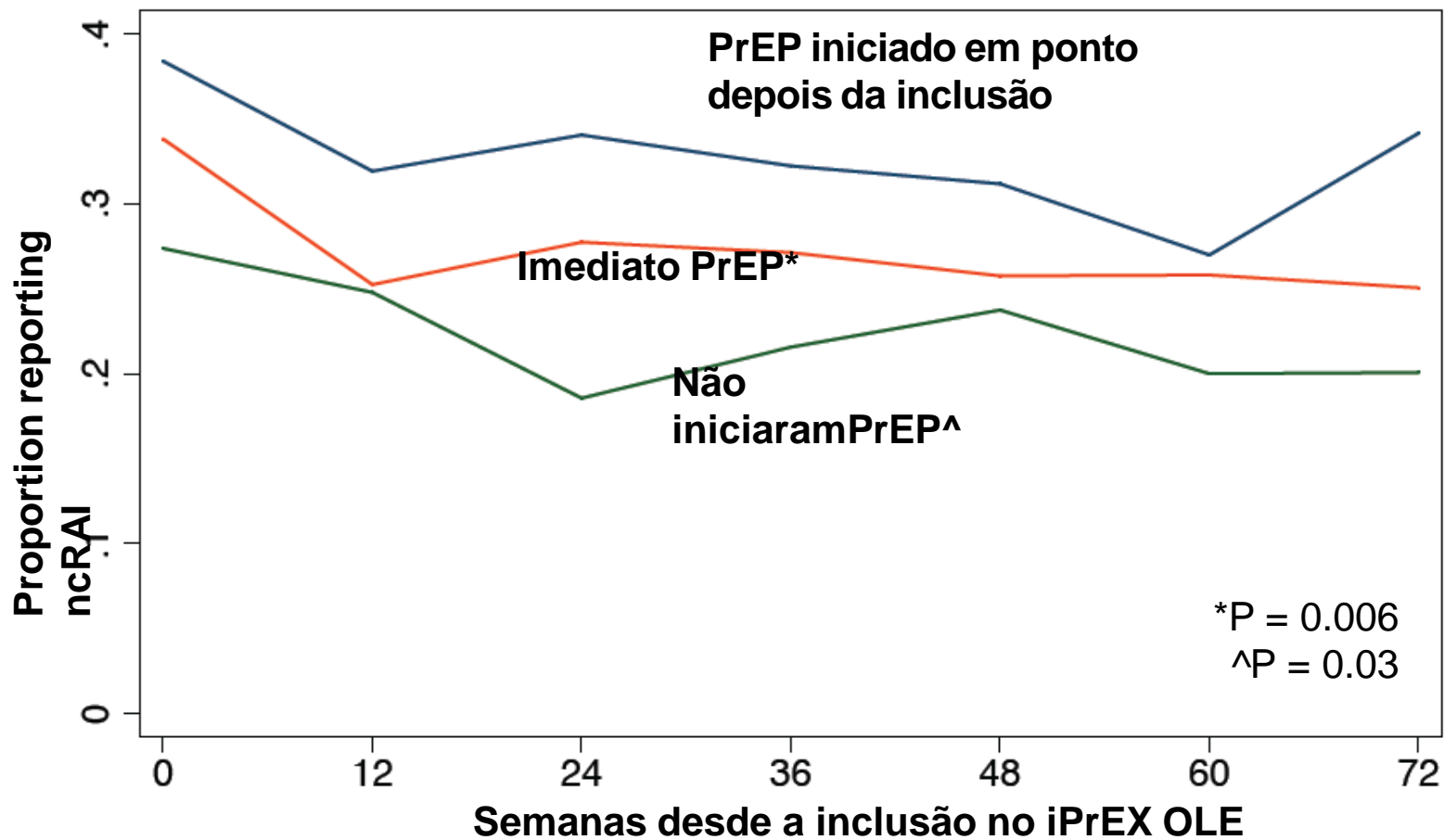


# Comportamento sexual





## Sexo Anal Receptivo sem Preservativo (ncRAI)



# Seat Belt Use in Cars with Air Bags

**Abstract:** Seat belt use was observed in 1,628 cars with air bags and manual belts and 34,223 cars with manual seat belts only. Sixty-six percent of drivers in cars with air bags wore seat belts compared to 63 percent of drivers in cars with manual belts only. The study found no evidence for the speculation that drivers with air bags will reduce their seat belt use because they believe an air bag alone provides sufficient protection. (*Am J Public Health* 1990; 80:1514–1516.)

# Uso de preservativo na década de 80, antes dos antirretrovirais

## PUBLIC HEALTH BRIEFS

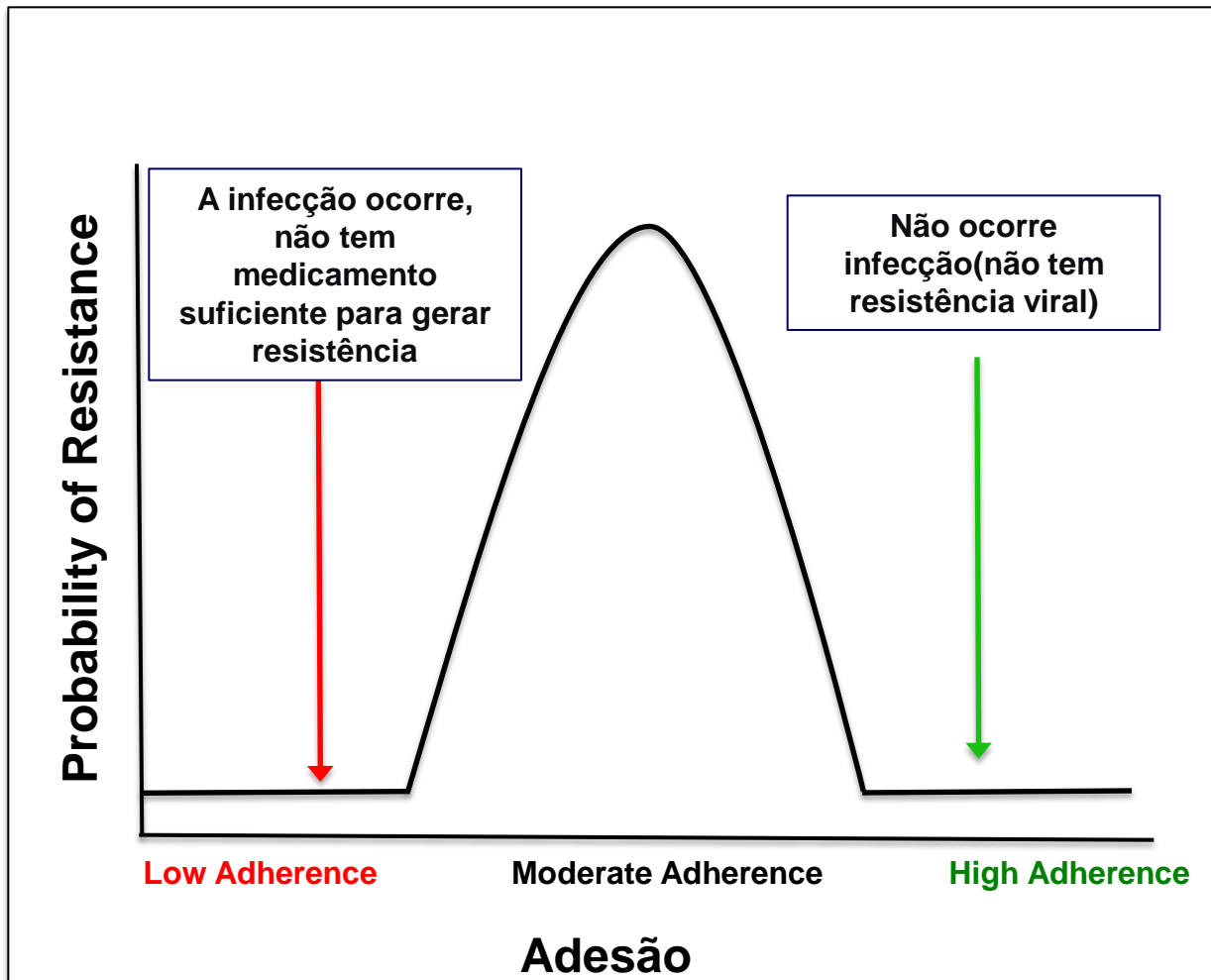
**TABLE 1—Serial Cross-Sectional Prevalence of Condom Use in Receptive Anal Sex at Visit 4 (V4) and Visit 5 (V5)**

	V4 N (%)	V5 N (%)
No receptive anal sex	375 (52)	341 (53)
Consistent condom use	66 (9)	78 (12)
Inconsistent condom use	96 (13)	94 (15)
Condoms never used	192 (26)	129 (20)
Total	729	642

### Discussion

Intra-individual fluctuations in individual risk-relevant behaviors have been reported in many longitudinal studies of homosexual men.<sup>6</sup> As early as 1985, a report from San Francisco noted that over the course of one year, approximately half the men observed in one cohort had changed their behavior, from completely or probably safe to probably or definitely risky.<sup>7</sup> Aggregate measures, as we demonstrated, can underestimate the magnitude of change to safer sexual practices, but even more important, they often fail to convey important information on adoption, maintenance and relapse in individual patterns of behavior over time. They are therefore, an essential part of evaluating long-term behavioral change, whether the change is related to HIV/AIDS or to other conditions.

# Qual é a Relação entre Resistência e Adesão ?



# Resistência

- A resistência foi rara nos ensaios clínicos de PrEP
  - infecção aguda não diagnosticada ao iniciar ARV
  - resistência: K65R (TDF) ou M184V/I (FTC)

Número de Soroconvertores (HIV) em PrEP Ativo com Resistência ao HIV			
Trial	HIV Infected After Enrollment, n/N	Seronegative Acute HIV Infection at Enrollment, n/N	HIV Infections Averted, n
iPrEx <sup>[1,2]</sup>	0/36	2/2	28
Partners PrEP <sup>[3]</sup>	0/30	2/8	74
TDF2 <sup>[4]</sup>	0/10	1/1	16

1. Liegler T, et al. J Inf Dis. 2014 [Epub ahead of print]

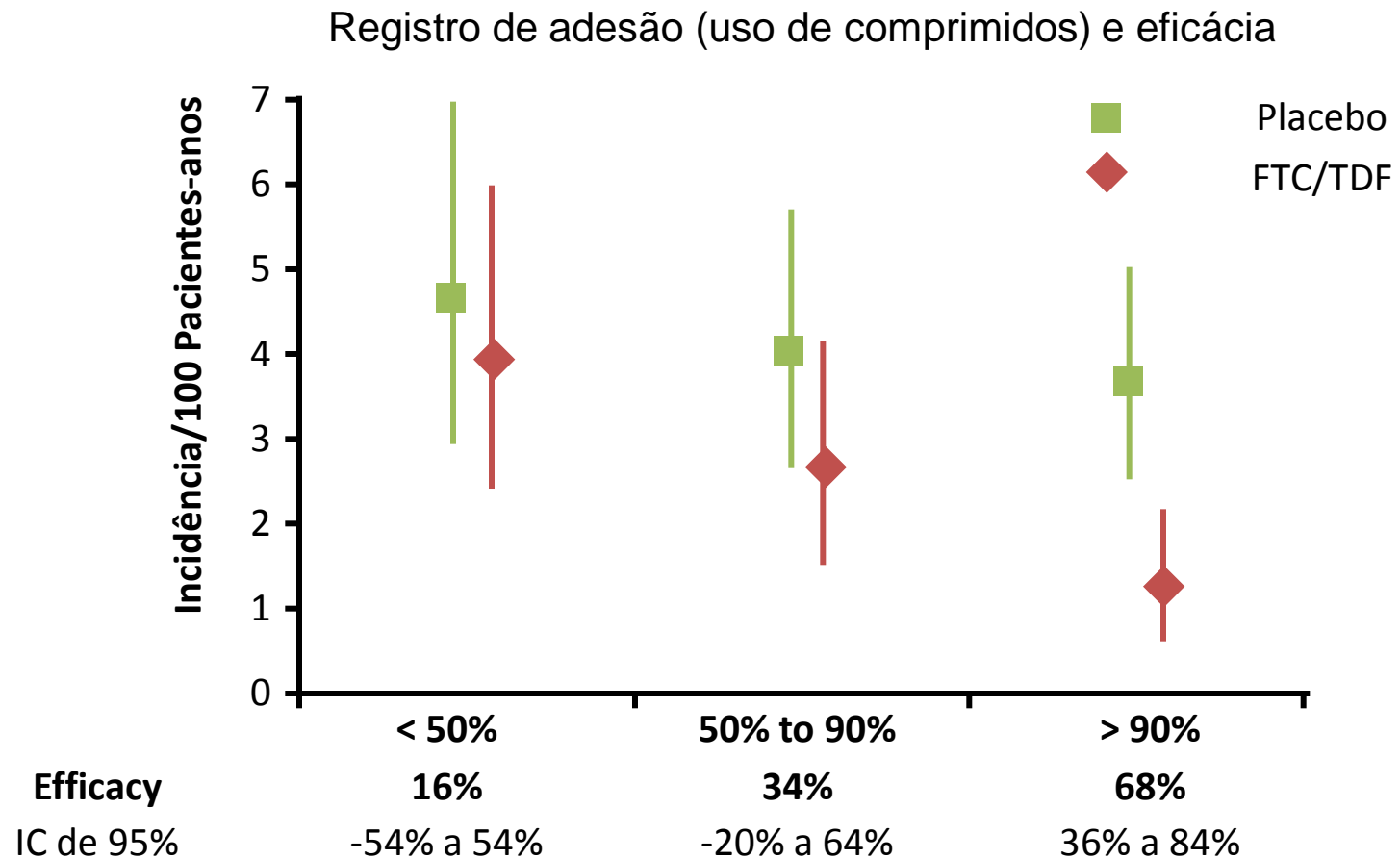
2. Grant RM, et al. N Engl J Med. 2010;363:2587-2599.

