

Impact du traitement antirétroviral sur la transmission

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Décision, et Coût-Efficacité en Maladies Infectieuses"

Université Paris Diderot: site Bichat



**HIV testing and
counselling**

Condoms

**Mass media
campaigns**

**Blood supply
screening**

**Education/behavior
modification**

**ARVs to prevent
MTCT**

**Proven HIV
prevention
strategies**

**Adult male
circumcision**

Clean syringes

PEP

**Treatment/prevention
of drug/alcohol
abuse**

Fauci. CROI 2010

Antiretroviral treatment of HIV-1 prevents transmission of HIV-1: where do we go from here?

Myron S Cohen, M Kumi Smith, Kathryn E Muessig, Timothy B Hallett, Kimberly A Powers, Angela D Kashuba

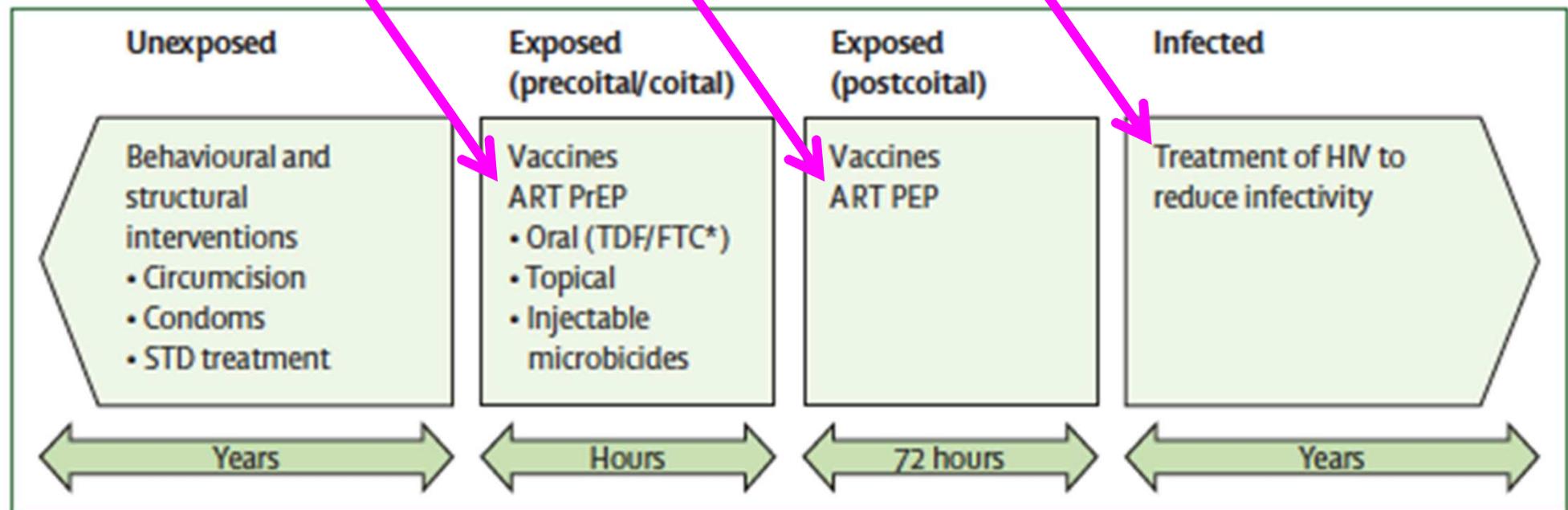


Figure 1: Four opportunities for HIV prevention

Lancet 2013

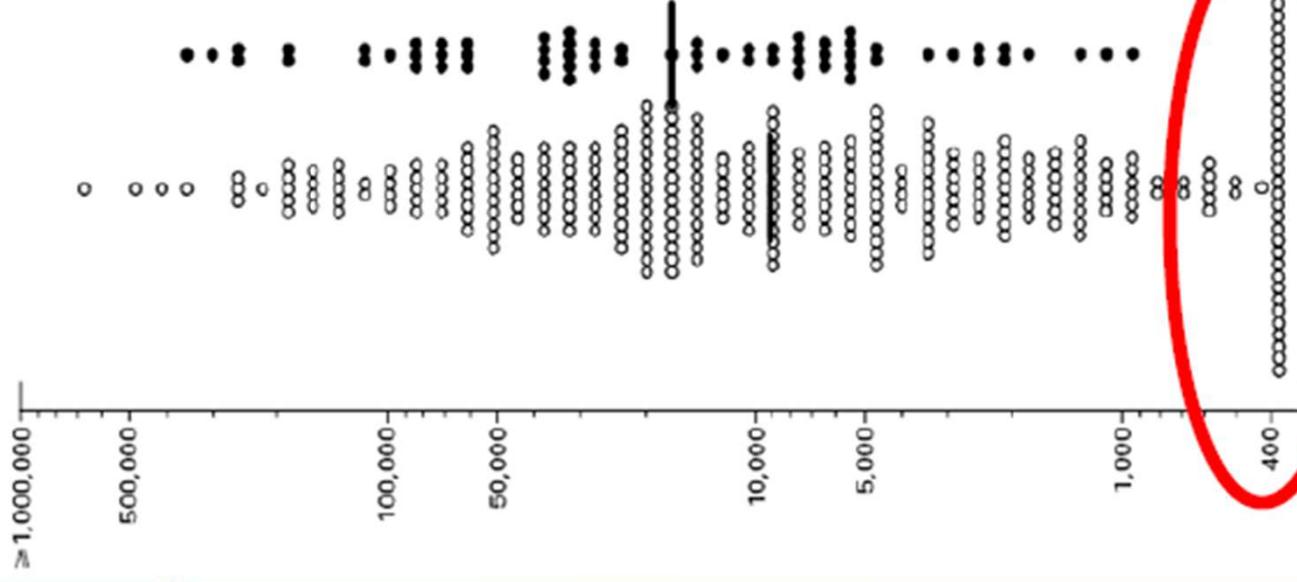
N Engl J Med 1999;341:394-402

Maternal levels of plasma HIV RNA and the risk of perinatal transmission

PATRICIA M. GARCIA, M.D., M.P.H., LESLIE A. KALISH, D.Sc., JANE PITT, M.D., HOWARD MINKOFF, M.D.,
THOMAS C. QUINN, M.D., SANDRA K. BURCHETT, M.D., JANET KORNEGAY, Ph.D., BROOKS JACKSON, M.D.,
JOHN MOYE, M.D., CELINE HANSON, M.D., CARMEN ZORRELLA, M.D., AND JUDY F. LEW, M.D.,
FOR THE WOMEN AND INFANTS TRANSMISSION STUDY GROUP*

- Mother's viremia of a non infected new born
- Mother's viremia of an infected new born

**Absence de transmission
lorsque la virémie
maternelle est < 1000/ml**



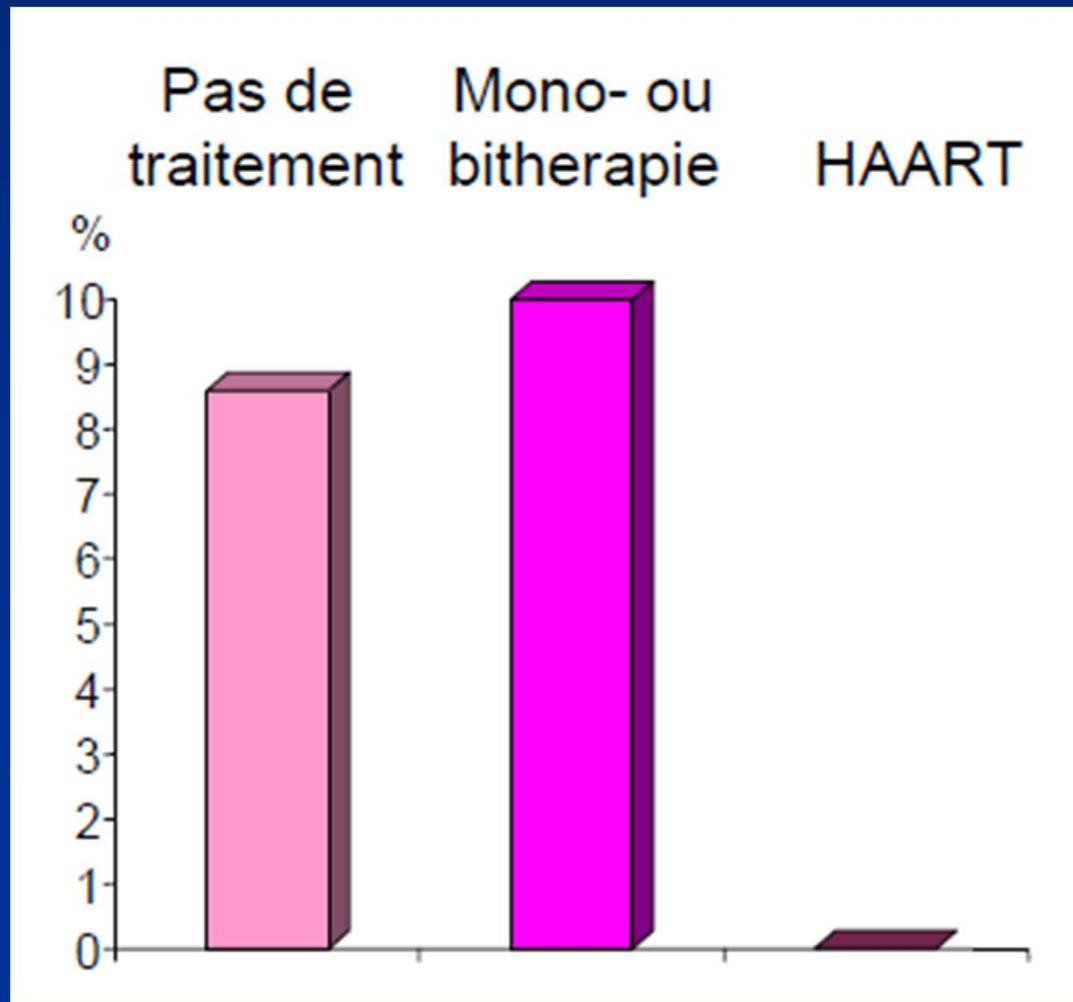
Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda

Ronald H Gray, Maria J Wawer, Ron Brookmeyer, Nelson K Sewankambo, David Serwadda, Fred Wabwire-Mangen, Tom Lutalo, Xianbin Li, Thomas vanCott, Thomas C Quinn, and the Rakai Project Team*