3. Baeten JM, et al. N Engl J Med. 2012; 367:399-410. (supplementary appendix).

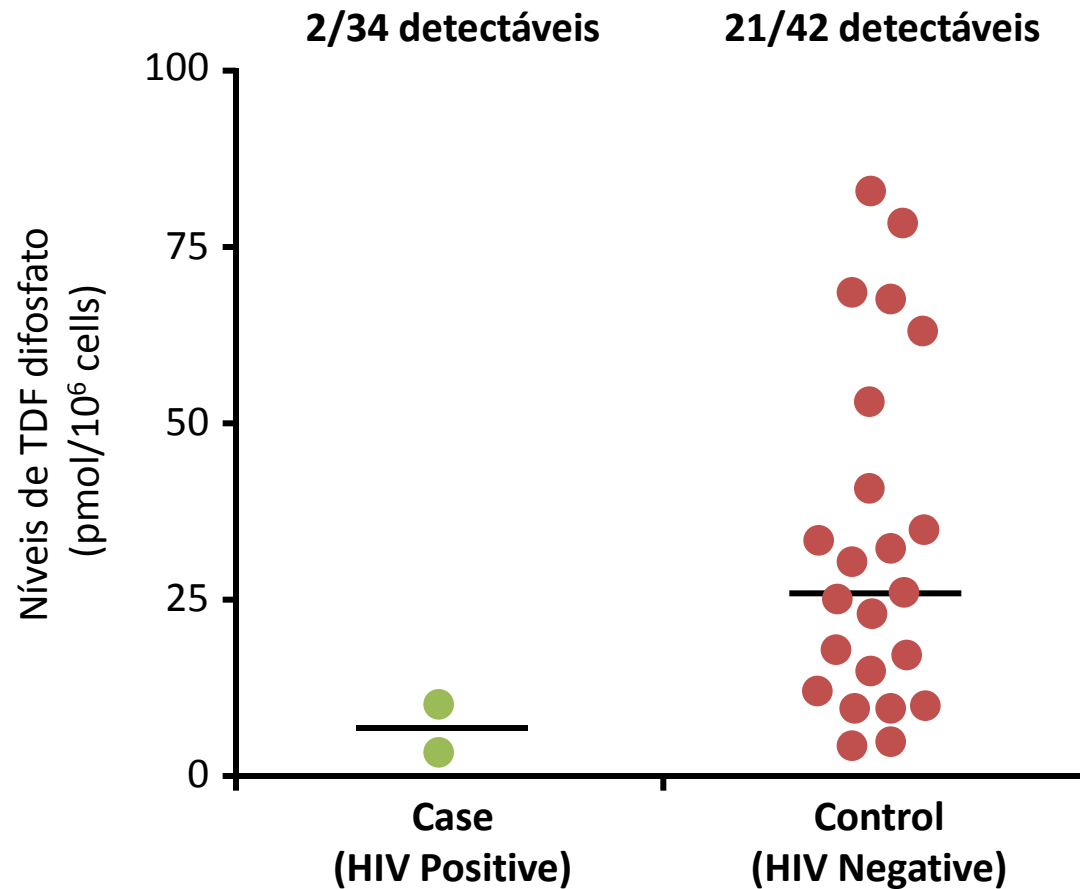
4. Thigpen MC, et al. N Engl J Med. 2012; 367:423-434. (supplementary appendix).



# iPrEx: Registro de adesão e eficácia

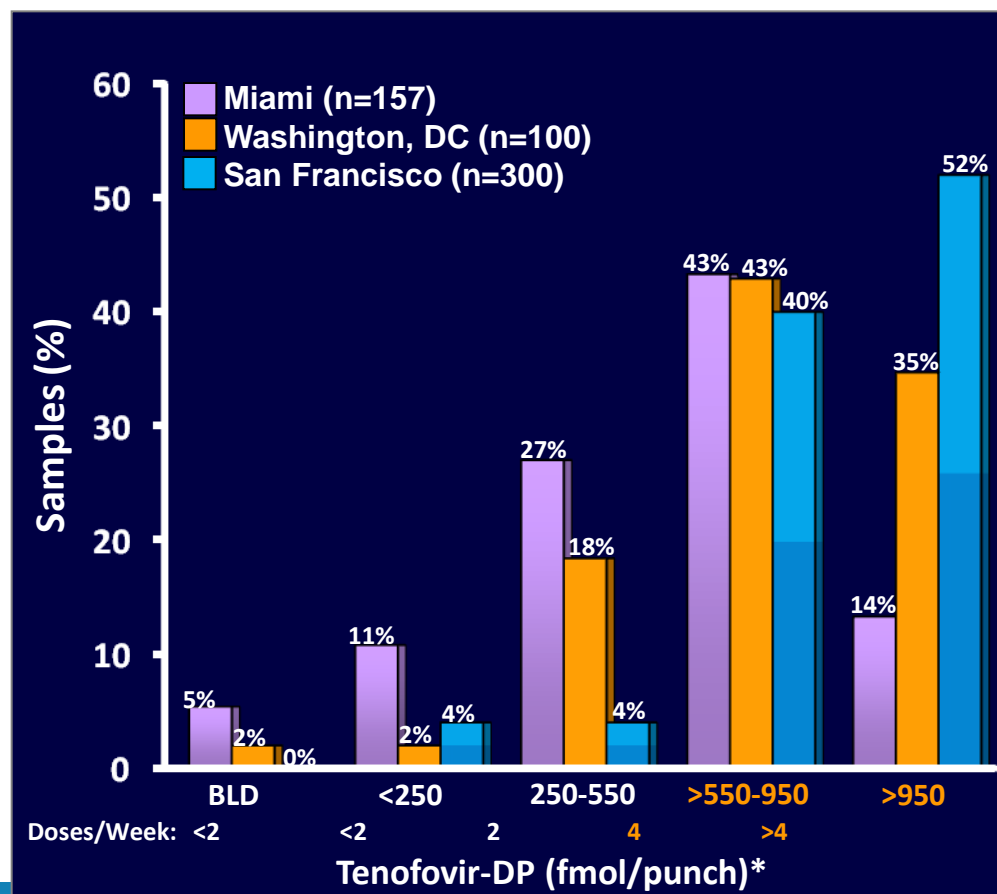


# iPrEx: Níveis de medicamentos pelo *status* de HIV no grupo de FTC/TDF



# É possível alcançar altos níveis de Adesão: Projeto de Demonstração de PrEP nos EUA (2012-2014)

- Clínica de DST em São Francisco, Miami e Washington, DC (n=831)
- 48 semanas de Truvada
  - Aceitação: 60.4%
    - 77% com níveis detectáveis de Tenofovir equivalentes a tomada de  $\geq 4$  doses/semana
- Os que mais usaram PrEP foram os que relatavam comportamento de maior risco



BLD: below limit of detection.

\*femtomole/punch: measure of flux density.





# Próximas etapas

---

- Resultados finais dos projetos de Demonstração de dose diária de FTC/TDF
- Dose intermitente de FTC/TDF (HPTN 066, 067, ANRS Study in France/Quebec)
- Dose diária de agentes alternativos(HPTN 069)
- Formulações com ação de longa duração (TMC278LA and GSK1265744), adesivos (patch), anéis vaginais/filmes (Dapivirina, TDF, others)



# Estratégias para melhorar a Execução e a Aderência à PrEP

Novas drogas e estratégias de dosagem para PrEP



Novas estratégias de aderência



Sistemas de execução e formulações alternativas

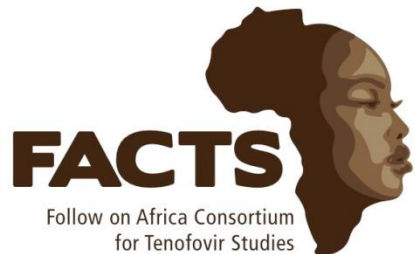


Microbicidas Retais:  
MTN-017 (TFV gel retal)



Injetáveis:  
Rilpivirine-LA  
GSK744

# “Sob Demanda” Produtos



## ❖ Tenofovir Gel (Estudo CONRAD)

- Efetivo na prevenção do HIV (39%) e HSV-2 (51%) no estudo CAPRISA 004, mas não verificado no VOICE
- Ensaio Clínico de Confirmação (FACTS 001) Coito dependente. Resultados esperados para 2015
  - 2,900 mulheres, 8-30 anos (África do Sul)
- Gel Retal: MTN 017 Fase II, 360 HSH e Travestis
  - Peru, South Africa, Thailand and US

## ❖ Novos produtos tópicos (Gel)

- MIV-150 (ITRNN) + Acetato de Zinco + LNG (Pop Council)
- Griffithsin: inibe a ligação com gp120 e gp41 (NCI/Palmer)
- 5P12-RANTES: bloqueador de co-receptor (Mintaka)
- IQP-0528: ITRNN e bloqueador de entrada (IMquest)





Sites	11
Total enrolled in OLE	1770
PrEP Eligible	1603
Average age	2
	8

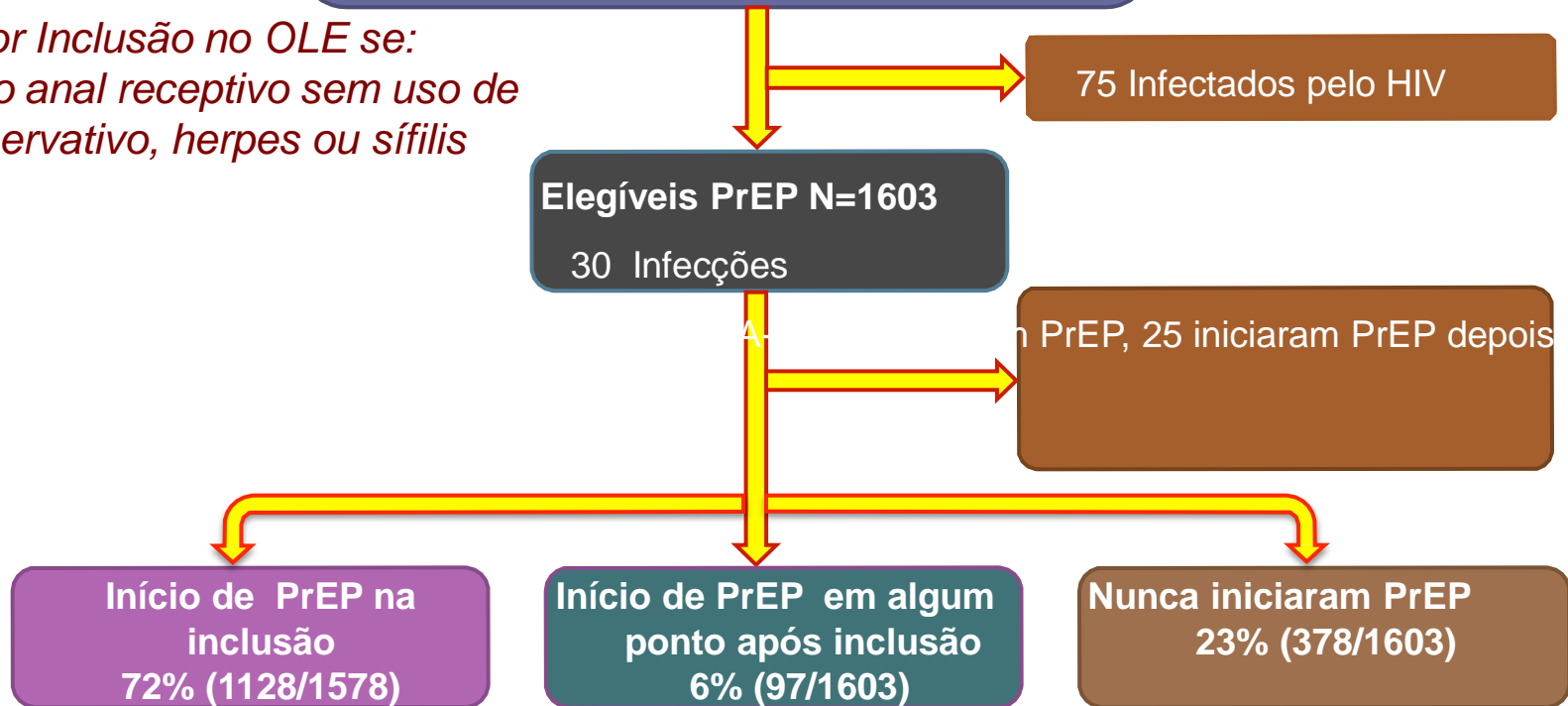




# iPrEX OLE (não infectados)

<i>Trial</i>	<i>Incluídos/OLE Eligible</i>	<i>%</i>
iPrEx	1526/2336	65%
ATN 082	46/68	68%
US Safety Study	106/271	39%
<b>Total</b>	<b>1678/2680</b>	<b>62%</b>

*Maior Inclusão no OLE se:  
Sexo anal receptivo sem uso de preservativo, herpes ou sífilis*





# Razão para não iniciar PrEP

CASI no momento da inclusão (mais de uma opção possível de ser marcada) N=373

Razão para não iniciar PrEP	%
Preocupação com efeitos colaterais do medicamento	50%
Não deseja tomar medicamentos todos os dias	16%
Não gosta de tomar medicamentos	13%
Pode prevenir o HIV de outras formas	14%
Preocupação que possam pensar que estou HIV+ por estar tomando Truvada	7%
Preocupação que as pessoas saibam que tenho sexo com homens e/ou travestis porque estou tomando Truvada	3%

*Reasons did not differ by prior randomized assignment to active vs. placebo*



# Decisão de iniciar PrEP

	% Coorte do estudo	% Início de PrEP	Início de PrEP P Value
Sexo Anal Receptivo sem Preservativo			0.003
Não	68%	75%	
Sim	32%	81%	
HSV +			0.03
Não	87%	75%	
Sim	13%	77%	

*Sem diferença na decisão de iniciar PrEP: idade, escolaridade, identidade transsexual, grupo de randomização no iPrEX, uso de drogas (álcool, anfetamina ou cocaína)*



# iPrEX OLE

- As Travestis: quase 30% menos prováveis de ter altas concentrações nos cartões de sangue coletados para medir tenofovir (aOR 0.72, P = 0.02).
- Nenhum participante que usou Truvada 4 a 6 vezes por semana ou diariamente se infectou durante o estudo
  - Incidência do HIV segundo uso estimado do Truvada
    - Nenhum comprimido: 4,7 por 100 pessoas-ano
    - < 2 comprimidos por semana: 2,3 por 100 pessoas-ano
    - 2 a 3 comprimidos por semana: 0,6 por 100 pessoas-ano
    - 4 a 6 comprimidos por semana: 0 por 100 person-years
    - 7 comprimidos por semana: 0 por 100 pessoas-ano





# Principais Conclusões do iPrEx OLE

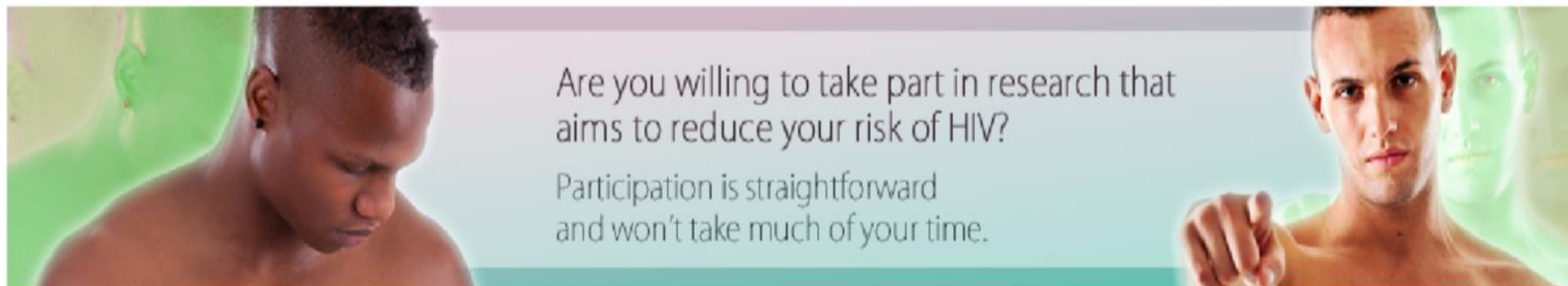
- Escolha de usar PrEP foi alta em todo o espectro demográfico
- O comportamento sexual de risco foi associado a ...
  - Maior retenção entre a fase randomizada (IpREX) e a fase aberta (OLE),
  - Maior uso de PrEP e maior adesão
- Adesão precisa ser boa, mas não necessariamente perfeita:
  - Redução do risco 84% (95% CI: 21 to 99%) com 2-3 comprimidos/semana;
  - Redução do risco 100% (95% CI: 86 to 100%) com  $\geq 4$  comprimidos/semana
- PrEP falha se as pessoas param de usar enquanto estão mantendo comportamento de risco par ao HIV
- As Travestis: quase 30% menos prováveis de ter altas concentrações nos cartões de sangue coletados para medir tenofovir (aOR 0.72, P = 0.02) - Mais estudos de PK são necessários
- A concentração de Tenofovir difosfato nos cartões de DBS é um marcador conveniente de média de longo tempo de uso de PrEP com proteção

# iPrEX OLE

---

- 1.603 voluntários que haviam participado da etapa inicial do estudo, quando não se sabia se o Truvada era eficaz e uma parte usou placebo
- 76% decidiram usar PrEP
  - Sexo anal receptivo sem proteção e infecção pelo HSV-2
  - Incidência: 2.6/100PY vs. 1.8/100PY
  - iPrEX 3.9 placebo, 2.2 TDF/FTC
- Muito bem tolerado (apenas 3 alterações de exame de creatinina)
- Nenhum caso de infecção entre os que tinham drogas detectável no sangue indicando uso de 4 a 7 doses/semana
- Diminuição de sexo anal desprotegido
- Sem alteração na incidência de sífilis





[▶ PROUD Study Summary](#)

[▶ Volunteers](#)

[▶ Participant Information Sheet](#)

[▶ Where are we recruiting?](#)

[▶ Frequently Asked Questions](#)

[▶ Study Protocol](#)

[▶ Contact Us](#)

[▶ Acknowledgments](#)

[▶ Further reading](#)

[▶ Useful Links](#)

[▶ Publications](#)

[Home Page](#) > [Volunteers](#)

## Volunteers

### Why take part?

The study will give us more information about how PrEP could be used to prevent new HIV infections amongst gay men.