HIV-1 viral load (copies/mL)				
<1700	1/43	10.40	26.0	1.00
1700-12 499	11/45	9.38	22.0	16.1 (3.11-295.71)
12 500-	11/42	7.98	23.0	17.91 (3.44-328.65)
38 499				
>38 500	15/44	7.91	18.8	27.7 (5.42-506.79)

Taux d'infection du partenaire, étude espagnole

◆ Traitement du patient index



Castilla, et al. JAIDS 2005; 40:96-101

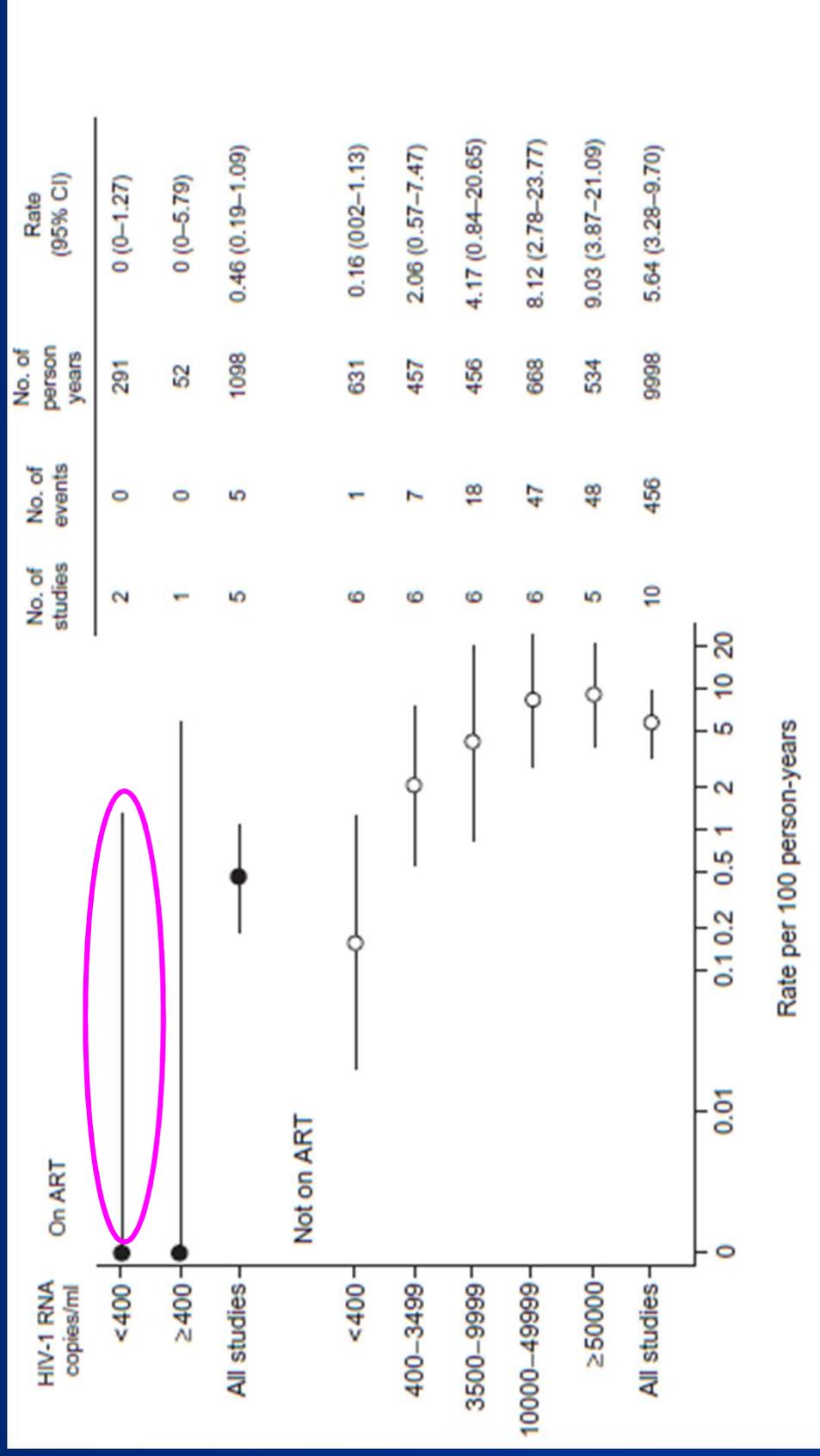
Les personnes séropositives ne souffrant d'aucune autre MST et suivant un traitement antirétroviral efficace ne transmettent pas le VIH par voie sexuelle

Commission fédérale
pour les problèmes liés
au Sida
*Bulletin des médecins
suisses 2008*



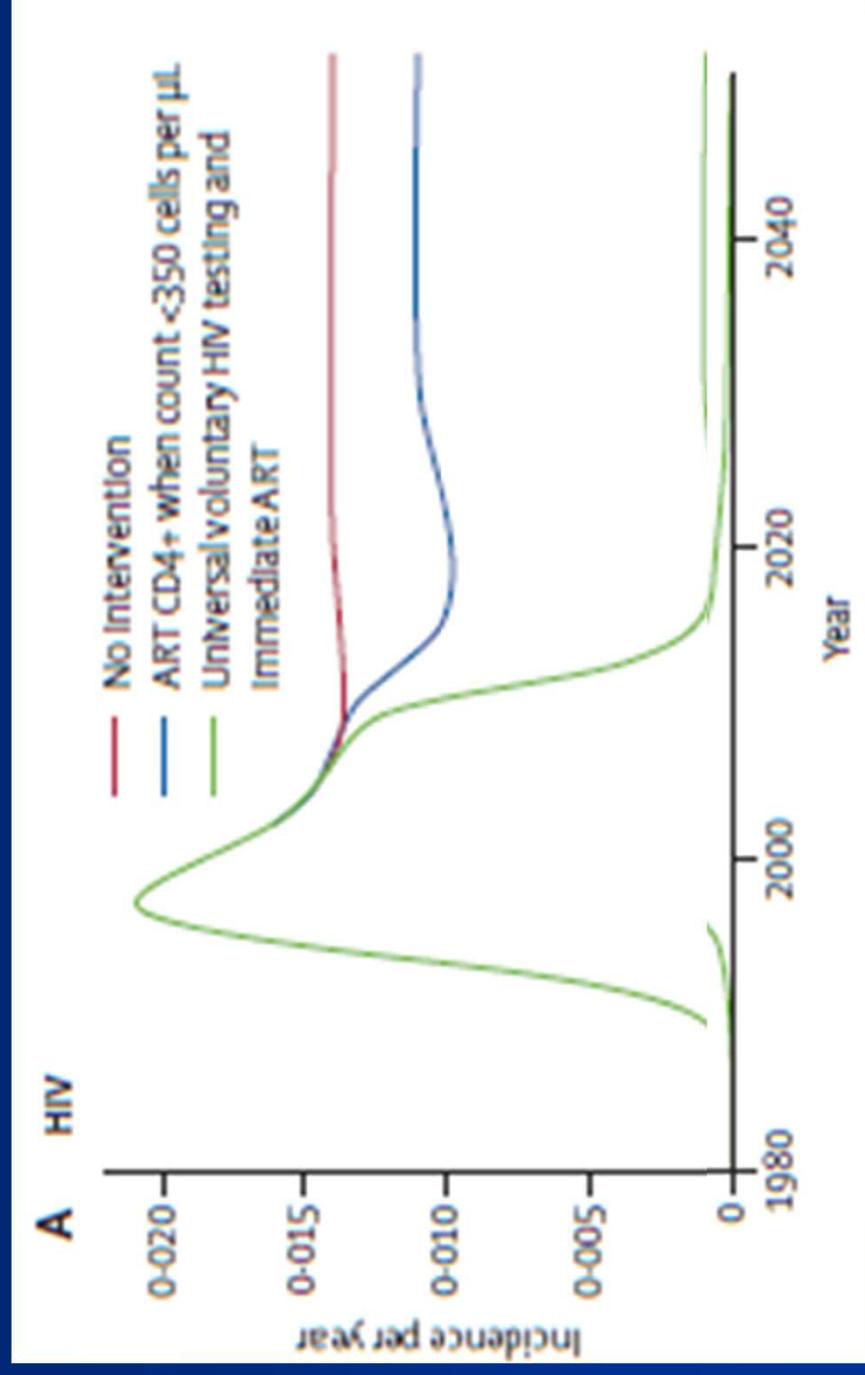
Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis

Suzanna Attia^a, Matthias Egger^{a,b}, Monika Müller^a, Marcel Zwahlen^a and Nicola Low^{a,b}



Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model

Reuben M Granich, Charles F Gilks, Christopher Dye, Kevin M De Cock, Brian G Williams



EDITORIAL



Antiretroviral Treatment as Prevention

Scott M. Hammer, M.D.

ORIGINAL ARTICLE

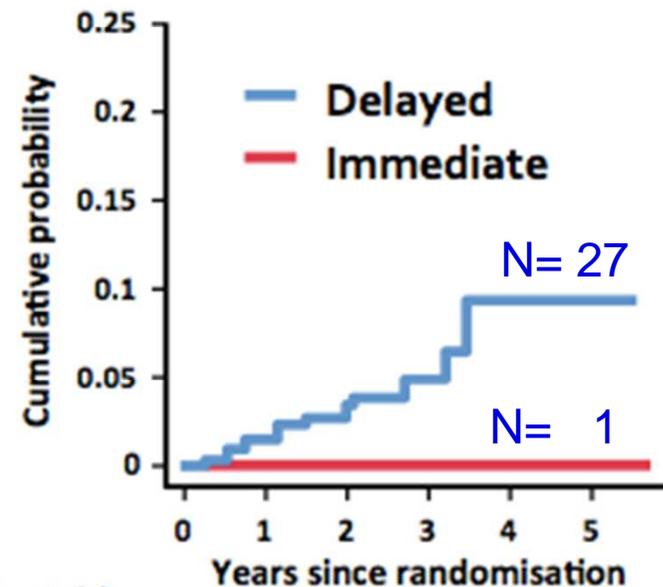
Prevention of HIV-1 Infection with Early Antiretroviral Therapy