By taking part, you could reduce your own risk of catching HIV.

Our team will help and support you to be healthy.

You can take part in the study if you:

- Are HIV negative
- Are 18 or older
- Have had anal sex without a condom in the last three months.
- Are likely to do this again in the next three months.
- Can visit the clinic for blood tests every three months.

# IPIRGAY

## Study Design

### Effectiveness of “on demand” PrEP Randomized placebo-controlled trial

- High risk MSM
- Condomless anal sex with  $\geq 2$  partners

Full prevention services\*  
TDF/FTC before and after sex  
(n=950)

Full prevention services\*  
placebo before and after sex  
(n=950)

Counseling, testing for STI, condoms, vaccination, PEP  
Primary endpoint : HIV infection, 64 events expected  
Incidence of HIV-infection: 3%PY, 50% efficacy, ~ 2000 pts


# **Dose Intermitente de Truvada (FTC/TDF)**

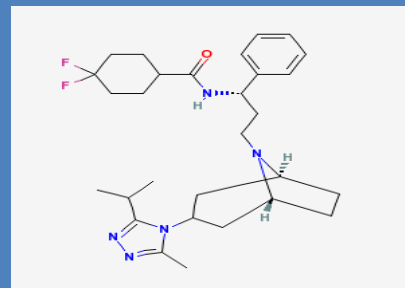
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- **HPTN 066 – PK (plasma, compartimentos genitais/lumens) de esquemas em DOT: semanal, 2 X na semana, 2 comprimidos 2 X/semana e diário**
- **HPTN 067 – PK e outras avaliações de 3 iPrEP strategies – diária, 2 X/semana, + reforço 2hr pós-coito, 24-48hs pré-coito, 2 hr pós-coito, N=540 (Gays, HSH, Travestis/WSM)**



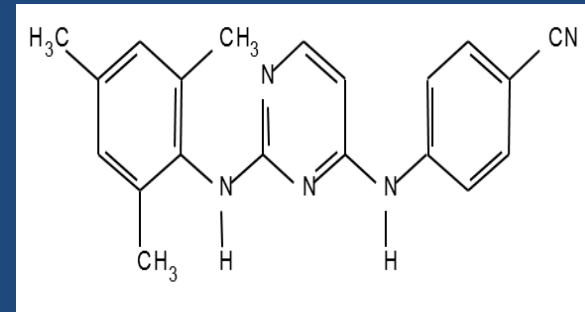
# Maraviroc

- Inibidor de entrada com perfil de segurança estabelecido para uso terapêutico oral (Pfizer/ViiV)
-  Phase II study for oral PrEP +/-FTC or TDF (HPTN 069) 400 HSH/200 mulheres
- Licença para a IPM in 2008
- Em desenvolvimento clínico:
  - Anéis com Maraviroc ou Maraviroc + Dapivirina
- Próxima Geração:
  - Maraviroc gel (uso retal)- Magee Women's Research Institute
  - Maraviroc/tenofovir gel – estágio inicial de desenvolvimento



# Dapivirine (TMS 120)

- ARV de alta potência: ITRNN
- Desenvolvido pela Janssen
- Testado para tratamento oral
- Licença para a IPM em 2004
  - Em desenvolvimento como microbicida vaginal para prevenção do HIV
- 15 estudos de Fase I/II (segurança) (Anel ou gel
  - Bom perfil de segurança em todos os estudos ) > 700 participantes)
- O programa de desenvolvimento do Anel começou em 2012, resultados esperados para 2015/2016



# PrEP de Longa duração/Depósito

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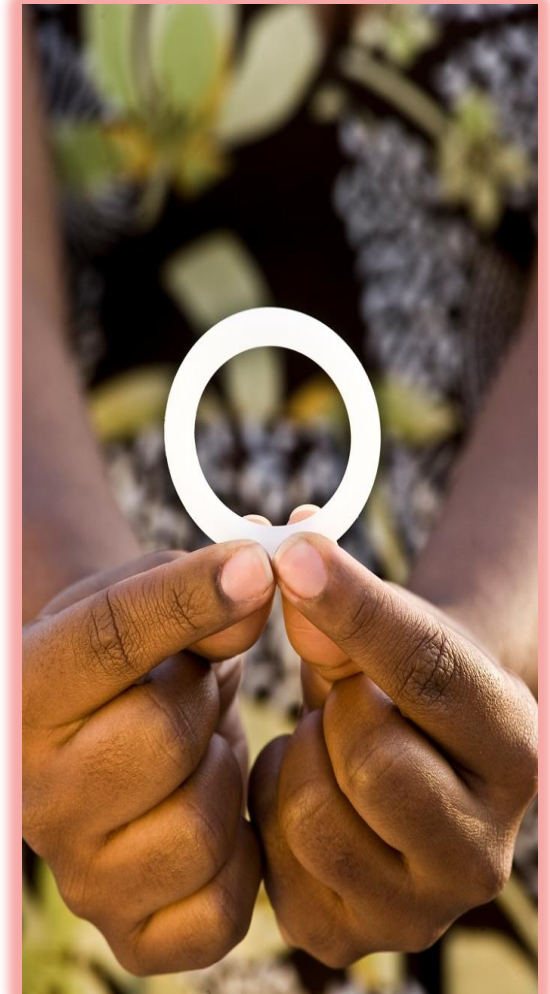
- **HPTN 076 – Fase II – segurança do TMC278LA em mulheres não infectadas e com baixo risco de infecção**
- **HPTN 077 – Fase II – segurança do GSK1265744 (cabotegravir) homens e mulheres não infectados pelo HIV, com baixo risco de adquirir a infecção(a iniciar)**
- **ÉCLAIR – Fase II segurança do GSK1265744 (cabotegravir) homens e mulheres não infectados, com baixo risco de adquirir a infecção pelo HIV (inclusão encerrada)**





# Anéis com Microbicida

- **Longa ação: mensal ou tempo maior**
  - Potencial para melhorar a adesão
  - Melhor adesão, maior efetividade
- **Fácil de usar, confortável**
  - Anel flexível, inserido pela própria mulher
  - Raramente percebido pela mulher ou pelo parceiro
  - Pouco ou nenhum impacto na atividade sexual
- **Viável para o mundo em desenvolvimento**
  - Baixo custo de produção
  - Boa segurança e aceitabilidade
- **Potencial para combinação de medicamentos no mesmo anel**



# Sistemas de Liberação contínua: Combination Intravaginal Rings (IVRs)



## ❖ 60-day Dapivirine + LNG IVR (IPM)

- Combines the ARV dapivirine (DPV) + LNG (silicon ring)
- DPV+LNG ring formulation and testing are underway

## ❖ 90-day Tenofovir + LNG IVR (CONRAD; IPM)

- Combines TFV with the hormonal contraceptive, LNG
- Segment or matrix formulation



## ❖ 30-day MZL Combination IVR (Population Council)

- Combines MIV-150 + Zinc Acetate + LNG
- Early pharmacology studies underway



**NUVARING®**  
(etonogestrel/ethinyl estradiol vaginal ring)  
delivers 0.120 mg/0.015 mg per day



- 44 million users since 2002
- Matrix, non-latex, novel polymer
- Vicriviroc and MK-2048 (ISTI) combinations under study



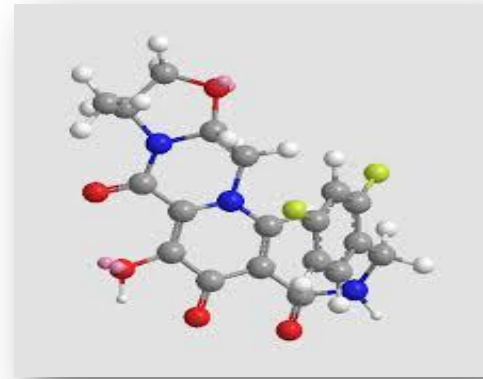
# Nano formulações de antirretrovirais

## TMC278LA (Rilpivirine; PATH)



- NNRTI (Rilpivirine)
- Oral formulation in Complera™
- Long acting: up to 3 months?
- Multiple trials:
  - Dose ranging PK; PK/PD
  - Phase-2: HPTN 076

## Cabotegravir (GSK '744; ViiV)



- Integrase inhibitor
- Similar to Dolutegravir
- Safe in humans with oral run-in
- Activity up to 3 months?
- NHP model efficacy
- Phase 2: Éclair and HPTN 077

# Medicamentos Injetáveis com Ação de Longa Duração

➤ 2 ou mais medicamentos administrados simultaneamente

ARV Injetáveis  
de Longa  
Duração  
Rilpivirina  
Cabotegravir



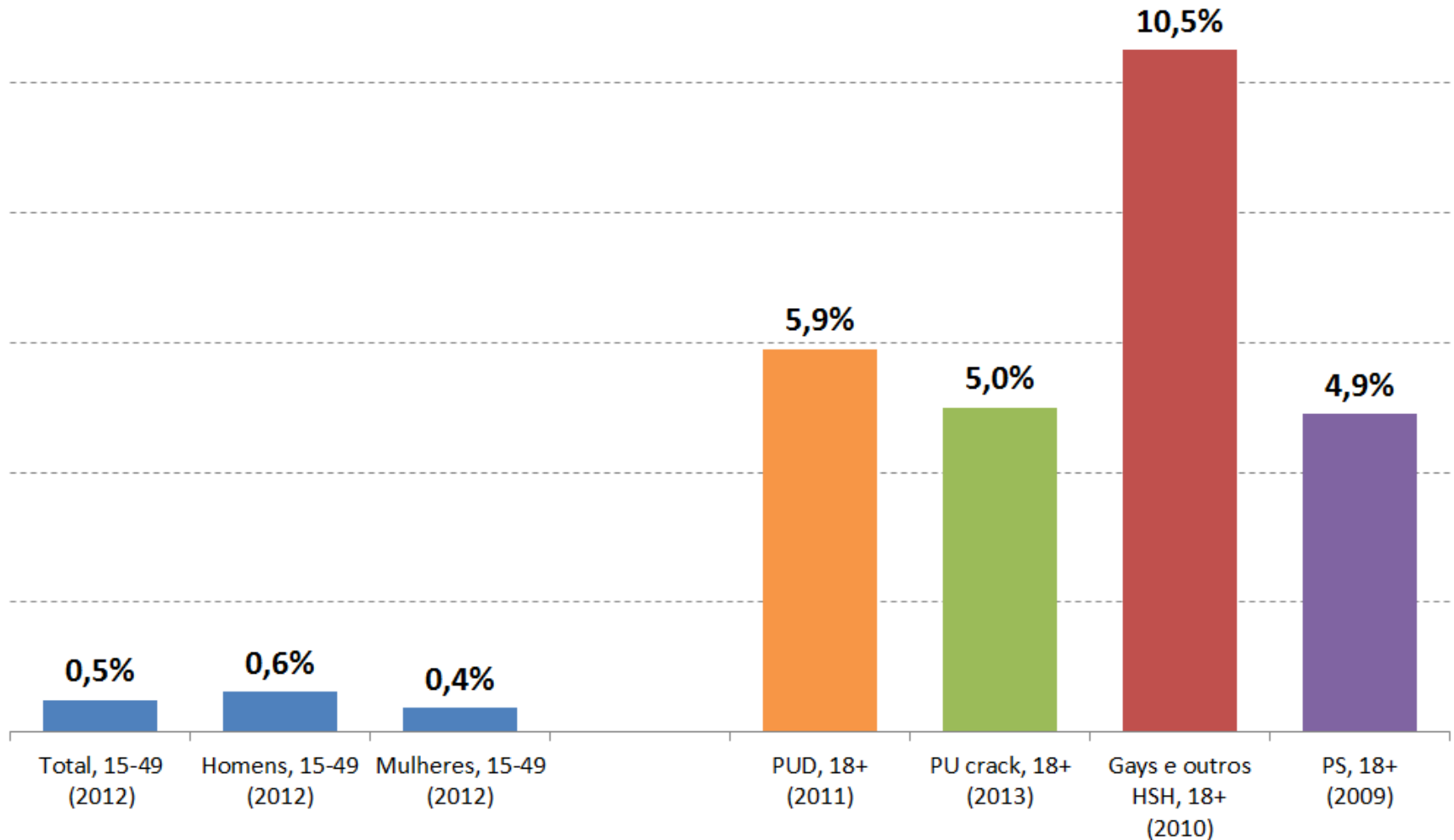
Depo Provera



Cyclofem



# Taxa de prevalência de HIV



# Implementação da Profilaxia Pré-Exposição ao HIV

Um projeto de demonstração- PrEP Brasil



# PrEP Brasil: Informações Gerais

- Estudo multicêntrico de iniciativa nacional
- Centros participantes:
  - LapClinAIDS-IPEC/FIOCRUZ (**centro coordenador**)
  - CRT-AIDS (SP)
  - USP
- Financiamentos:
  - Rio de Janeiro: edital PROEP/Pesquisa Clínica do CNPq
  - São Paulo: edital FAPESP
  - Medicação do estudo (Truvada<sup>®</sup>) doada pelo fabricante

# Esquema do Estudo

- **OBJETIVO:** Avaliar a **aceitabilidade, segurança** e viabilidade da PrEP administrada em 3 centros de pesquisa no Brasil
- **DELINEAMENTO:** Projeto demonstrativo de PrEP, aberto e multicêntrico.
- **POPULAÇÃO:** Gays, HSH e Travestis com risco de contrair o HIV.
- **AMOSTRA:** 400 voluntários (200 IPEC + 100 CRT + 100 USP)
- **TRATAMENTO:** FTC/TDF 01CP VO 1X/DIA
- **DURAÇÃO:** 3 anos. Período de inclusão de 12 meses e período de acompanhamento de 12 meses. Análises no terceiro ano.



# Objetivos Primários

- Descrever a **aceitação da PrEP** diária oferecida a homens gays, HSH e travestis
- Descrever **efeitos adversos e toxicidade** da PrEP
- Descrever **padrões e correlações da adesão** à PrEP
- Mensurar as **mudanças no comportamento sexual de risco**

# Objetivos Secundários

- **Descrever o conhecimento da PrEP** entre gays, HSH e Travestis;
- **Descrever os motivos** que levam à escolha de iniciar ou recusar PrEP;
- Descrever o número de **soroc conversões**;
- Descrever os **padrões de resistência** de ARV entre pessoas que soroc converteram;
- Avaliar o **auto-relato de desvios** (venda/partilha) da PrEP;
- Descrever os possíveis **danos sociais** do uso da PrEP;
- Descrever a **prevalência de doenças sexualmente transmissíveis** (sífilis, herpes simples-2, clamídia, gonorréia).

# Desenho do estudo

- Estudo de Demonstração, Multicêntrico (IPEC, CRT e USP – expansão para Porto Alegre)
- **População do estudo:** gays, HSH e Travestis, não infectados pelo HIV
- **Study size:** 400 a 500 participantes
- **Treatment Regimen:** FTC/TDF (emtricitabine 200 mg / TDF 300 mg) – Truvada, dose única diária
- Medicamento doado pela Gilead Sciences
- **Study Duration:** Aproximadamente 2.5 years. Inclusão em 12 meses, e acompanhamento de cada participante por 12 meses em uso do medicamento

# Sub estudos

- Intervenção de adesão – mensagens de SMS. UM grupo vai receber mensagens e o outro não
- Mensuração de tenofovir intracelular e em sangue coletado em cartão DBS para medir adesão (Rio vs SP)
- Sindemia – avaliar a associação do uso de álcool e outras drogas, depressão e violência com o padrão do uso de PrEP

# Situação do PrEP Brasil

## Agosto 2014

Centro	Voluntários Pré-Triados	Voluntários Elegíveis	Voluntários Triados	Voluntários Incluídos
IPEC	166	102	74	56
CRT	50	43	24	5
USP	25	18	18	13
Total:	241	163	116	74

**1**  
**COMPRIMIDO  
POR DIA  
PODE  
PREVENIR O  
HIV/AIDS**

Uma pesquisa do IPEC/FIOCRUZ, indica que um novo medicamento, em forma de comprimido, tomado uma vez ao dia, pode prevenir o HIV. Essa pesquisa vai avaliar aceitação, viabilidade e a melhor forma de oferecê-lo à população brasileira como prevenção ao HIV.

**PrEP**  
PROFILAXIA  
PRÉ EXPOSIÇÃO *Brasil*

# 1 COMPRIMIDO POR DIA PODE PREVENIR O HIV/AIDS

ISSO PODE FUNCIONAR PARA VOCÊ TAMBÉM!  
PARTICIPE DESSA PESQUISA COM A FIOCRUZ

9090 (21) 2260-6700



# 1 COMPRIMIDO POR DIA PODE PREVENIR O HIV/AIDS

Uma pesquisa do IPEC/FIOCRUZ, indica que um novo medicamento, em forma de comprimido, tomado uma vez ao dia, pode prevenir o HIV. Essa pesquisa vai avaliar aceitação, viabilidade e a melhor forma de oferecê-lo à população brasileira como prevenção ao HIV.

PARTICIPE!

(21) 2260-6700

 [facebook.com/LAPCLIN-AIDS](https://facebook.com/LAPCLIN-AIDS)

 [twitter.com/LAPCLIN\\_AIDS](https://twitter.com/LAPCLIN_AIDS)



Ministério da Saúde

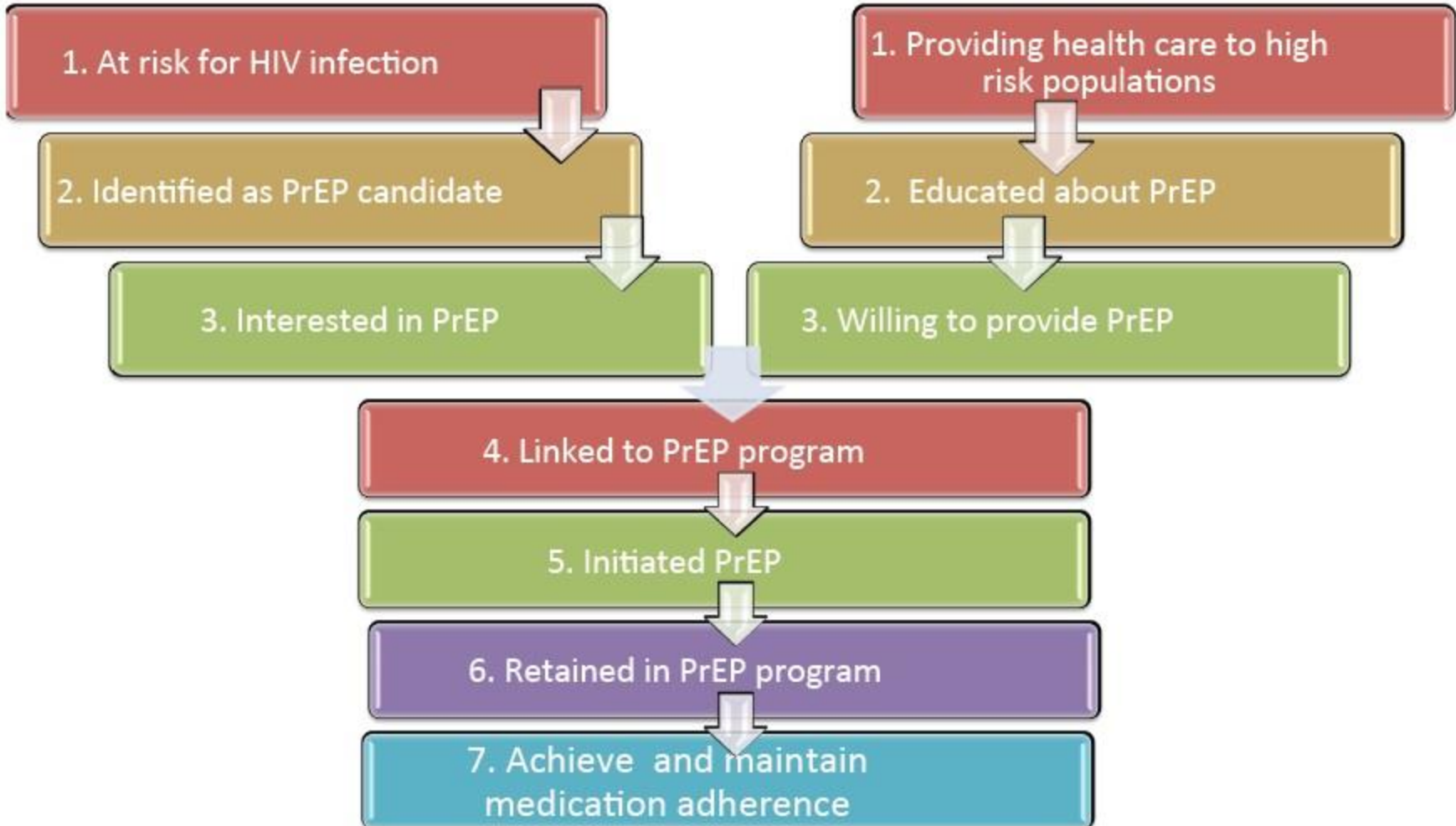
FIOCRUZ  
Fundação Oswaldo Cruz

# PrEP Cascade

(D. Smith, CDC and Al Liu, SFDPH)

Patients

Providers

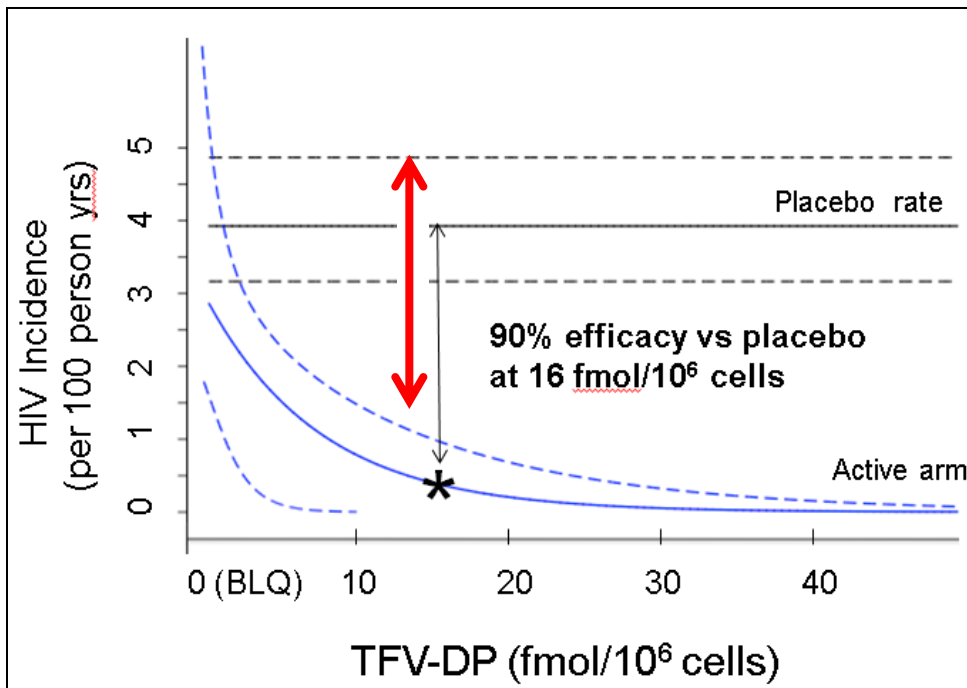


# **Início e Duração da Proteção**



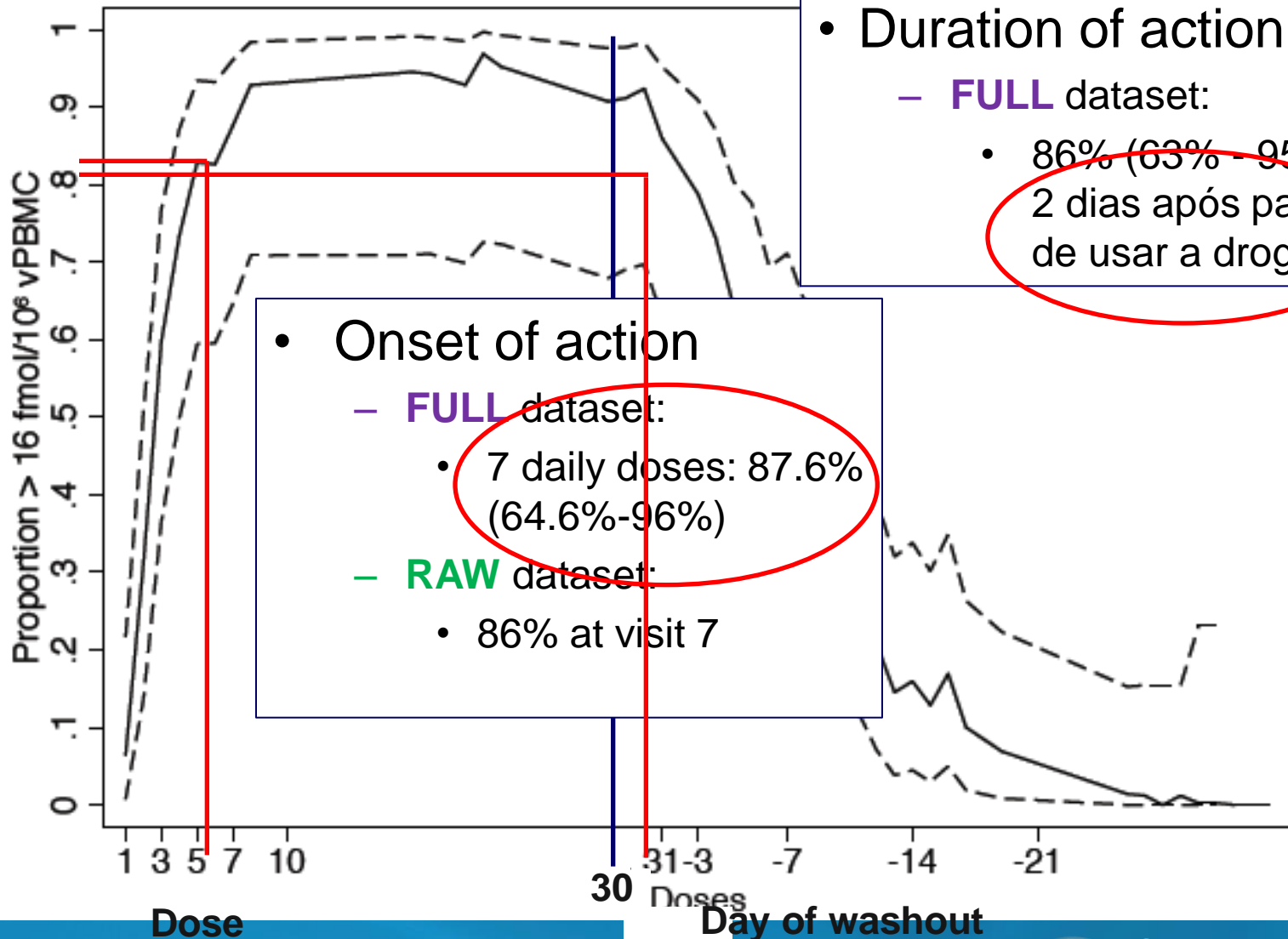
# Estabelecendo o $EC_{90}$

## Regression of HIV-infection risk relative to placebo

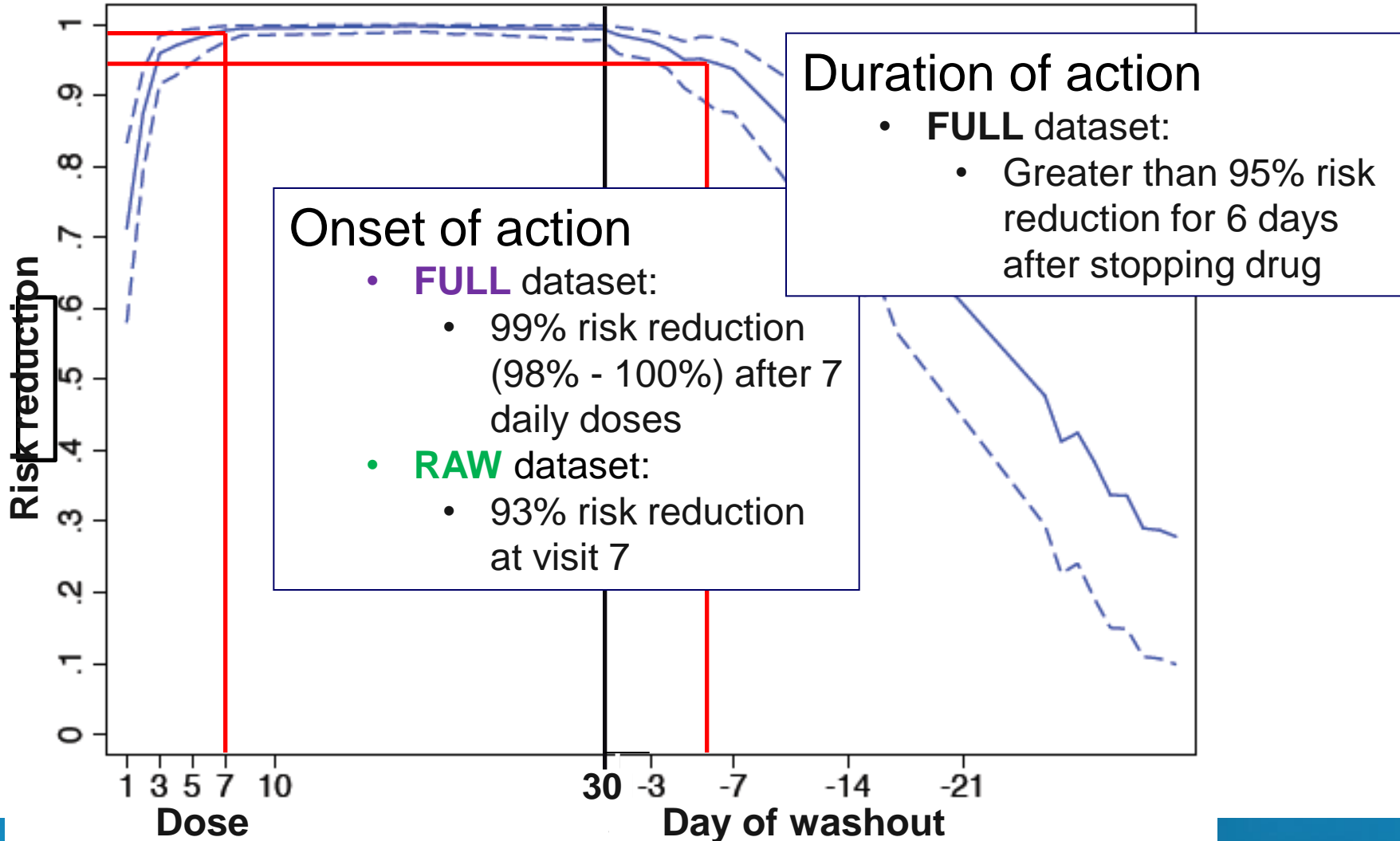


- iPrEx post hoc analysis
  - Proportional hazards regression equation for HIV-infection risk relative to placebo
  - Intracellular TFV-DP in vPBMC
- $EC_{90} = 16 \text{ fmol}/10^6 \text{ cells}$  (95% CI: 3 to 28)