Myron S. Cohen, M.D., Ying Q. Chen, Ph.D., Marybeth McCauley, M.P.H.,
 Theresa Gamble, Ph.D., Mina C. Hosseinipour, M.D.,
 Nagalingeswaran Kumarasamy, M.B., B.S., James G. Hakim, M.D.,
 Johnstone Kumwenda, F.R.C.P., Beatriz Grinsztejn, M.D., Jose H.S. Pilotto, M.D.,
 Sheela V. Godbole, M.D., Sanjay Mehendale, M.D., Suwat Chariyalertsak, M.D.,
 Breno R. Santos, M.D., Kenneth H. Mayer, M.D., Irving F. Hoffman, P.A.,
 Susan H. Eshleman, M.D., Estelle Piwowar-Manning, M.T., Lei Wang, Ph.D.,
 Joseph Makhema, F.R.C.P., Lisa A. Mills, M.D., Guy de Bruyn, M.B., B.Ch.,
 Ian Sanne, M.B., B.Ch., Joseph Eron, M.D., Joel Gallant, M.D.,
 Diane Havlir, M.D., Susan Swindells, M.B., B.S., Heather Ribaud, Ph.D.,
 Vanessa Elharrar, M.D., David Burns, M.D., Taha E. Taha, M.B., B.S.,
 Karin Nielsen-Saines, M.D., David Celentano, Sc.D., Max Essex, D.V.M.,
 and Thomas R. Fleming, Ph.D., for the HPTN 052 Study Team*

N = 1763

Couples serodiscordants
 CD4 entre 350 et 550 mm³

HPTN 052:
 Linked HIV transmission



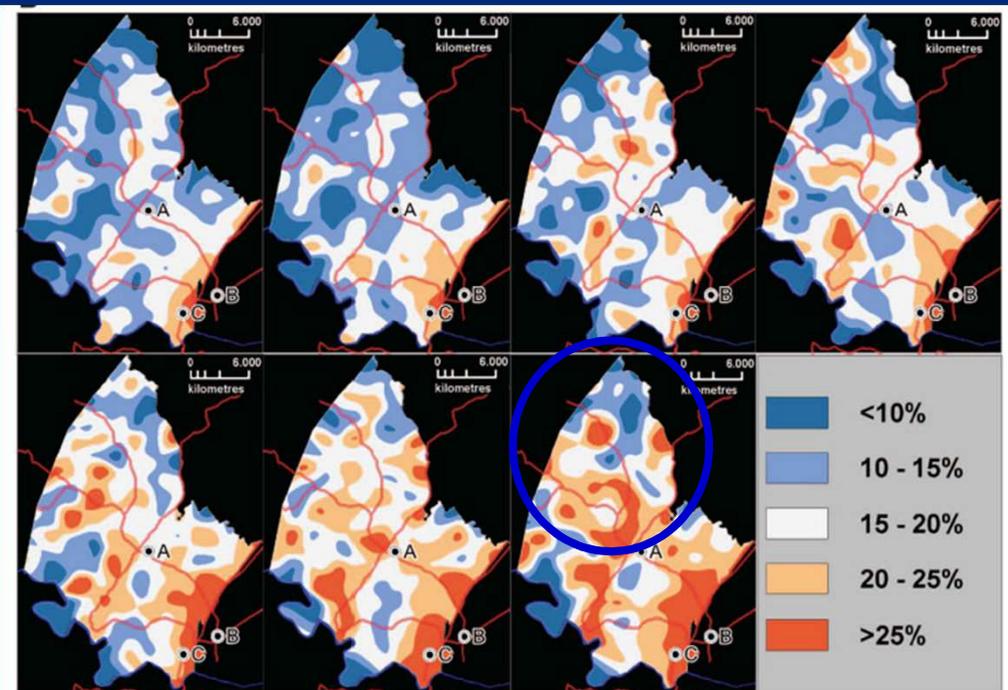
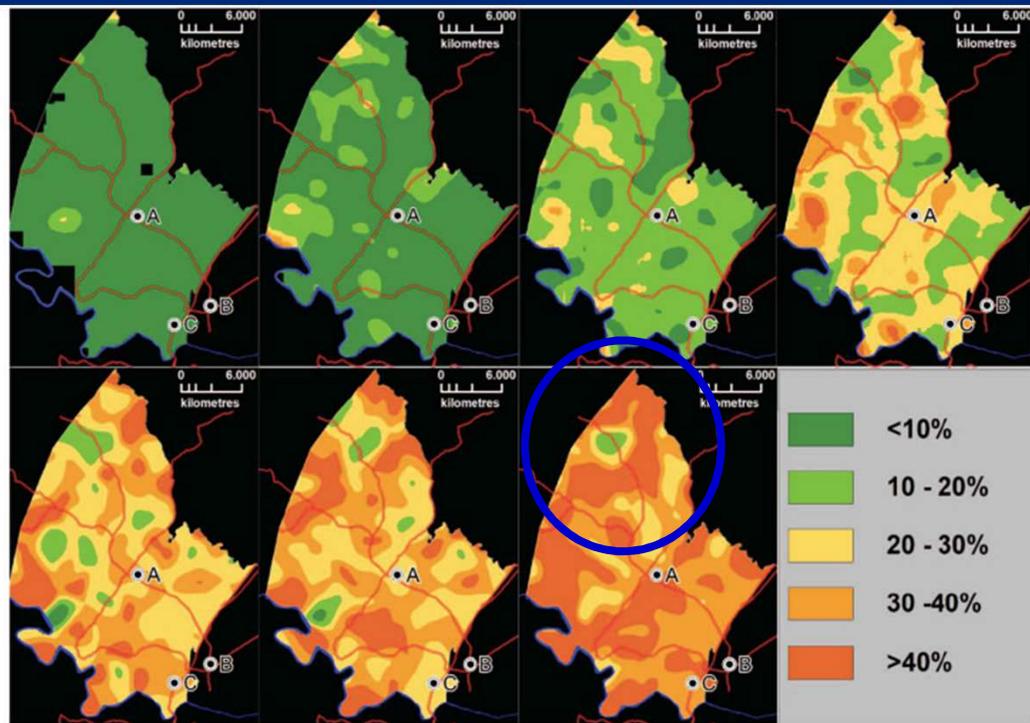
No. at risk	0	1	2	3	4	5
Immediate	893	658	298	79	31	24
Delayed	882	655	297	80	26	22

High Coverage of ART Associated with Decline in Risk of HIV Acquisition in Rural KwaZulu-Natal, South Africa

Frank Tanser^{1,*}, Till Bärnighausen^{1,2}, Erofilo Grapsa¹, Jaffer Zaidi¹, and Marie-Louise Newell^{1,3}

- N = 16,667
- Cohorte prospective de patients non infectés par le VIH
- 2004- 2011

Si proportion ART > 30%; risque d'être infecté 38% moindre que si ART <10%



Proportion ART

Prevalence VIH

Universal Voluntary Testing and Treatment for Prevention of HIV Transmission

Carl W. Dieffenbach, PhD

Anthony S. Fauci, MD

quire validation with research. Retrospective analyses of existing data from cohort studies and clinical trials and the design and execution of new prospective cohort studies and

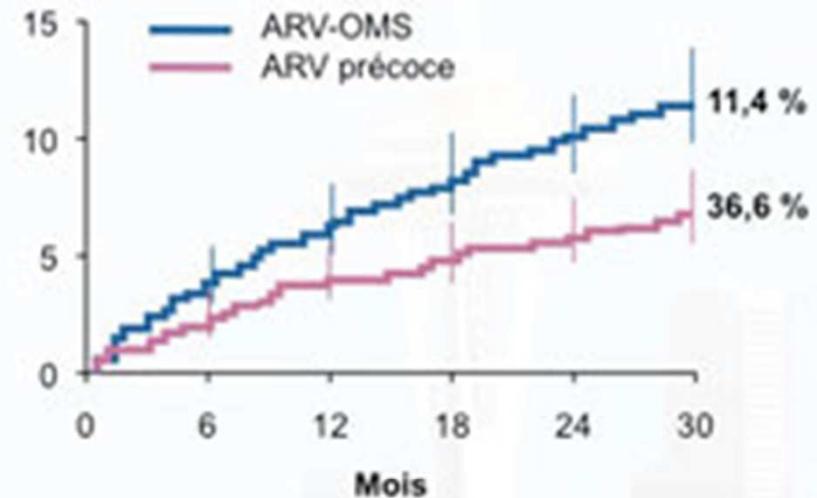
“For a test and treat strategy to be ethically sound, there must be a benefit of early treatment to the individual, as well as to society as a whole.”

JAMA, June 10, 2009—Vol 301, No. 22 (Reprinted)

Temprano

- ◆ Bénéfices et risques d'un traitement ARV précoce et/ou d'une chimioprophylaxie antituberculeuse chez des adultes infectés par le VIH

Probabilité d'avoir l'événement morbidity infectieuse ou tumorale sévère liée au VIH ou décès :



	n	Taux/100 patients. année	RRa	p
ARV-OMS	11	4,9		
ARV précoce	64	2,8	0,56	0,0002
Pas d'INH	104	4,7		
INH	64	3,0	0,65	0,005

« Desinhibition sexuelle; augmentation de la fréquence des prises de risque »