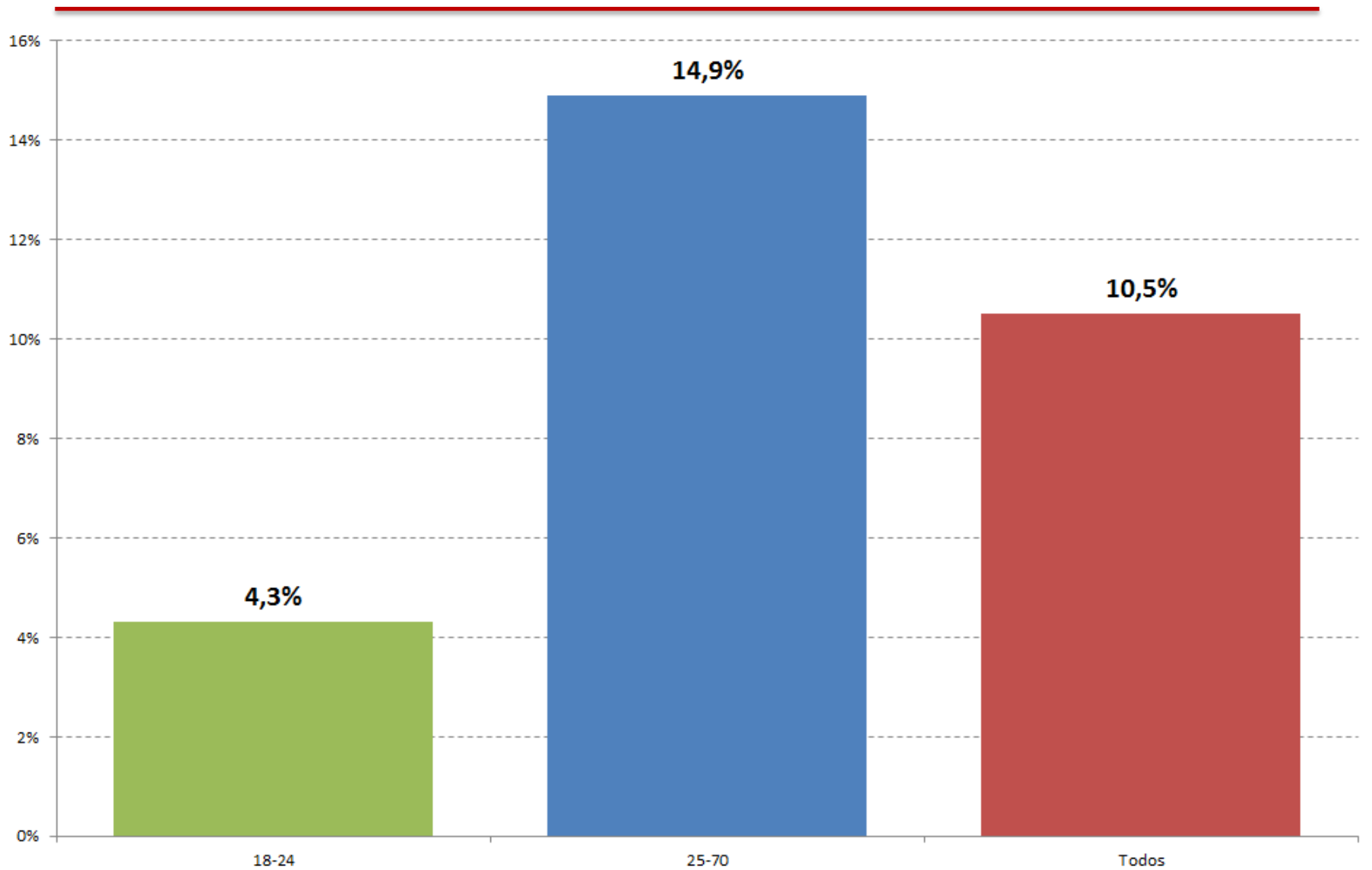
# Proporção > EC90 por tempo em uso da droga



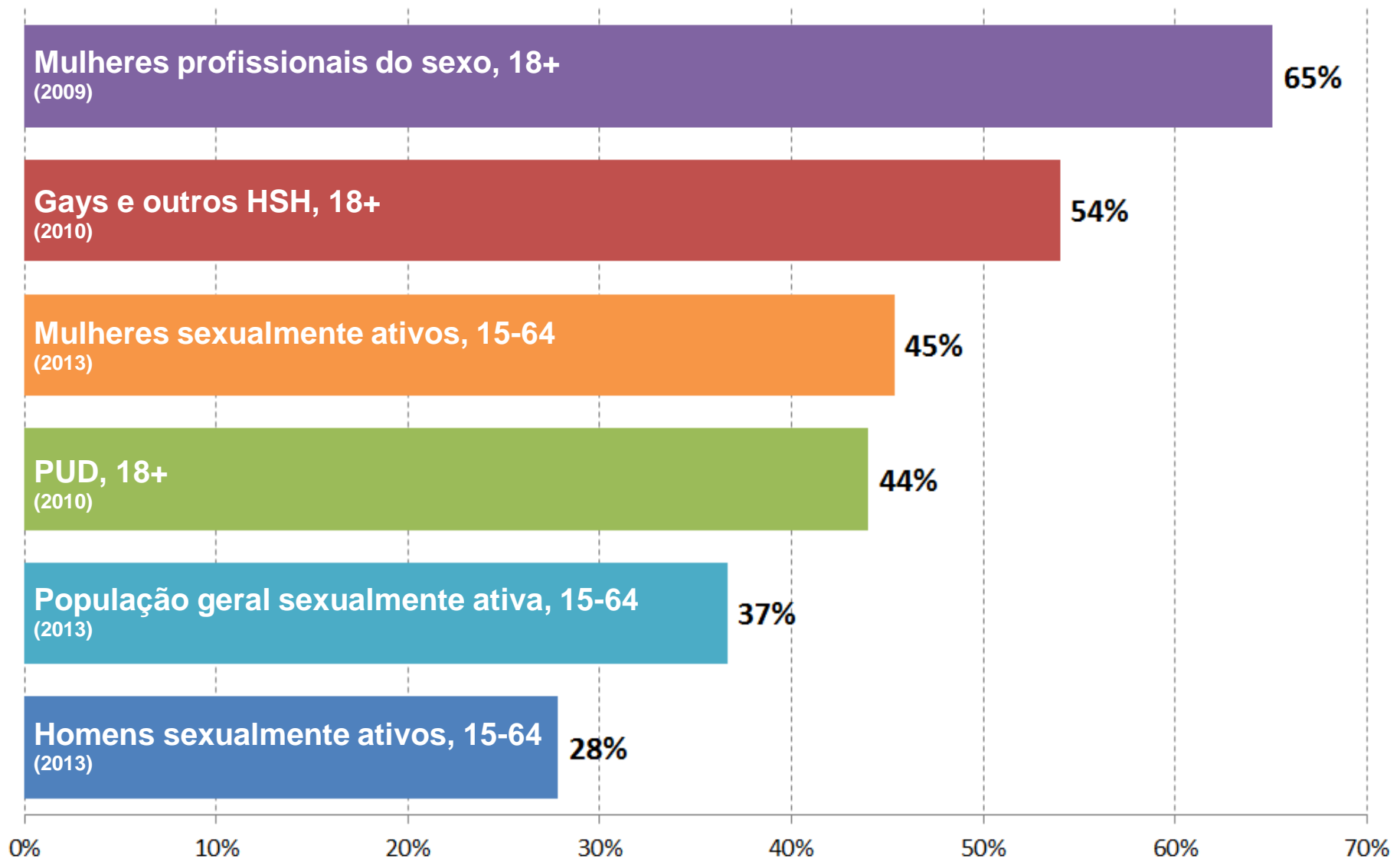
# Inferred HIV Risk Reduction



# Taxa de prevalência de HIV em HSH



# Cobertura de teste de HIV na vida



# Criando Demanda para os Testes de HIV

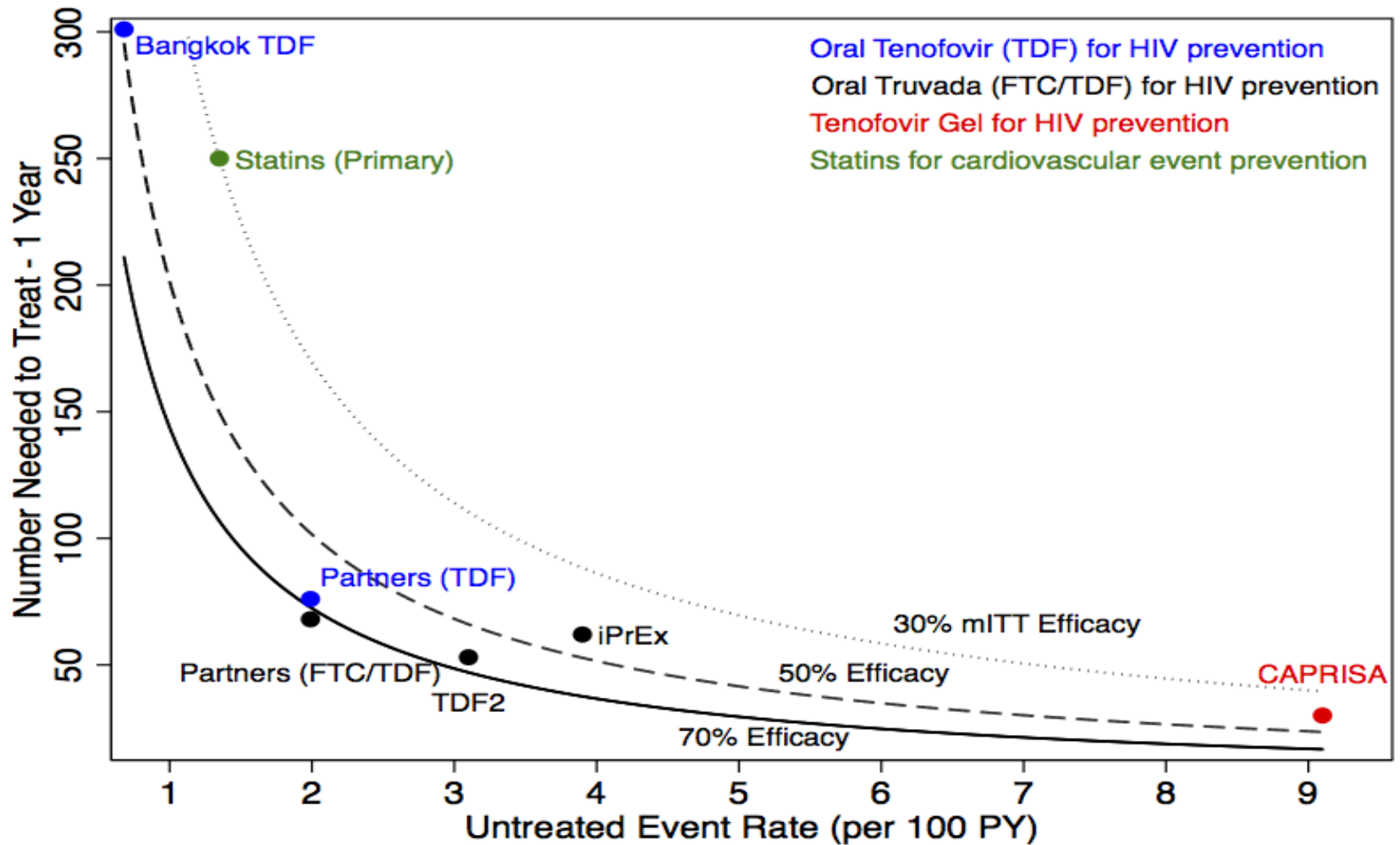


A screenshot of the Adam's Love website header. It features a green button that says "Become a Member SIGN UP HERE", a circular logo with "WE DESERVE IT", and the text "Adam's Love 'We Deserve It' Campaign". Below this is the "ADAM'S LOVE for Men who love Men" logo and a blue navigation bar with the text "Thailand's Official MSM Health Website" and search options.

An advertisement for HIV testing in Rio de Janeiro. It features a rainbow graphic and the text "Cariocas são DESCOLADOS Cariocas SE TESTAM!". It includes contact information: "Ativo, passivo, versátil, venha se testar com a gente! Temos novidades para você! Ligue grátis! 9090 (21) 2260-6700". Social media handles for Facebook and Twitter are also provided.

An advertisement for HIV testing with a large red "X" graphic. The text reads "A HORA É AGORA". It includes information about the test: "Se você é homem e fez sexo com outro homem nos últimos 30 dias, sem camisinha, venha fazer seu teste hoje mesmo! O diagnóstico ultraprecoce do HIV pode ajudar a controlar a ação do vírus no seu corpo. Ficou interessado? Ligue grátis! 9090 (21) 2260-6700". It also lists social media handles and logos for various organizations including the Ministry of Health, IPEC, and LaPClin.

# O custo-efetividade da PrEP aumenta quando disponibilizado para pessoas em alto risco



## Ongoing and Planned PrEP Trials and Demonstration Projects, as of June 2014

Trial/project	Sponsor/funder	Type/Category	Location	Population	Design/Key questions	Status
<b>VicPrEP Demonstration Project</b>	Monash University and Alfred Health at the Victorian AIDS Council/Gay Men's Health; funded by the Victorian Government	Demonstration Project	Australia	Gay men, IDUs, HIV-negative partners in serodiscordant heterosexual couples and people who have received non-occupational post-exposure prophylaxis (N-PEP) on more than two occasions in the previous 12 months	To determine the effectiveness of PrEP in the local setting and the factors contributing to its success. Truvada will be administered 100 participants for up to 12 months. The other 100 participants will elect not to use Truvada, but agree to provide relevant information through regular on-line surveys.	Expected to start late 2014.
<b>Partners Demonstration Project</b>	Led by a team of scientists from Kenya, Uganda and the US; funded by NIMH/NIH, USAID and BMGF	Demonstration Project	Kenya, Uganda	Serodiscordant couples	Evaluates HIV prevention preferences among approximately 1,000 HIV serodiscordant couples, adherence to PrEP and ART and interface of reproductive health priorities and ART-based prevention. Will implement PrEP as "bridge" to ART, providing PrEP to HIV-negative partner when HIV-positive partner is not yet on ART due to ineligibility based on country guidelines or personal decision.	All four sites open and enrolling as of August 2013; results expected in 2016.
<b>LVCT and SWOP</b>	Implemented by national partners in each country in collaboration with the World Health Organization, UNAIDS, O'Neill Institute of Georgetown University, London School of Hygiene and Tropical Medicine, Imperial College London; funded by Bill & Melinda Gates Foundation	Demonstration Project	Kenya	Young women, female sex workers and MSM	Aims to introduce PrEP into combination prevention interventions targeting young women, female sex workers and MSM. Formative research underway to assess consumer perceptions and identify potential barriers and opportunities related to introduction. Outcomes include criteria for PrEP indication among young women and a menu of interventions for target populations, including PrEP and feasible delivery options.	Formative research in planning phase; feasibility study reports results likely in December 2013.
<b>Nigerian National Agency for the Control of AIDS</b>		Demonstration Project	Nigeria	Serodiscordant couples	Evaluates the effectiveness of various models for the delivery of PrEP and TasP as part of a combination prevention strategy for 1,200 heterosexual, serodiscordant couples. Couples will be recruited from facilities that provide prevention of vertical transmission, ART and other services. Study sites include Plateau, Edo and Cross River State. Study findings will be used to inform the scale-up of PrEP and TasP as part of a comprehensive national HIV-prevention package.	Formative discussions underway. No start date for demonstration project.
<b>Wits Reproductive Health and HIV Institute</b>		Demonstration Project	South Africa	Female sex workers	Aims to assess whether oral PrEP and TasP can be rolled out within a combination prevention and care approach tailored to the needs of 605, both HIV-positive and negative, female sex workers age 18 and older. Study sites include Hillbrow and Waterval Boven.	Expected start date February 2014, with expected completion September 2016.
<b>Durbar (DMSC) and Ashodaya Samithi</b>		Demonstration Project	India	Female and transgender sex workers	Aims to assess the potential introduction of PrEP among female and transgender sex workers. The project includes sex workers part of the Durbar Mahila	Feasibility study underway from May September 2013, with



## Ongoing and Planned PrEP Trials and Demonstration Projects, as of June 2014

Trial/project	Sponsor/funder	Type/Category	Location	Population	Design/Key questions	Status
					Samanwaya Committee (DMSC), a brothel-based sex work project in Sonagachi, and also the Ashodaya Samithi project, a CBO for street-based sex workers based in Mysore.	results expected in October 2013.
<b>The Demo Project</b>	National Institute of Allergy and Infectious Diseases of the NIH	Demonstration Project	US (Miami, Florida; San Francisco, California; and Washington, DC)	MSM and transgender women	Aims to enroll 300 HIV-negative MSM and transgender women at City Clinic, while a sister project in Miami will enroll 200 participants in a PrEP regimen. Whitman Walker Clinic in Washington, DC, will also be a site, aiming to enroll approximately 100 participants.	Started October 2012. Expected completion by August 2014.
<b>East Bay Consortium/CRUSH (Connecting Resources for Urban Sexual Health)</b>	California HIV/AIDS Research Program of the University of California	Demonstration Project	US (East Bay, California)	Young MSM of color	Aims to test and link young MSM of color to sexual health services; enhance and evaluate engagement and retention strategies for HIV-positive young MSM of color; and engage and retain HIV-negative young MSM of color in sexual health services, including PrEP.	Started in December 2012.
<b>DemoPrEP</b>	University of Sao Paulo; Centro de Referência e Treinamento DST AIDS; Oswaldo Cruz Foundation	Demonstration Project	Brazil	MSM; transgender women	Plans to enroll 400 MSM and transgender women to assess the acceptability, feasibility and safety of daily, oral TDF/FTC as PrEP over 12 months.	Planned to start in January 2014. Expected completion date of January 2016.
<b>PAC PATH PrEP Demo Project</b>	California HIV/AIDS Research Program of the University of California; LA County HIV & STD Program; Los Angeles Gay and Lesbian Center; OASIS Clinic; AIDS Project LA; UCLA	Demonstration Project	US (Los Angeles, California)	MSM	Plans to enroll 375 high-risk MSM and transgender women who will receive a customized prevention package that may include PrEP.	Started in May 2013. Expected completion date of May 2017.
<b>California Collaborative Treatment Group Consortium/ALERT (Active Linkage, Engagement and Retention to Reduce HIV)</b>	California HIV/AIDS Research Program of the University of California, San Diego County HIV, STD, and Hepatitis Branch and the Long Beach Health and Human Services Agency	Demonstration Project	US (Long Beach, Los Angeles and San Diego, California)	MSM	Plans to enroll 400 eligible high-risk MSM, for two years who will receive daily TDF/FTC-based PrEP, into a randomized study that evaluates whether a text messaging-based adherence intervention can improve adherence to the PrEP medication.	Started in January 2013. Results expected October 2015.
<b>CDC Foundation Demonstration Project</b>	Funding pending	Demonstration Project	US	MSM and heterosexual women	Proposed to evaluate real-world PrEP use in MSM and heterosexual women at risk of HIV infection in health clinic settings, potentially in 1,200 participants.	Start date pending funding.

## Ongoing and Planned PrEP Trials and Demonstration Projects, as of June 2014

Trial/project	Sponsor/funder	Type/Category	Location	Population	Design/Key questions	Status
<b>Choices For Adolescent Methods Of Prevention In South Africa (CHAMPS)</b>	NIAID	Demonstration Project	South Africa	Heterosexual men and women	Designed to combine different HIV prevention strategies into an optimized prevention 'menu' for adolescents, from which young women and men at risk of HIV infection may choose a particular combination of strategies to meet their specific needs and circumstances, including PrEP, microbicides, HIV Counseling and Testing (HCT) and circumcision.	Started July 2011; results expected June 2015.
<b>SPARK Project NYC</b>	HART and Callen-Lorde Community Health Center (CLCHC); funded by the National Institute on Alcohol Abuse and Alcoholism (NIAAA)	Demonstration Project	US (New York)	MSM and transgender women	Designed to evaluate a program in which PrEP is introduced, provided, and supported as part of a comprehensive prevention package. The project is also designed to identify and examine social and behavioral factors associated with disparities in access to prevention and care services among gay, bisexual, and other men who have sex with men in NYC that might direct or impact PrEP implementation programs and policies.	Started October 2011
<b>Sisters Antiretroviral therapy Programme for Prevention of HIV –an Integrated Response (SAPPH-Ire)</b>	Centre for Sexual Health and HIV/AIDS Research Zimbabwe; University College London; London School of Hygiene and Tropical Medicine ; RTI; DFID; UNFPA	Open Label	Zimbabwe	Female sex workers	Seeks to enhance HIV treatment and prevention among 28,000 highway-based sex workers by increasing uptake and frequency of testing, demonstrate acceptability and feasibility of delivering PrEP, maximize retention in care, promote timely initiation of ART for those eligible, and maximize adherence to both ART and PrEP.	Started September 2013; results expected late-2015.
<b>Project PrEPare (Adolescents 18-22)</b>	Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN); funded by NICHD, NIDA, NIMH	Open Label Demonstration Project and Phase II Safety Study	US (Baltimore; Boston; Bronx, New York; Chicago; Washington, DC; Denver; Detroit; Houston; Los Angeles; Memphis; Miami; New Orleans; Philadelphia; Tampa)	MSM	Designed to explore the safety, acceptability and feasibility of PrEP among young men who have sex with men (YMSM) who are at risk for HIV infection. This study will take place at clinical sites across the US with about 300 HIV-uninfected YMSM.	Started November 2012; results expected November 2015.
<b>Project PrEPare (Adolescents 15-17)</b>				MSM		Estimated start date March 2016.
<b>HPTN 073</b>	HPTN; funded by NIAID/NIH	Open label demonstration project	US (Los Angeles, California; Washington, DC; Chapel Hill, North Carolina)	MSM	Designed to assess the initiation, acceptability, safety, and feasibility of PrEP for Black MSM (BMSM). A subset of participants will also be recruited to participate in qualitative interviews about facilitators and barriers regarding PrEP. Recruiting HIV-uninfected BMSM at risk for HIV infection in three US Cities. Enrollment will include those aged 18 and over with an effort to recruit an equal number of BMSM under age 25 and over age 25 with a total of 225 participants (75 per site).	Enrolling as of July 2013; results expected June 2015.

## Ongoing and Planned PrEP Trials and Demonstration Projects, as of June 2014

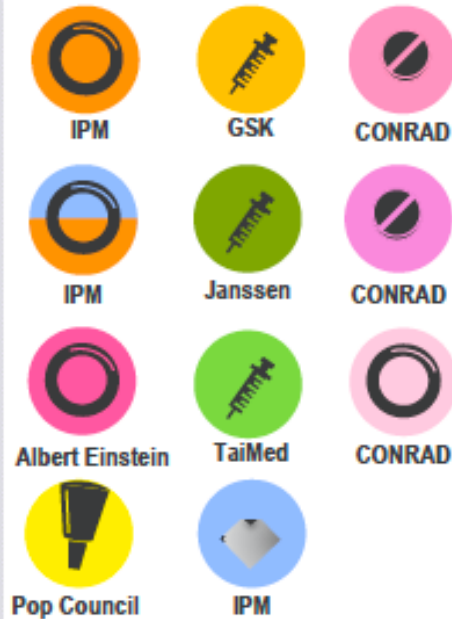
Trial/project	Sponsor/funder	Type/Category	Location	Population	Design/Key questions	Status
<b>Bangkok Tenofovir Study (BTS) Follow-Up</b>	Bangkok Metropolitan Administration, CDC, Gilead	Open label extension	Thailand	People who inject drugs	Follow-on trial of daily oral TDF in men and women who inject drugs	Expected start date in mid- to late-2013, with expected completion in late-2014.
<b>iPrEx OLE</b>	Sponsored/funded by DAIDS/NIH, through a grant to the Gladstone Institutes.	Open label extension	Brazil, Peru, Ecuador, South Africa, Thailand, US	MSM	Continuation of the iPrEx study designed to provide additional information about the safety of PrEP and the behavior of people taking PrEP over a longer term.	Fully enrolled and complete; results expected 2014.
<b>CDC 494 (TDF2 Follow-Up)</b>	Botswana Ministry of Health, CDC, Gilead	Open label extension	Botswana	Heterosexual men and women	Follow-on trial of daily oral TDF/FTC in heterosexual men and women.	Started in November 2012; results expected in 2014.
<b>PROUD (pilot trial)</b>	Sponsored/funded by UK MRC CTU, Public Health England	Open label pilot study for Phase IV trial	UK	MSM	Enrolling 500 MSM, aims to assess: whether or not a large trial is feasible; the level of interest in PrEP in clinic populations; acceptability of randomization; who takes up offer of PrEP; risk behavior over; change in risk following behavioral interventions; adherence behavior over time (self-report, pill count, and real time PK in a sub-set); facilitators and barriers to reducing risk and adhering to a daily pill.	Started in November 2012; results expected November 2015.
<b>IPERGAY</b>	Inserm-ANRS	III	Canada, France, Germany	MSM	Designed to evaluate a strategy for the prevention of HIV infection including "on demand" antiretroviral pre-exposure with Truvada versus placebo, associated with overall prevention in MSM, exposed to the risk of HIV infection.	Started in Canada and France; start pending in Germany; results expected December 2016.
<b>HPTN 067 (ADAPT)</b>	DAIDS, Gilead, HPTN, NIMH	Phase II open label	South Africa, Thailand, US	MSM	Designed to examine the feasibility of different methods of dosing for a PrEP regimen. Three methods of delivery will be compared: daily, time-based, and event-based.	Started in August 2011; results expected late-2013.
<b>HPTN 069/ACTG 5305 (NEXT-PrEP)</b>	ACTG, HPTN, NIAID	Phase II	US (Baltimore, Boston, Chapel Hill, Cleveland, Los Angeles, New York, Newark, Philadelphia, Pittsburgh, Raleigh, San Francisco, San Juan, Seattle, Washington)	MSM and at-risk women	Designed to evaluate the safety and tolerability of four ARV regimens in preventing HIV infection in a population of men who have sex with men who may be at risk of getting HIV infection through sex. The four ARV regimens being evaluated are maraviroc (MVC), MVC plus emtricitabine (FTC), MVC plus tenofovir disoproxil fumarate (TDF), and TDF plus FTC.	Started in February 2012; results expected December 2014.

# → ARV-Based Prevention Pipeline (March 2014)

## PRE-CLINICAL



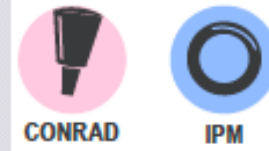
## PHASE I



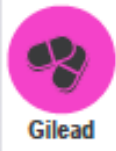
## PHASE II



## PHASE III



## PHASE IV



### DELIVERY SYSTEM

Oral pills	Vaginal tablet
Vaginal gel	Rectal gel
Vaginal ring	Long acting injectable
Vaginal film	Thin film polymer
PBS Phosphate buffered saline	Nano-fiber

### ACTIVE DRUG

TFV Tenofovir	DAR Darunavir
TFV Tenofovir prodrug	DAP Dapivirine
TDF Tenofovir disoproxil fumarate	GRF Griffithsin
TFV/FTC Tenofovir/emtricitabine	DS003 DS003 (BMS793)
TDF/FTC Tenofovir disoproxil fumarate/emtricitabine	IQP IQP-0528
MIV 150 MIV 150	5P12 5P12-RANTES
TMC 278 Ripilvirine	744 GSK 744
MVA Maraviroc	MAb Monoclonal antibody
RAL Raltegravir	No drug tested currently



# Tecnologias disponíveis e em desenvolvimento

*Preservativo feminino*



*Preservativo masculino*

Baixas taxas de uso consistente e dificuldade de negociação

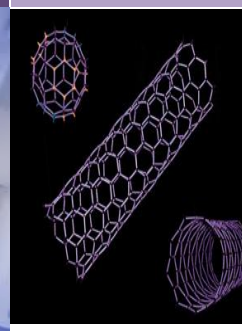
Drug/device combinations



Injetáveis  
ART, mAbs, HC



Electrospun  
Nanofibers/Films



*The future of MPTs...protection from HIV, other STDs, +/- pregnancy*

**Tratamento das  
infecções genitais  
(DST)**



**Microbicidas**



**Barreiras cervicais**



**Preservativos**

**PREVENÇÃO  
DO HIV**

**Circuncisão  
masculina**



**Aconselhamento  
comportamental  
e testagem**

**Quimioprofilaxia  
na prevenção da  
transmissão vertical  
PEP - PrEx**

**Vacinas**



**Terapia  
supressora**

**HSV-2**



# Resistência a Inovações

A F Williams, J K Wells, and A K Lund. Seat belt use in cars with air bags. American Journal of Public Health December 1990: Vol. 80, No. 12, pp. 1514-1516.  
doi: 10.2105/AJPH.80.12.1514

## Seat belt use in cars with air bags.

A F Williams, J K Wells, and A K Lund

### ABSTRACT

Seat belt use was observed in 1,628 cars with air bags and manual belts and 34,223 cars with manual seat belts only. Sixty-six percent of drivers in cars with air bags wore seat belts compared to 63 percent of drivers in cars with manual belts only. The study found no evidence for the speculation that drivers with air bags will reduce their seat belt use because they believe an air bag alone provides sufficient protection.