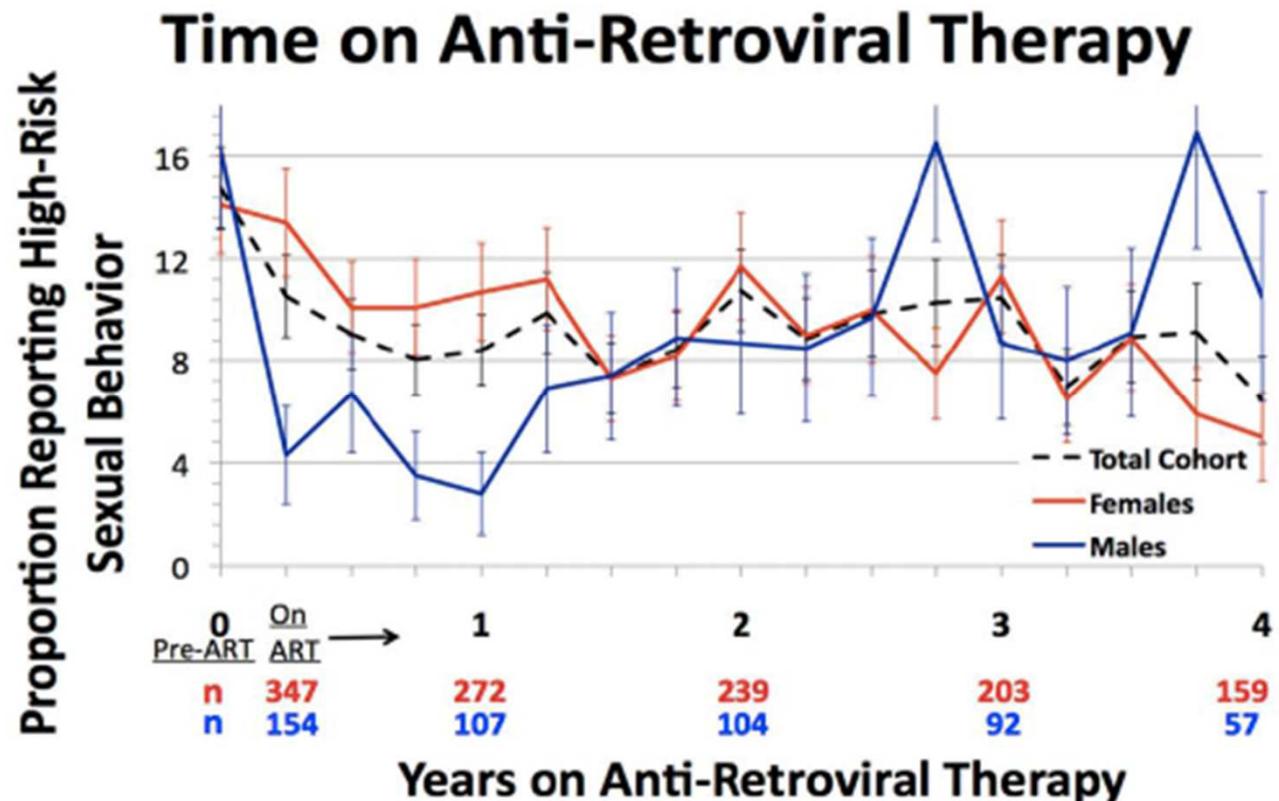
OPEN ACCESS Freely available online

PLOS ONE

Disinhibition in Risky Sexual Behavior in Men, but Not Women, during Four Years of Antiretroviral Therapy in Rural, Southwestern Uganda

Annet Kembabazi^{1*}, Francis Bajunirwe², Peter W. Hunziker³, Jessica E. Haberer⁵, David R. Bangsberg^{5,6}, Mark J. Silliman^{1,4}

1A.



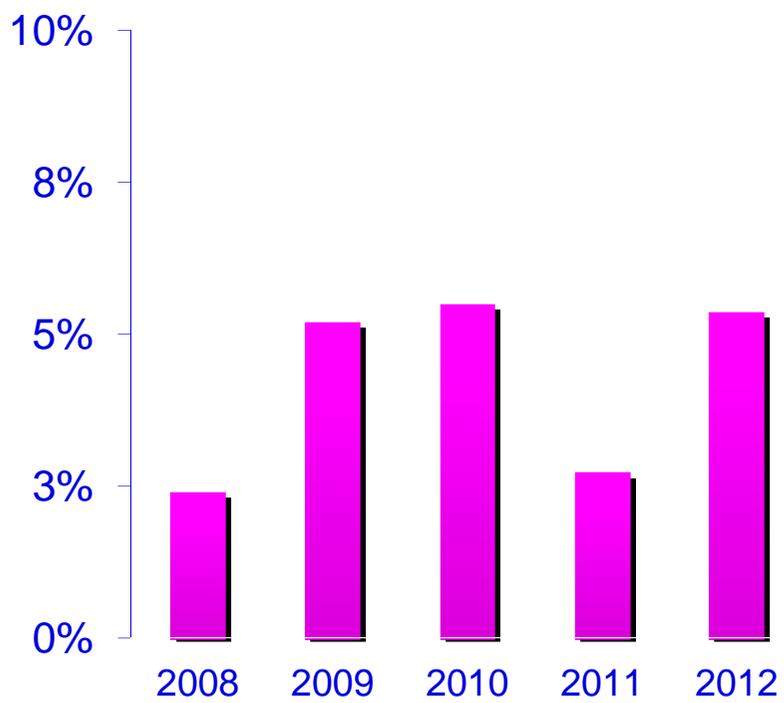
Résistance

Low Prevalence of Transmitted Drug Resistance of HIV-1 During 2008–2012 Antiretroviral Therapy Scaling up in Southern Vietnam

Junko Tanuma, MD, PhD, Vo Minh Quang, MD,† Atsuko Hachiya, PhD,‡ Akane Joya, BSc,* Koji Watanabe, MD, PhD,* Hiroyuki Gatanaga, MD, PhD,* Nguyen Van Vinh Chau, MD, PhD,† Nguyen Tran Chinh, MD, PhD,† and Shinichi Oka, MD, PhD**

TABLE 4. Prevalence of Transmitted Drug Resistance Mutations in Specific HIV Risk Categories

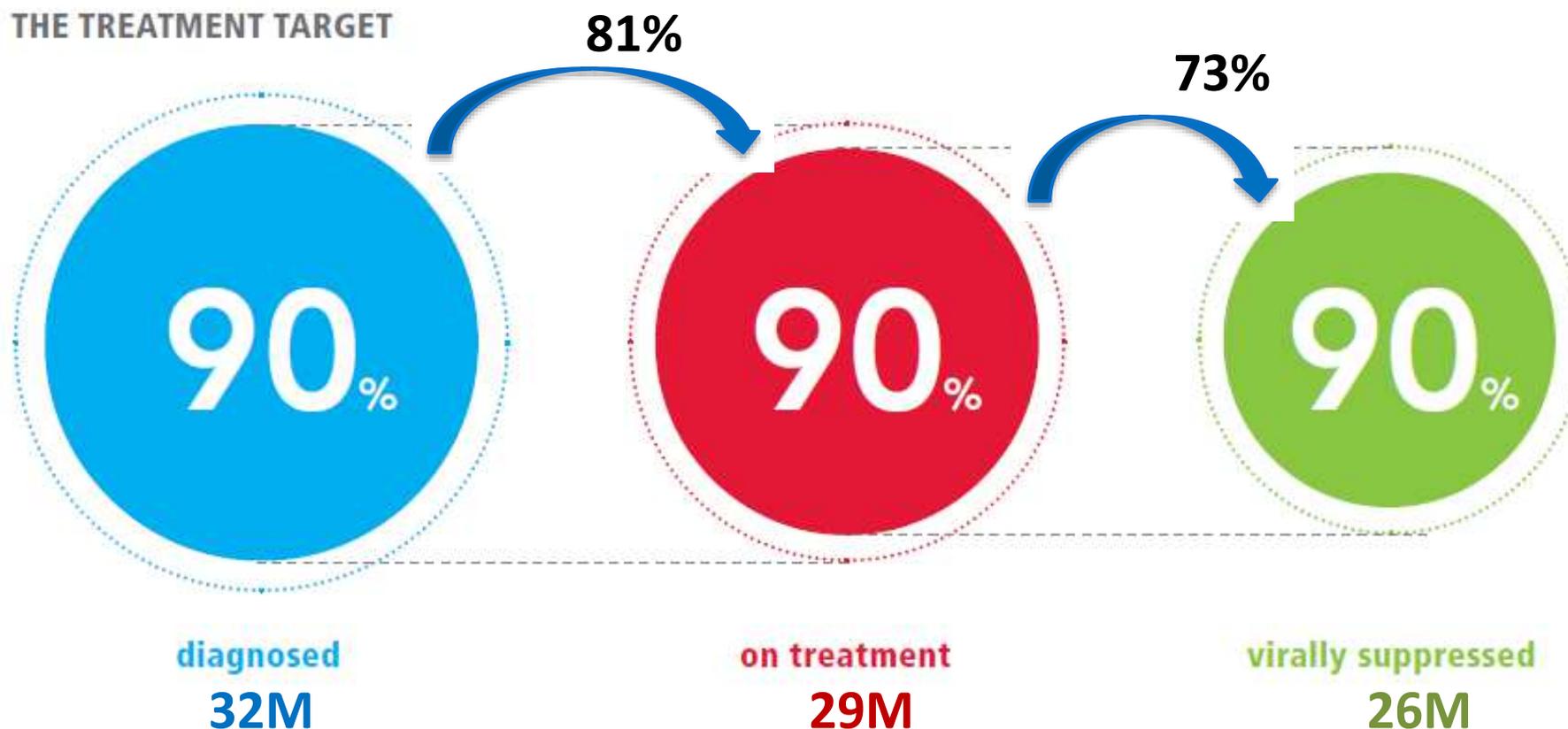
	Total	2011	2012
Total TDR rate [% (n/total)]	4.18 (5)	2.72 (8/294)	5.36 (14/261)
TDR rate in HIV risk categories [% (n/total)]			
Heterosexual contact alone	3.33 (2)	1.92 (4/208)	5.02 (10/199)
IDU alone	5.41 (1)	2.27 (1/44)	7.69 (3/39)
IDU plus heterosexual	2.78 (2)	3.57 (1/28)	0 (0/7)
Homosexual contact alone	0 (0)	- (0/0)	- (0/0)
Other	0 (0)	0 (0/3)	- (0/0)
Unknown	7.80 (1)	18.2 (2/11)	6.25 (1/16)





qui influenceront sur notre travail

THE TREATMENT TARGET

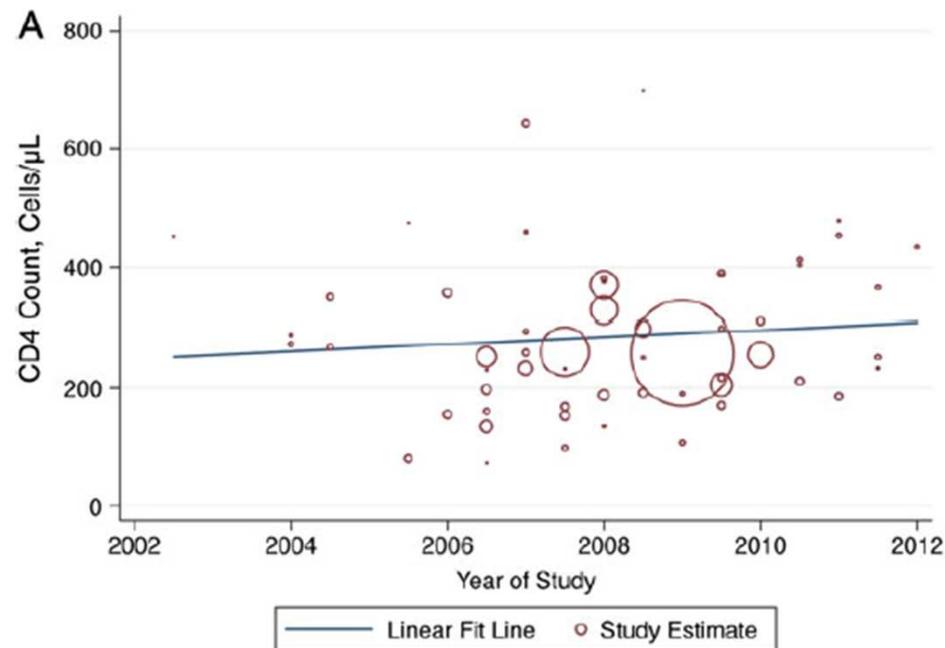


De nouvelles initiatives mondiales:

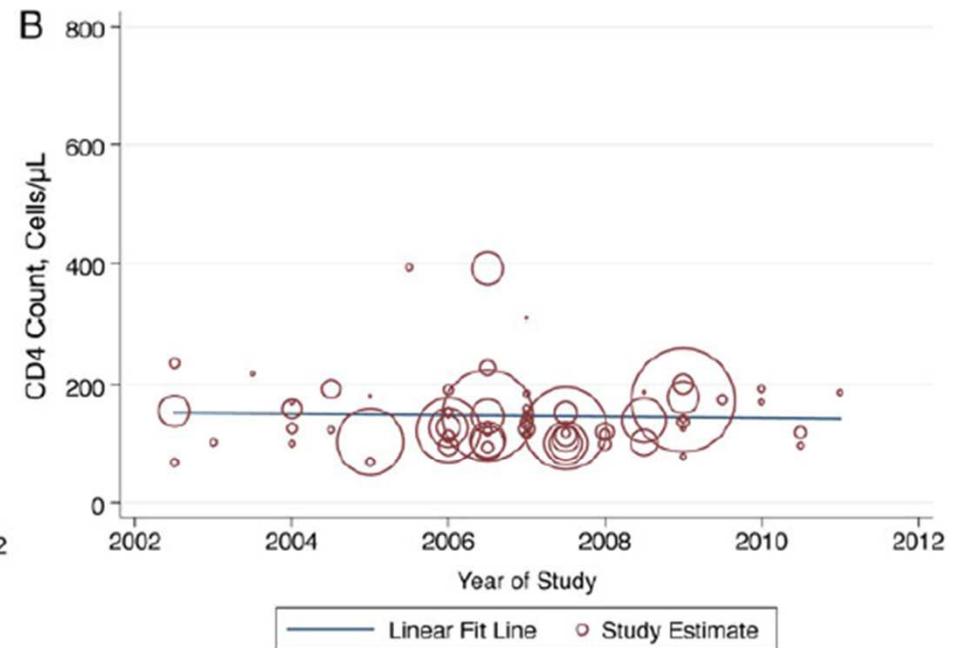
- 1) Un traitement précoce - FAST TRACK, le PEPFAR 3.0
- 2) Initiative Accès aux Diagnostiques (DAI)
- 3) Pédiatrie - ACT, Double dividendes, PHTI, Adolescents - Tous compris!

Trends in CD4 Count at Presentation to Care and Treatment Initiation in Sub-Saharan Africa, 2002–2013: A Meta-analysis

Mark J. Siedner,^{1,2,3} Courtney K. Ng,¹ Ingrid V. Bassett,^{2,3,4} Ingrid T. Katz,^{1,3,5} David R. Bangsberg,^{1,2,3,6} and Alexander C. Tsai^{1,3,6,7}



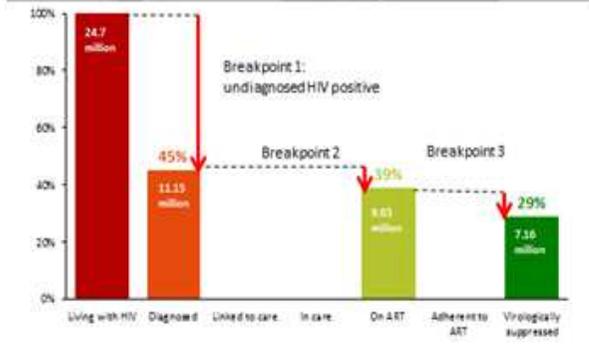
CD4 au diagnostic



CD4 au début de traitement

Même dans les contextes avec une bonne couverture du traitement antirétroviral, les cascades de traitement montrent des fuites importantes

Cascade of HIV care – Sub-Saharan Africa



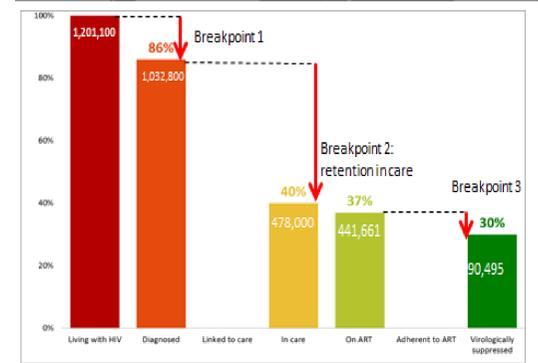
Reference: UNAIDS Gap Report 2014

Cascade of HIV Care – Brazil, 2013



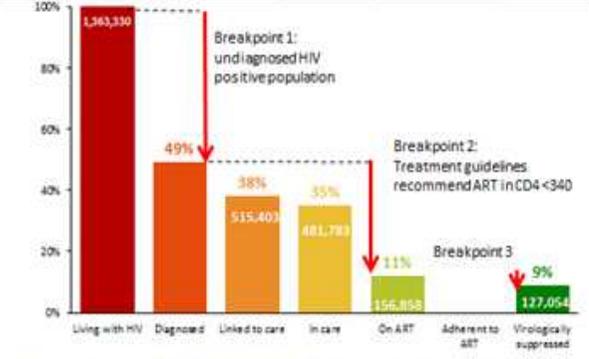
Reference: Brazilian Ministry of Health, Cascade of continuous care in Brazil, 2013. HIV epidemiology news, October 2014, Brazil.

Cascade of HIV care – United States



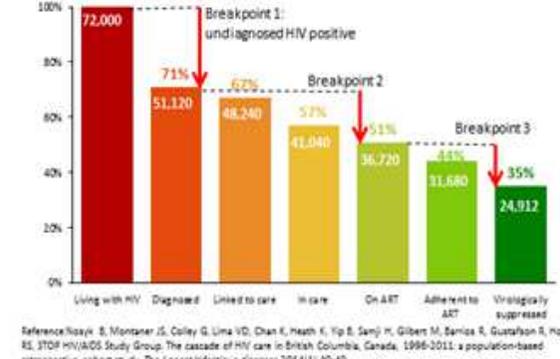
Reference: Heather Bradley, PhD 1, H. Irene Hall, PhD 1, Richard J. Wolitski et al: HIV Diagnosis, Care, and Treatment Among Persons Living with HIV – United States, 2011. November 28, 2014 / 63(47):1113-1117 available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6347a5.htm?cid=mm6347a5_w11tab1

Cascade of HIV care – Russia



Reference: Petrova, A., Finkelstein, A., Johnson, V., et al. The cascade of HIV care in Russia. *AIDS* 2012;26(10):2401-2408. <http://dx.doi.org/10.1097/QAD.0b013e3182401000>

Cascade of HIV care – British Columbia (CA)



Reference: Naayik, S., Montaner, J.S., Colley, G., Lima, V.D., Chan, K., Heath, K., Yip, S., Sanji, H., Gilbert, M., Baril, R., Gustafson, P., Hogg, R.S. STDF HIV/AIDS Study Group. The cascade of HIV care in British Columbia, Canada, 1996-2011: a population-based retrospective cohort study. *The Lancet Infectious Diseases* 2014;14:40-49.

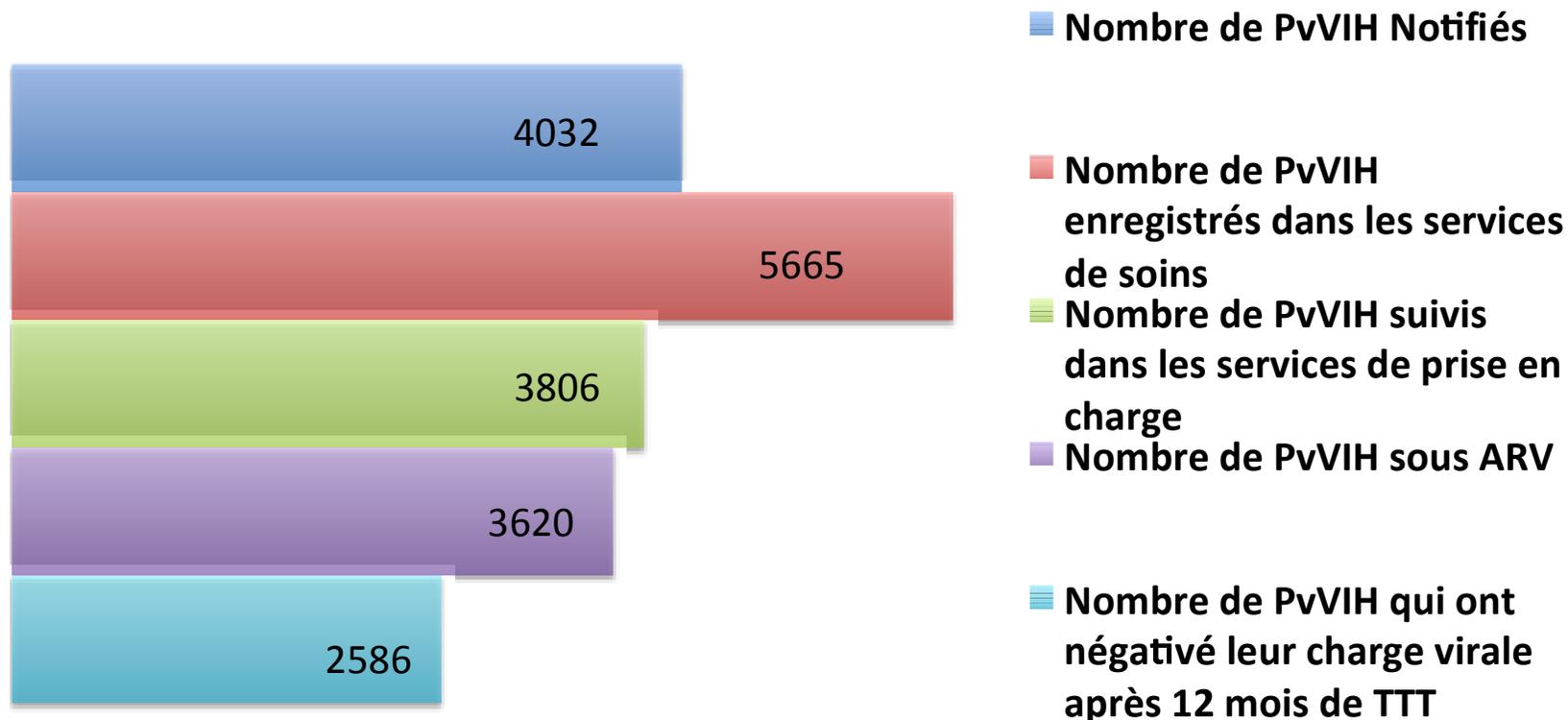
Hill et al. CROI 2015 [abstr 1118]