4/09/2009 3:46 © INNOVACT Cartoon www.innovact.com.au



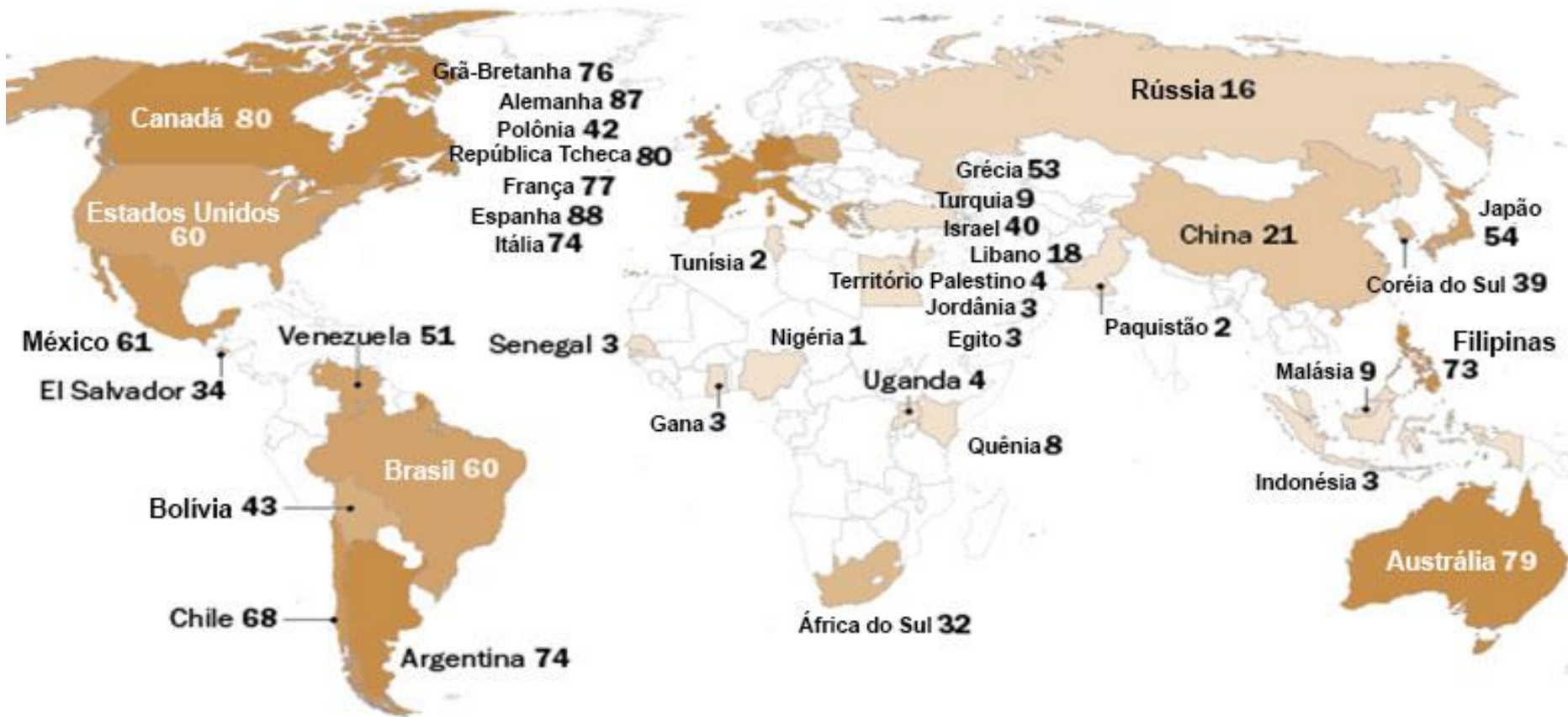
# Riscos Estruturais

Porcentagem de quantos dizem que a homossexualidade dever ser aceita pela sociedade