Analyse de la cascade VIH 2009-2013

Maroc



33% des PvVIH sont perdues entre l'enregistrement et le suivi dans les services de prise en charge

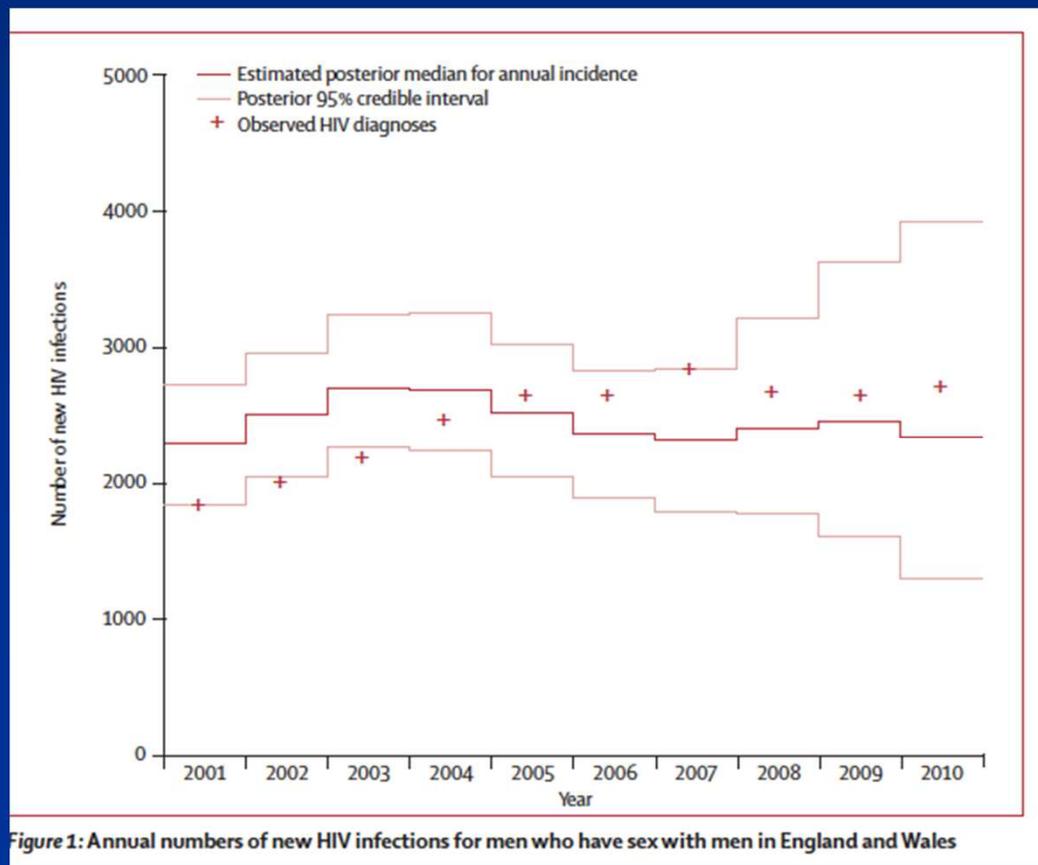
71% des PvVIH ont négativé leur charges virales après 12 mois de traitement

45% des personnes diagnostiquées et enregistrées ont un CV indétectables

-
- ◆ Dépistage
 - ◆ Lien avec le système de soins
 - ◆ Rétention dans le système de soins
 - ◆ Adhérence au traitement

“WHO ‘Treatment as Prevention’ guidelines are unlikely to decrease HIV transmission in the UK unless undiagnosed HIV infections are reduced”

Alison E. Brown, Anthony Nardone and Valerie C. Delpech; AIDS 2013



Lancet Infect Dis 2013

HIV sexual transmission risk among serodiscordant couples: assessing the effects of combining prevention strategies

Arielle Lasry, Stephanie L. Sansom, Richard J. Wolitski, Timothy A. Green, Craig B. Borkowf, Pragna Patel and Jonathan Mermin

Strategies	1 year	10 years
Receptive anal sex (RAS)	20.0%	89.0%
vaginal sex only, no anal sex (base-case)	6.0%	44.0%
Consistent <u>condom</u> * use and RAS	4.0%	35.0%
Consistent <u>condom</u> use	1.0%	11.0%
<u>ART</u> ** and RAS	0.9%	8.0%
<u>ART</u> and Consistent <u>condom</u> use and <u>PrEP</u>	0.05%	0.5%

*80% de protection; **96% de protection

AIDS 2014

Prophylaxie Pre-exposition (PreP)

- ◆ **Antirétroviraux ayant propriétés de diffusion dans les muqueuses vaginales et anales**

- Viread
- Truvada
- Maraviroc
- Rilpivirine
- Dapivirine
- Dolutegravir

- ◆ **Formulation: gélules, gel vaginal, anneau imprégné**

- ◆ **Modalités de prise:**

- Tous les jours
- Intermittent

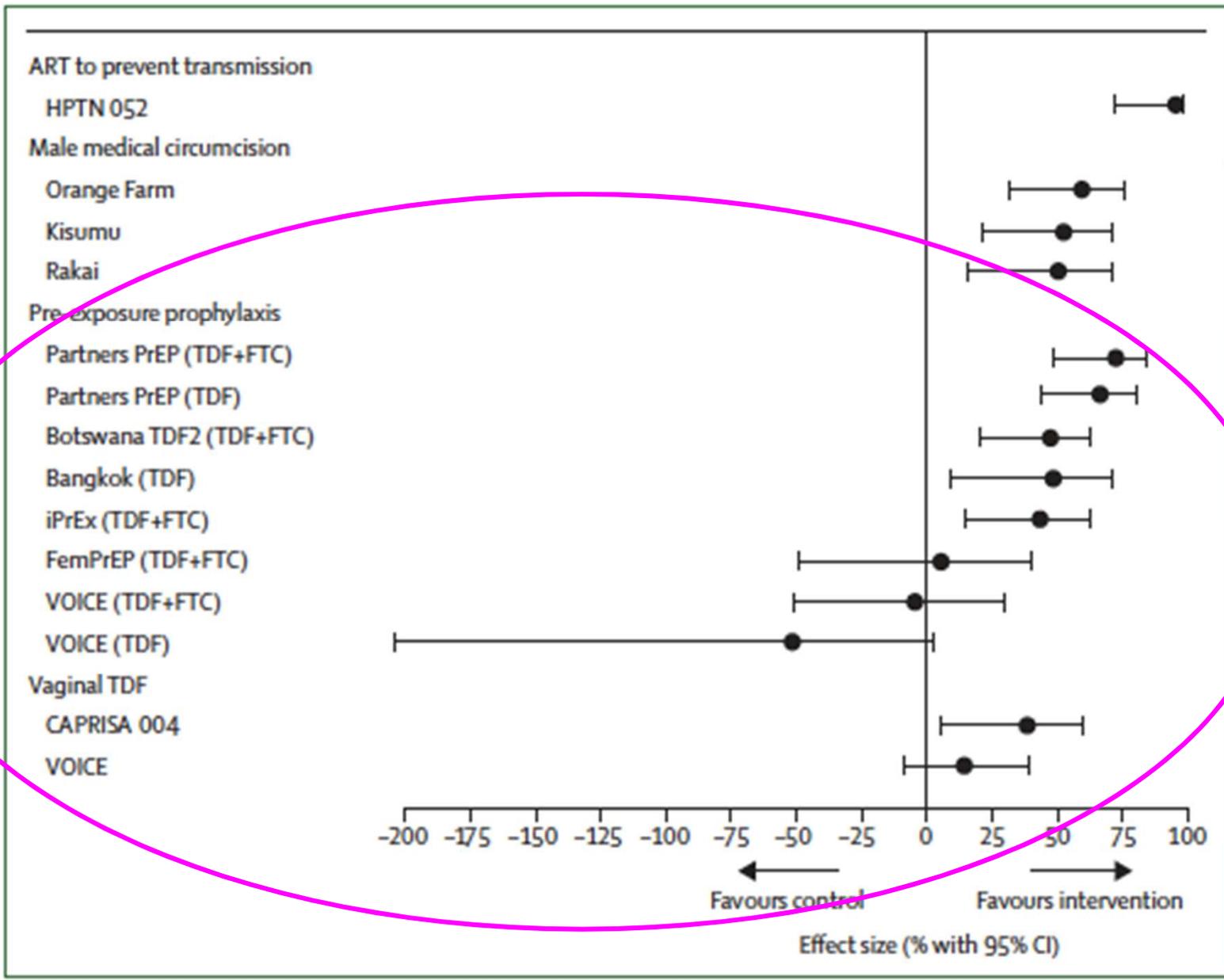


Figure 5: Clinical trials of interventions to prevent sexual transmission of HIV-1