Mais aceitável



Menos aceitável



CENTRO DE PESQUISA PEW

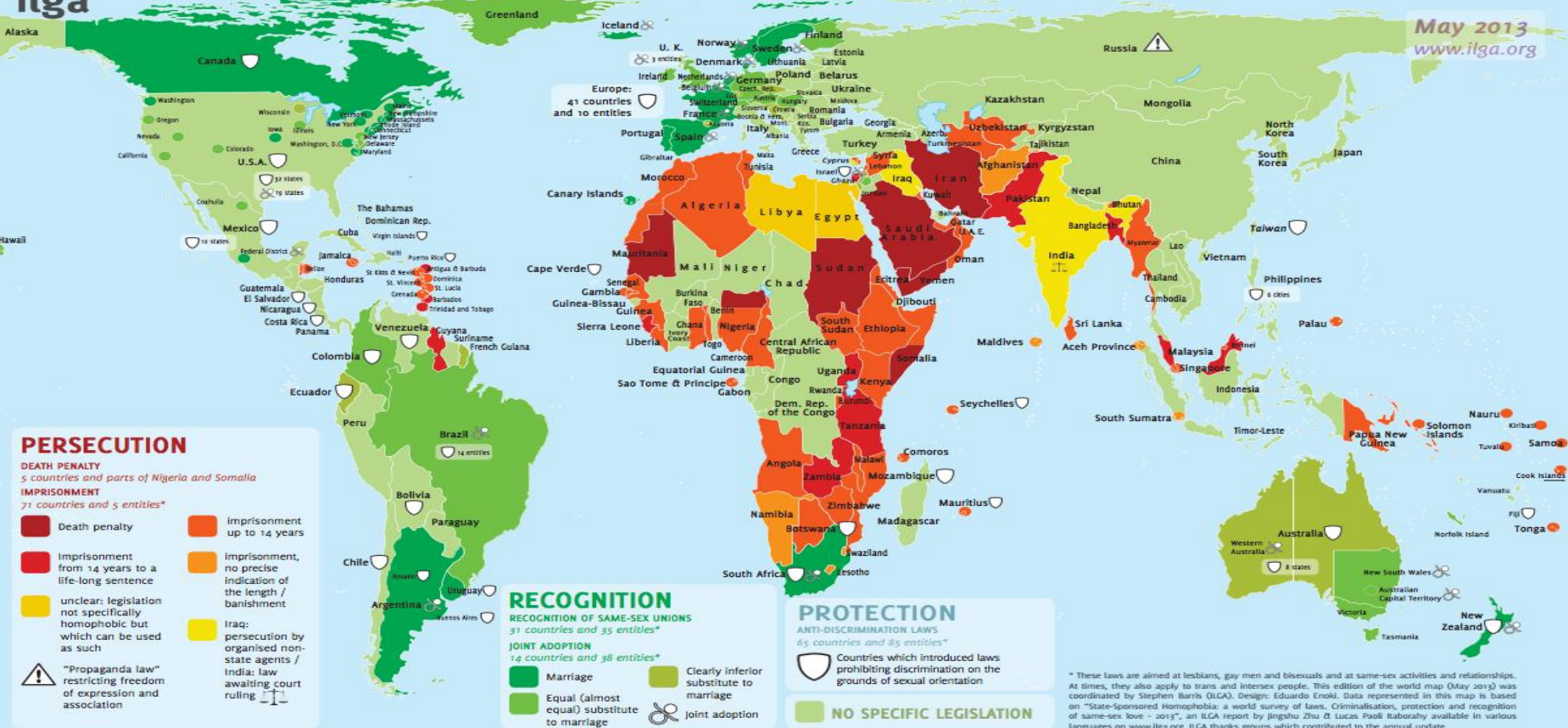
# Riscos Estruturais Criminalização



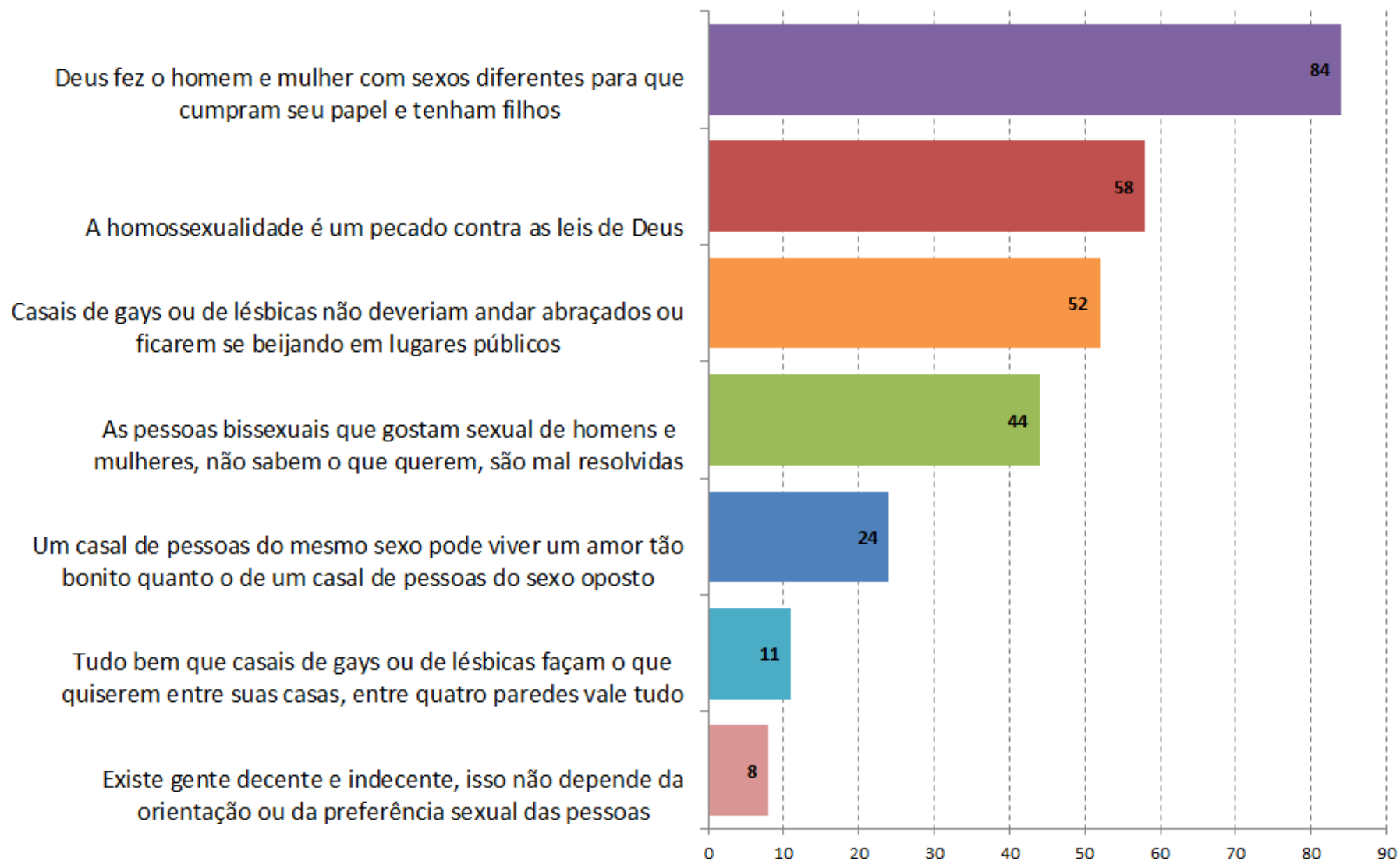
## LESBIAN AND GAY RIGHTS IN THE WORLD

ILGA, THE INTERNATIONAL LESBIAN, GAY, BISEXUAL, TRANS AND INTERSEX ASSOCIATION

May 2013  
www.ilga.org

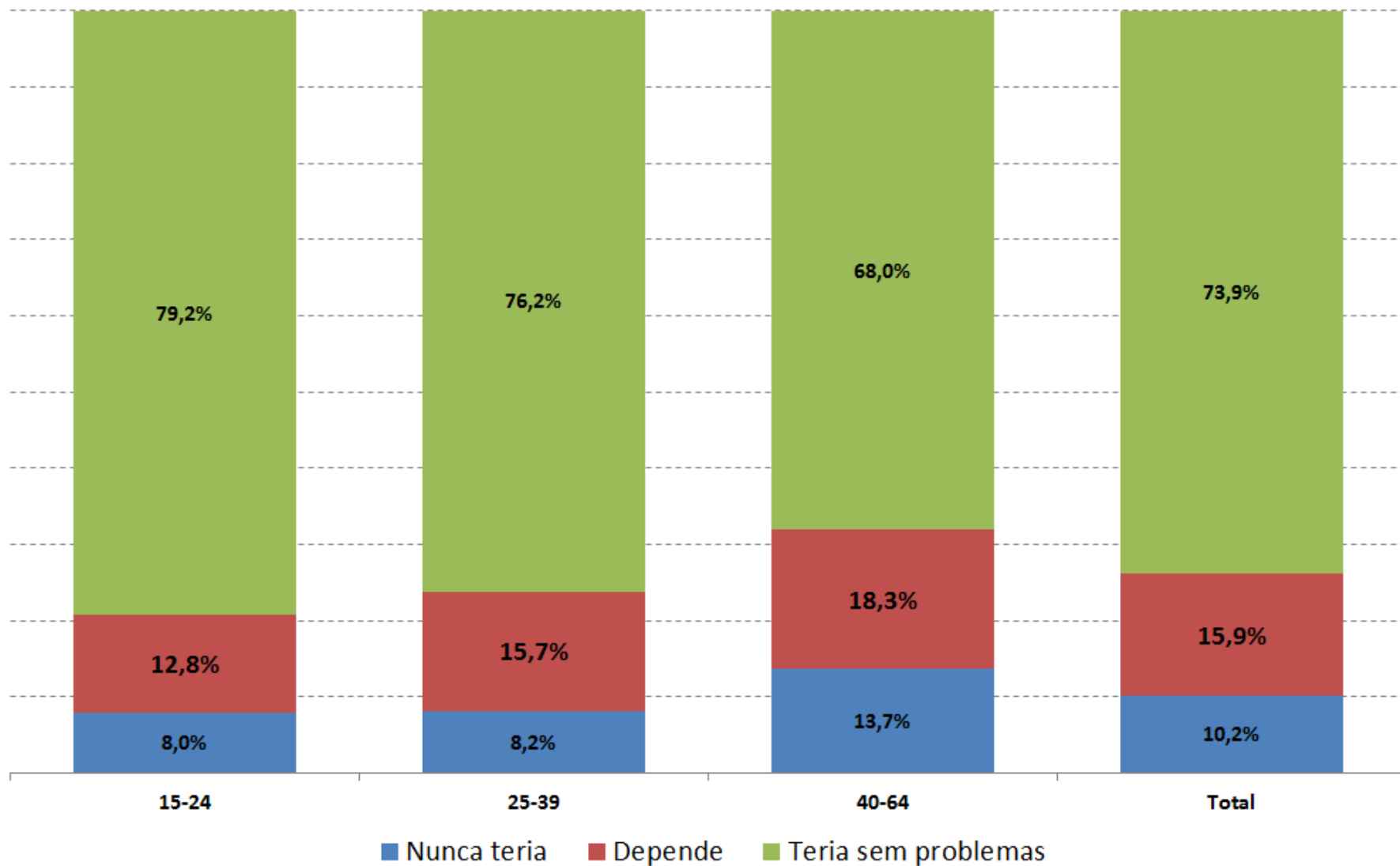


# Estigma e discriminação



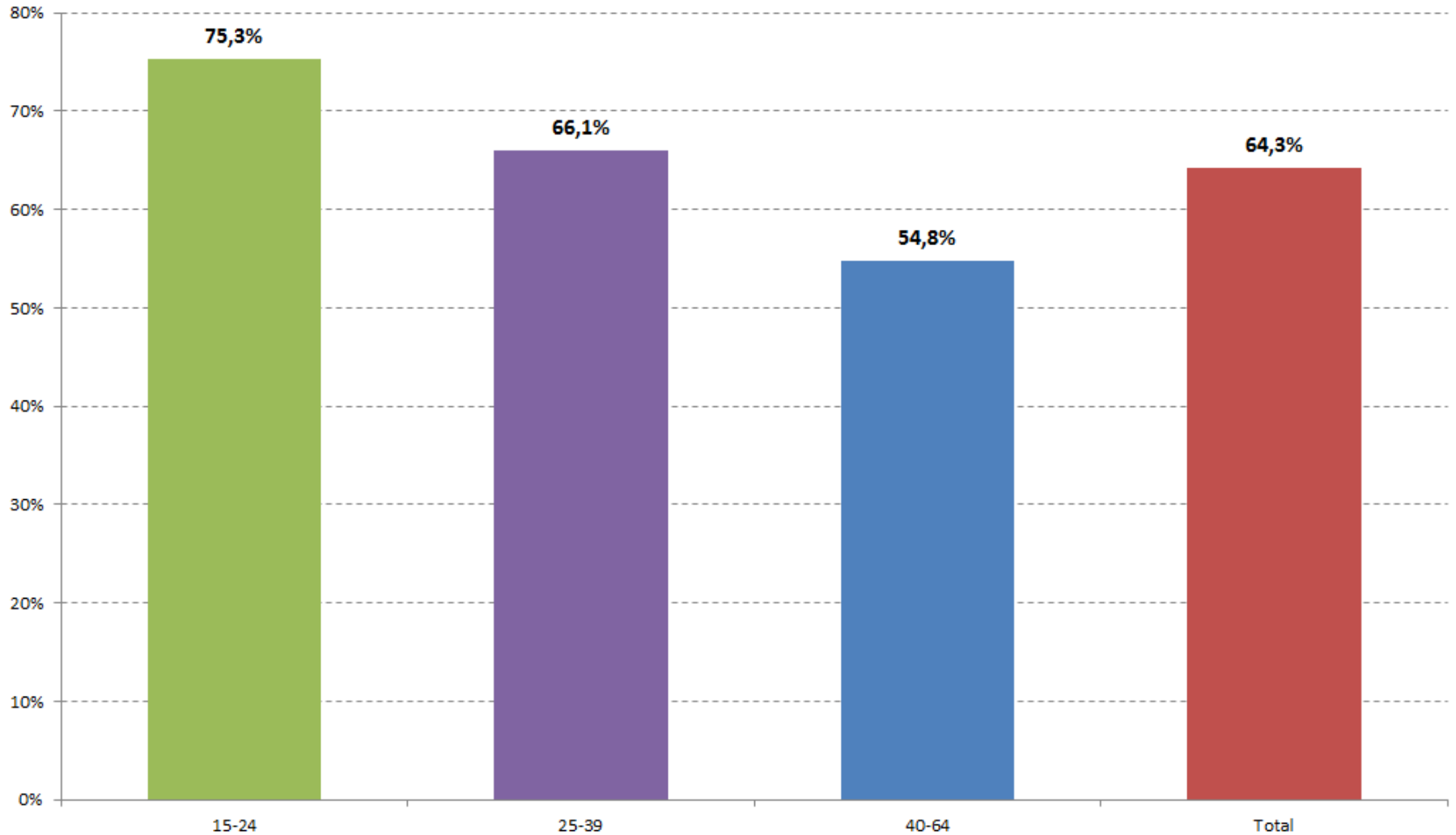
**P16. Eu vou falar coisas que costumam ser ditas sobre os homossexuais, que são os gays e as lésbicas – coisas que algumas pessoas acreditam e outras não – e gostaria que o/a sr/a. dissesse se concorda ou discorda de cada uma delas.**

# Em relação a ter amigos gays:



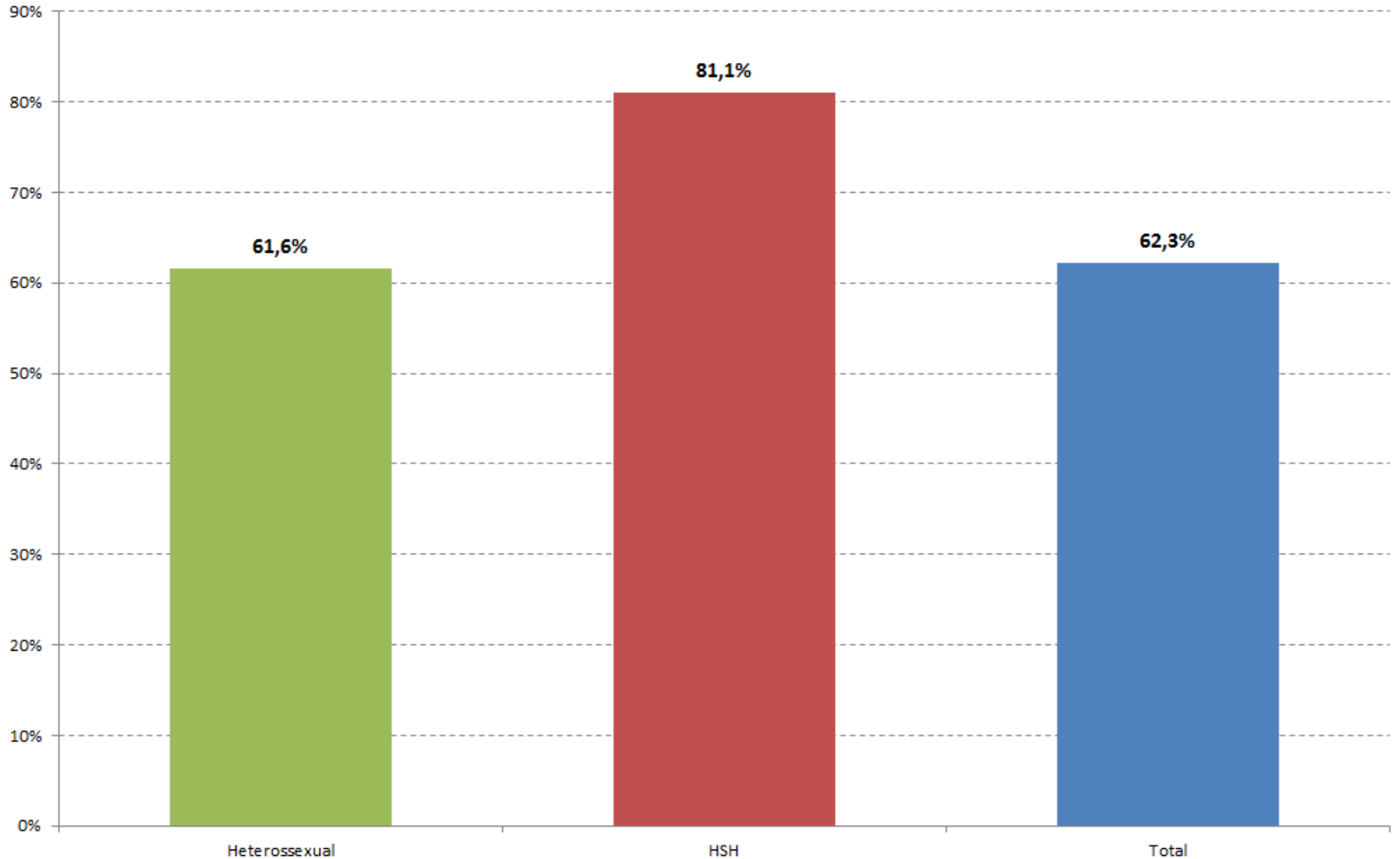
# Um casal gay tem direito a adotar uma criança

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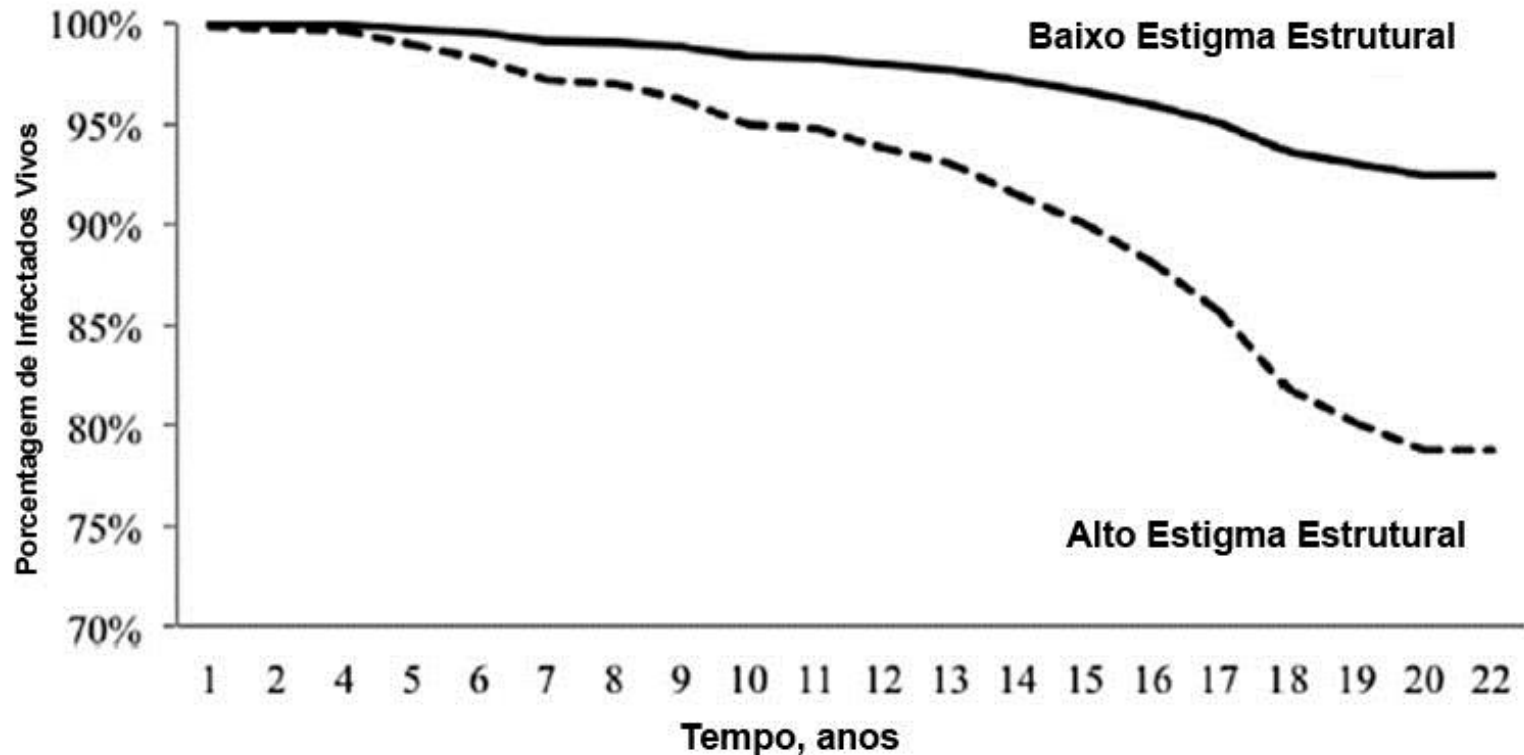
# Um casal gay tem direito a adotar uma criança

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# Estigma Estrutural e Mortalidade por todas as causas

**Fig. 2.** Tempo de sobrevivência por tipo de área residencial, Pesquisa Social Geral/Índice de Mortalidade Nacional, 1988 - 2002

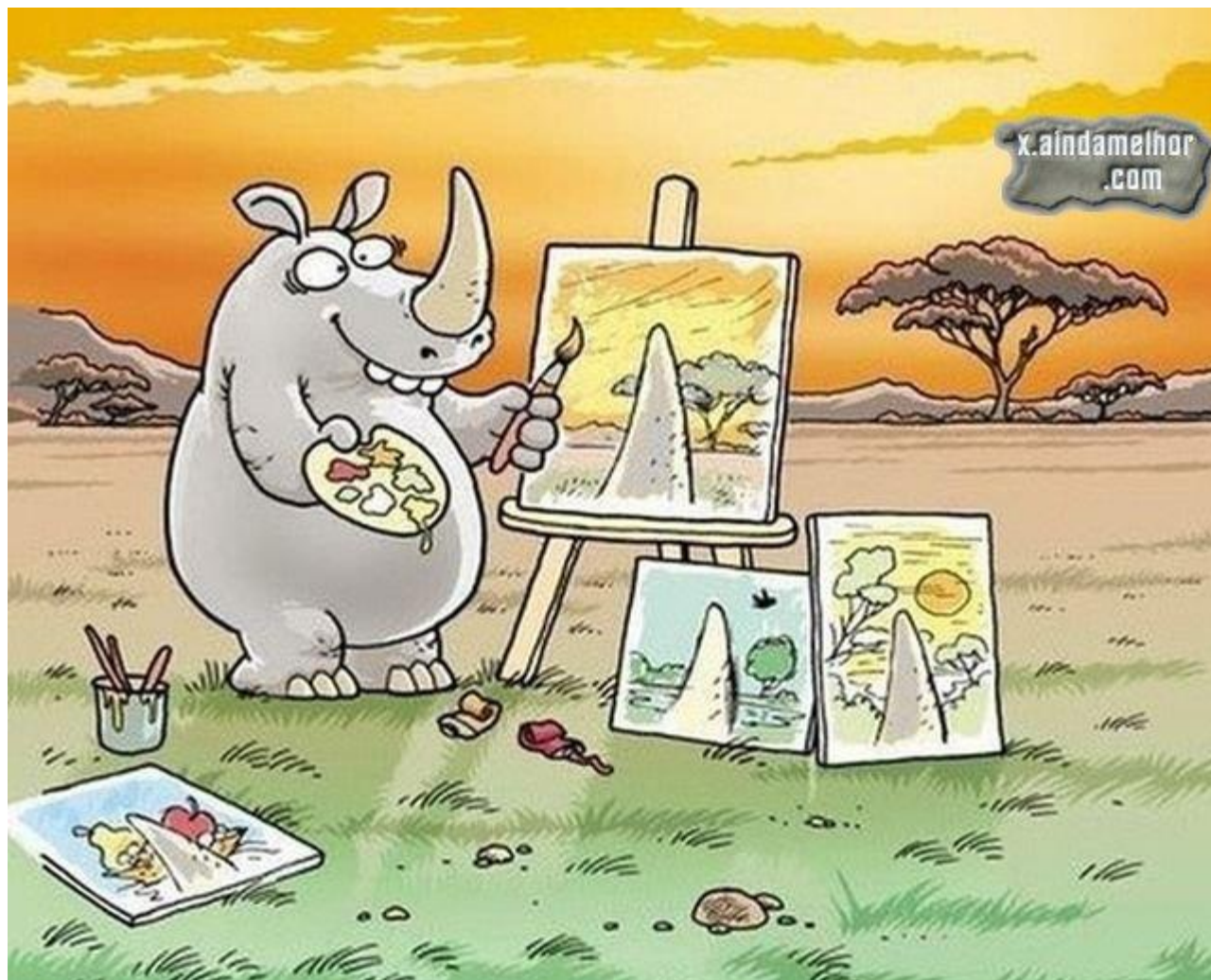


# To Optimize New Prevention Opportunities

- Aumentar os investimentos  
Short term ↑ expense = long term cost ↓
- Aumentar a vontade política
- Compromisso com a equidade
- Respeito aos Direitos humanos
- A participação da comunidade é fundamental









**Obrigada!**