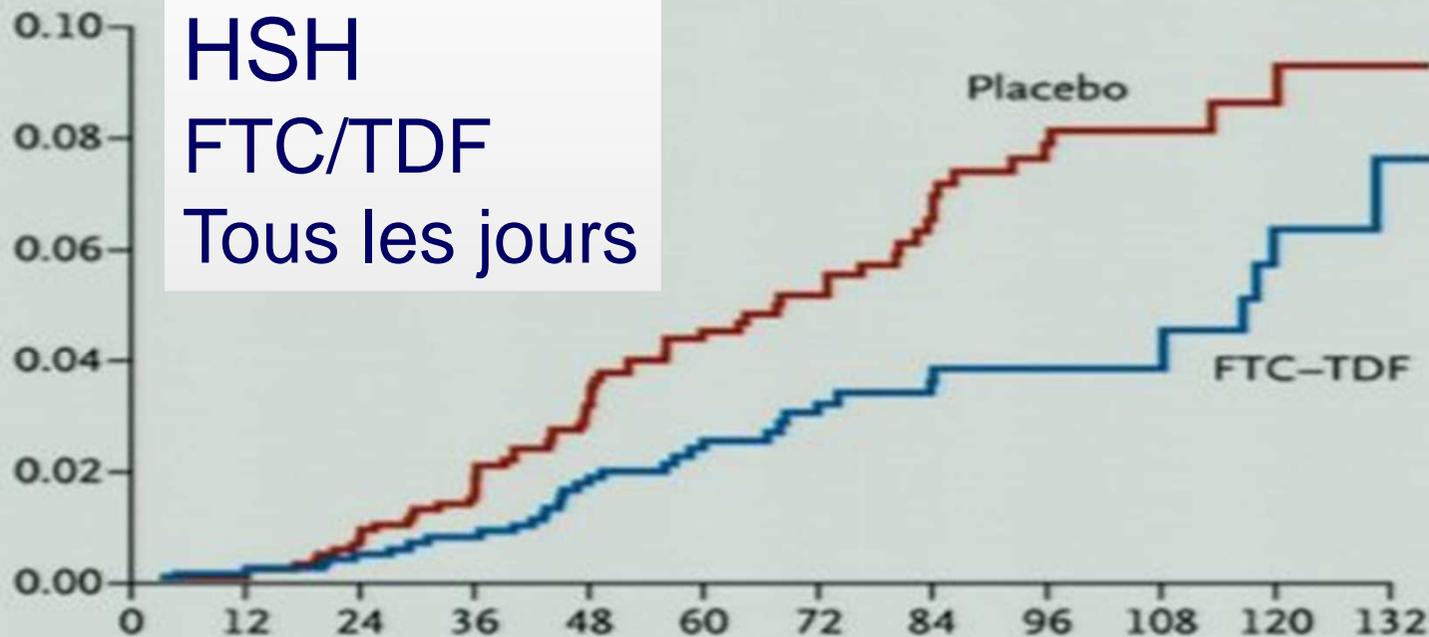
	Efficacy of tenofovir-emtricitabine compared with placebo	Adherence*
Partners PrEP ¹⁴⁴	75%	82%
Botswana TDF2 ¹⁴⁵	62%	79%
Bangkok Tenofovir Study ¹⁴⁶	49%	67%
iPrEx ¹⁴⁷	44%	51%
Fem-PrEP ¹⁴⁸	6%	26%
VOICE ¹⁴⁹	-4.2%	29%

* Assessed by plasma tenofovir concentrations.

Table 2: Association between adherence and efficacy of oral tenofovir-emtricitabine for the prevention of HIV-1 acquisition in trials of pre-exposure prophylaxis



iPREX : KM Estimates of Time to HIV Infection (mITT Population)



After a median follow-up of 14 months, 100 subjects became infected, 36 in the TDF/FTC arm and 64 in the placebo arm :

44% reduction in the incidence of HIV (95% CI : 15-63, p=0.005)

Update at CROI 2011 : 42% at 144 weeks

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

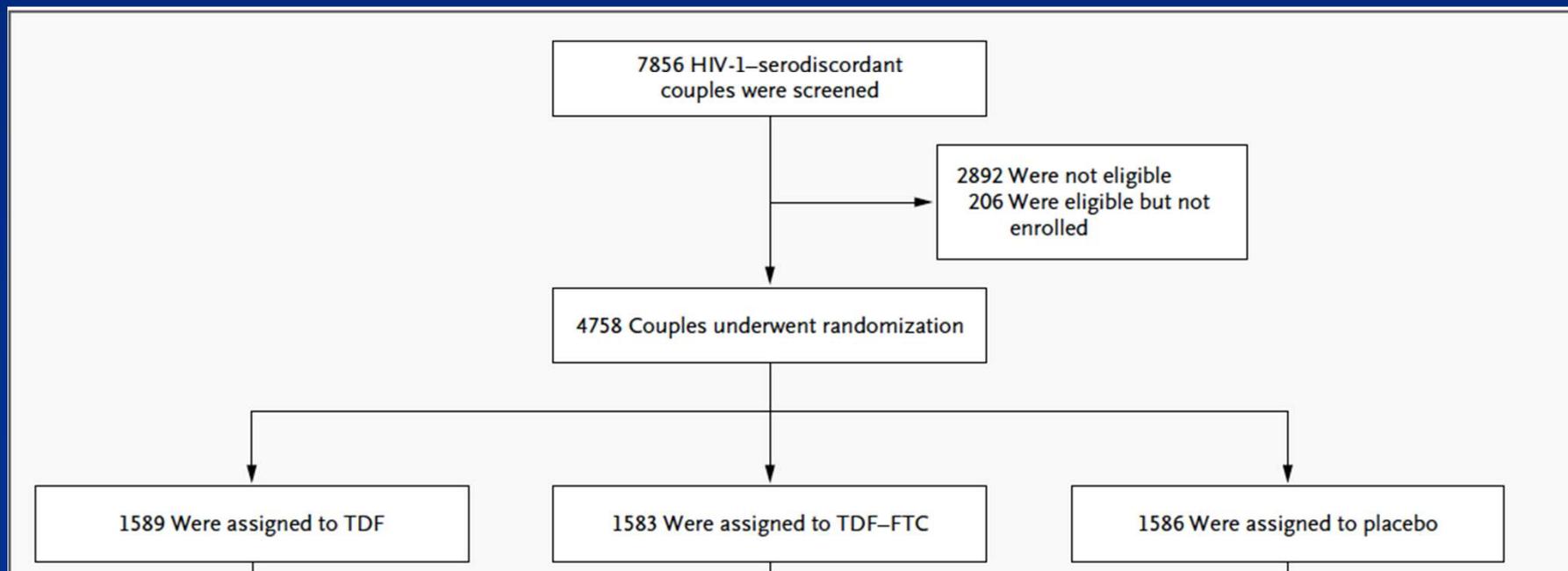
AUGUST 2, 2012

VOL. 367 NO. 5

Antiretroviral Prophylaxis for HIV Prevention in Heterosexual Men and Women

J.M. Baeten, D. Donnell, P. Ndase, N.R. Mugo, J.D. Campbell, J. Wangisi, J.W. Tappero, E.A. Bukusi, C.R. Cohen, E. Katabira, A. Ronald, E. Tumwesigye, E. Were, K.H. Fife, J. Kiarie, C. Farquhar, G. John-Stewart, A. Kakia, J. Odoyo, A. Mucunguzi, E. Nakku-Joloba, R. Twesigye, K. Ngure, C. Apaka, H. Tamooh, F. Gabona, A. Mujugira, D. Panteleeff, K.K. Thomas, L. Kidoguchi, M. Krows, J. Revall, S. Morrison, H. Haugen, M. Emmanuel-Ogier, L. Ondrejcek, R.W. Coombs, L. Frenkel, C. Hendrix, N.N. Bumpus, D. Bangsberg, J.E. Haberer, W.S. Stevens, J.R. Lingappa, and C. Celum, for the Partners PrEP Study Team*

Hétérosexuel
FTC/TDF ou TDF
Tous les jours



Couples séro-discordants 62% hommes; 38% femmes

Efficacité

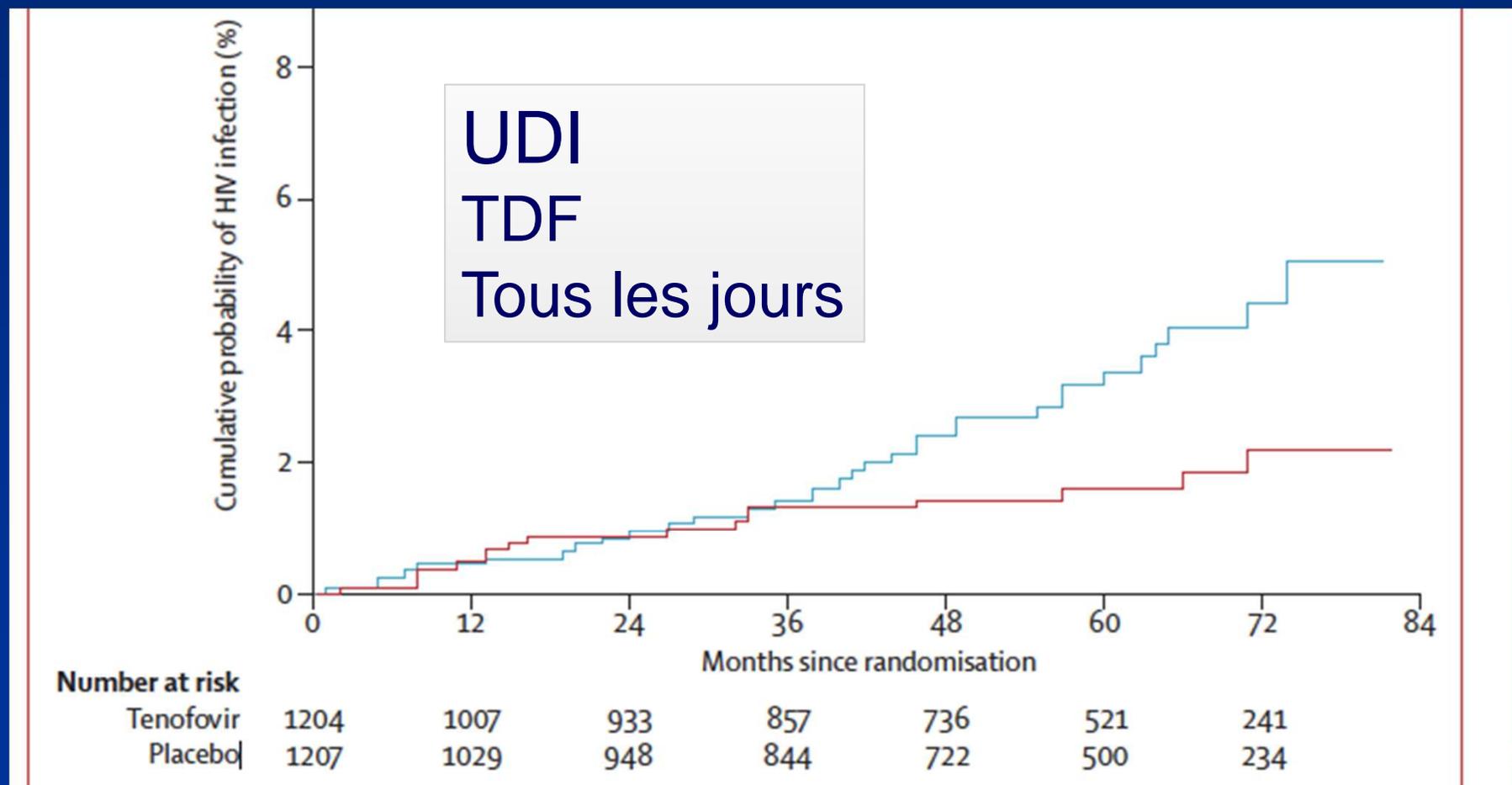
- ◆ 82 contaminations au total,
- ◆ 52 bras placebo,
- ◆ 17 bras Ténofovir (67% de protection)
- ◆ 13 bras Truvada (75% de protection).

Même efficacité de la PrEP chez les hommes et chez les femmes

Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial



Kachit Choopanya, Michael Martin, Pravan Suntharasamai, Udomsak Sangkum, Philip A Mock, Manoj Leethochawalit, Sithisat Chiamwongpaet, Praphan Kitisin, Pitinan Natrujirote, Somyot Kittimunkong, Rutt Chuachoowong, Roman J Gvetadze, Janet M McNicholl, Lynn A Paxton, Marcel E Curlin, Craig W Hendrix, Suphak Vanichseni, for the Bangkok Tenofovir Study Group



On Demand PrEP with Oral TDF/FTC in MSM Results of the ANRS Ipergay Trial

Molina JM, Capitant C, Spire B, Pialoux G, Chidiac C,
Charreau I, Tremblay C, Meyer L, Delfraissy JF,
and the ANRS Ipergay Study Group

Hospital Saint-Louis and University of Paris 7, Inserm SC10-US019
Villejuif, Hospital Tenon, Paris, Hospital Croix-Rousse, Lyon, UMR912
SEAS Marseille, France, CHUM, Montreal, Canada
and ANRS, Paris, France



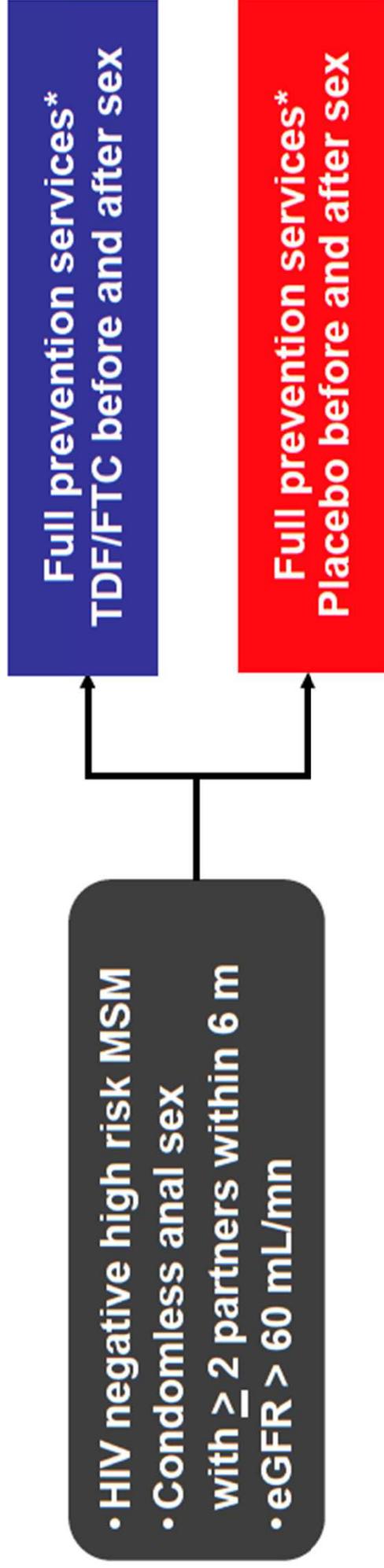
Agence autonome de l'Inserm



www.ipergay.fr

Study Design

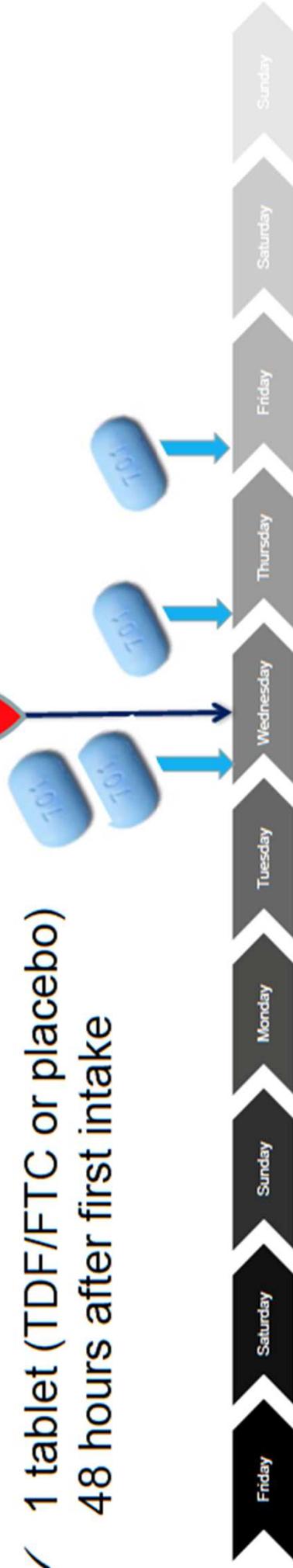
Double-Blinded Randomized Placebo-Controlled Trial



- * Counseling, condoms and gels, 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

Ipergay : Event-Driven iPrEP

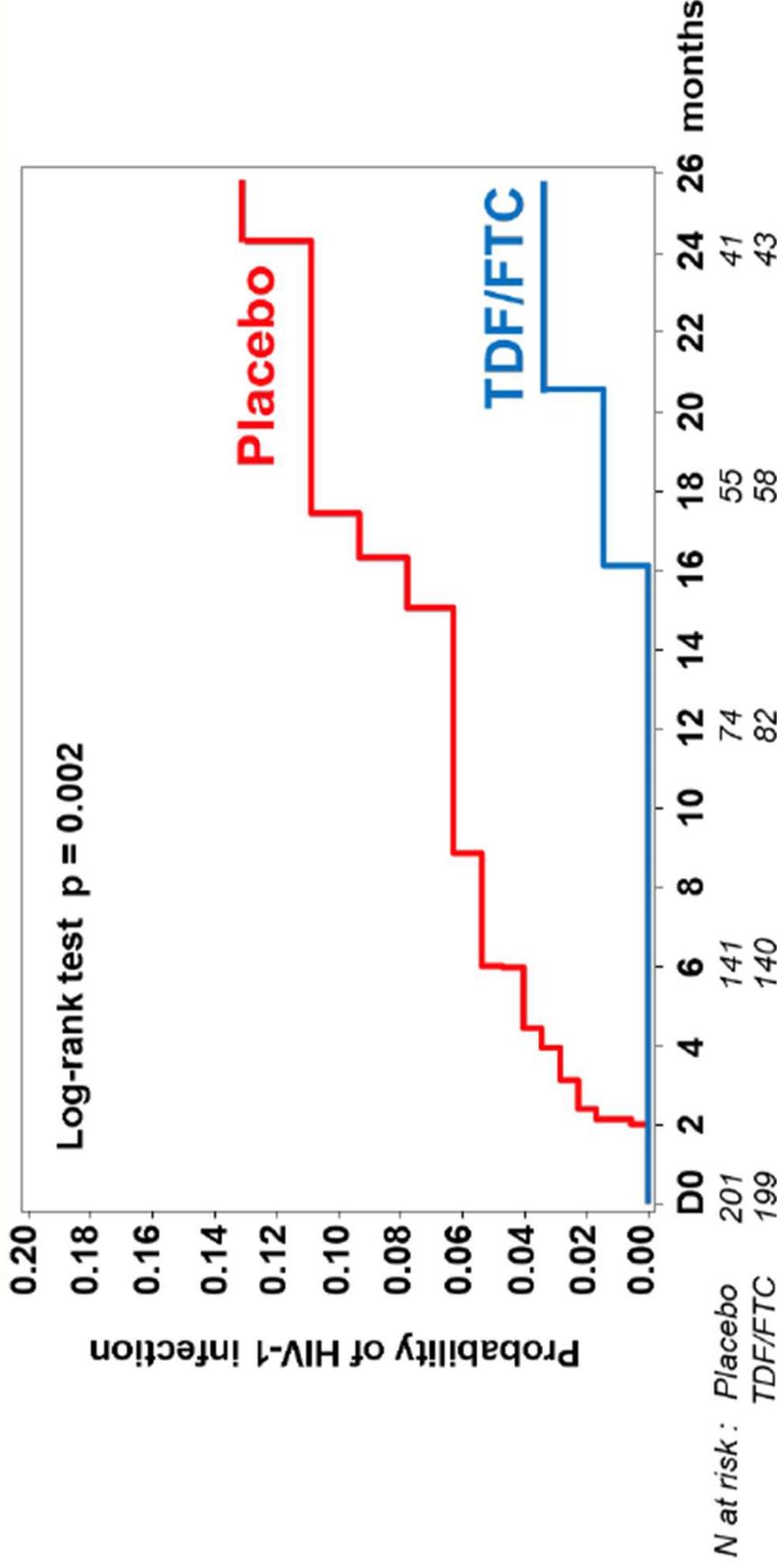
- ✓ 2 tablets (TDF/FTC or placebo)
2-24 hours before sex
- ✓ 1 tablet (TDF/FTC or placebo)
24 hours later
- ✓ 1 tablet (TDF/FTC or placebo)
48 hours after first intake





ipergay
ANRS
Intervention Préventive
de l'Exposition aux Risques
avec et pour les Gays

KM Estimates of Time to HIV-1 Infection (mITT Population)



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: 0.94 per 100 PY)

86% relative reduction in the incidence of HIV-1 (95% CI: 40-99, $p=0.002$)

NNT for one year to prevent one infection : 18

HIV sexual transmission risk among serodiscordant couples: assessing the effects of combining prevention strategies

Arielle Lasry, Stephanie L. Sansom, Richard J. Wolitski, Timothy A. Green, Craig B. Borkowf, Pragna Patel and Jonathan Mermin

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*80% de protection; **96% de protection

AIDS 2014

◆ Stratégies de prévention combinée

En Conclusion

The Uptake and Accuracy of Oral Kits for HIV Self-Testing in High HIV Prevalence Setting: A Cross-Sectional Feasibility Study in Blantyre, Malawi

Augustine Talumba Choko^{1*}, Nicola Desmond^{1,2}, Emily L. Webb³, Kondwani Chavula¹, Sue Napierala-Mavedzenge⁴, Charlotte A. Gaydos⁵, Simon D. Makombe⁶, Treza Chunda¹, S. Bertel Squire², Neil French⁴, Victor Mwapasa¹, Elizabeth L. Corbett^{1,7}

“Whatever the next hottest, scientifically proven HIV treatment or prevention strategies are :

- PreP
- TasP

they will share a common denominator for implementation: the HIV test.

They all begin with learning one’s HIV status.”

Walensky et al. Plos Med 2011