PREVENCIÓ DE LA INFECCIÓ PEL VIH

Dr. Josep Cucurull

Fundació Salut Empordà

Prevenció de la infecció

- Informació i Educació per modificar hàbits de conducta
- Control MTS
- Vacunes
- Circumcisió
- Gels vaginals amb activitat microbicida
- Profilaxi post-exposició (PPE)
- Profilaxi pre-exposició (PrEx)
- Prevenció de la transmissió mare-fill
- Diagnòstic i tractament precoç

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Estudis amb vacunes

- **VAX003 i VAX004 basades en gp120 recombinant, capaces de produir Acs neutralitzants però l'amplia variabilitat de la coberta vírica va frustrar la seva eficàcia**
    - **Flynn NM et al. J Infect Dis 2005**
    - **Pitisuttihum P et al. J Infect Dis 2006**
- **ALVACVIH es va aturar l'assaig als USA**
    - **Rusell ND et al. AIDS Vaccine 2006**
- **Vacuna de Merk (MRKAd5) basada amb els gens gag, pol i nef inserits en l'adenovirus p5 com a vector.**
  - **No va prevenir la infecció**
  - **No va reduir la CV en cas de infecció**
    - **D Kim et al. Infect Dis Clin N Am 2007**

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 3, 2009 VOL. 361 NO. 23

Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand

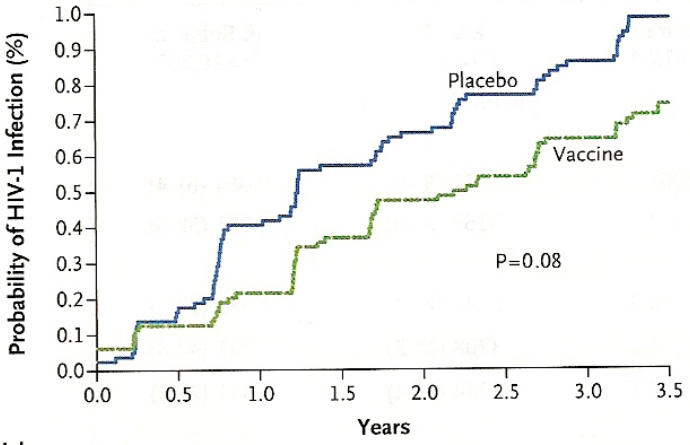
Supachai Rerks-Ngarm, M.D., Punnee Pitisuttithum, M.D., D.T.M.H., Sorachai Nitayaphan, M.D., Ph.D., Jaranit Kaewkungwal, Ph.D., Joseph Chiu, M.D., Robert Paris, M.D., Nakorn Premsri, M.D., Chawetsan Namwat, M.D., Mark de Souza, Ph.D., Elizabeth Adams, M.D., Michael Benenson, M.D., Sanjay Gurunathan, M.D., Jim Tartaglia, Ph.D., John G. McNeil, M.D., Donald P. Francis, M.D., D.Sc., Donald Stablein, Ph.D., Deborah L. Birx, M.D., Supamit Chunsuttiwat, M.D., Chirasak Khamboonruang, M.D., Prasert Thongcharoen, M.D., Ph.D., Merlin L. Robb, M.D., Nelson L. Michael, M.D., Ph.D., Prayura Kunasol, M.D., and Jerome H. Kim, M.D., for the MOPH–TAVEG Investigators*

Table 1. Baseline Characteristics of the Subjects (Modified Intention-to-Treat Population).

Variable	Vaccine (N=8197)	Placebo (N=8198)	All Subjects (N=16,395)
		number (percent)	
Sex			
Male	5033 (61.4)	5031 (61.4)	10,064 (61.4)
Female	3164 (38.6)	3167 (38.6)	6,331 (38.6)
Age group			
≤20 yr	2297 (28.0)	2246 (27.4)	4,543 (27.7)
21–25 yr	3633 (44.3)	3708 (45.2)	7,341 (44.8)
≥26 yr	2267 (27.7)	2244 (27.4)	4,511 (27.5)
Province			
Chon Buri	4107 (50.1)	4107 (50.1)	8,214 (50.1)
Rayong	4090 (49.9)	4091 (49.9)	8,181 (49.9)
Marital status			
Single	3353 (40.9)	3338 (40.7)	6,691 (40.8)
Married	4110 (50.1)	4169 (50.9)	8,279 (50.5)
Divorced	602 (7.3)	541 (6.6)	1,143 (7.0)
Widowed	50 (0.6)	64 (0.8)	114 (0.7)
Separated	82 (1.0)	86 (1.0)	168 (1.0)
No. of sex partners			
0	1864 (22.7)	1801 (22.0)	3,665 (22.4)
1	5428 (66.2)	5495 (67.0)	10,923 (66.6)
>1	619 (7.6)	620 (7.6)	1,239 (7.6)
Did not answer	280 (3.4)	273 (3.3)	553 (3.4)
Missing data	6 (0.1)	9 (0.1)	15 (0.1)
Risk group			
Low	3865 (47.2)	3924 (47.9)	7,789 (47.5)
Medium	2369 (28.9)	2292 (28.0)	4,661 (28.4)
High	1963 (23.9)	1982 (24.2)	3,945 (24.1)
Behavioral risk			
Needle sharing	68 (0.8)	65 (0.8)	133 (0.8)
No condom use			
With casual partner	497 (6.1)	439 (5.4)	936 (5.7)
With commercial sex worker	33 (0.4)	29 (0.4)	62 (0.4)
With same-sex partner	79 (1.0)	90 (1.1)	169 (1.0)
With HIV-infected partner	16 (0.2)	13 (0.2)	29 (0.2)
With partner who injects drugs	12 (0.1)	6 (0.1)	18 (0.1)
With multiple sex partners	128 (1.6)	130 (1.6)	258 (1.6)
Condom use with HIV-infected partner	113 (1.4)	114 (1.4)	227 (1.4)
Symptoms of an STD within past 6 mo*	246 (3.0)	233 (2.8)	479 (2.9)
Drug injection in jail	23 (0.3)	15 (0.2)	38 (0.2)
Occupation as a commercial sex worker	42 (0.5)	44 (0.5)	86 (0.5)
Occupation in the entertainment business	233 (2.8)	237 (2.9)	470 (2.9)

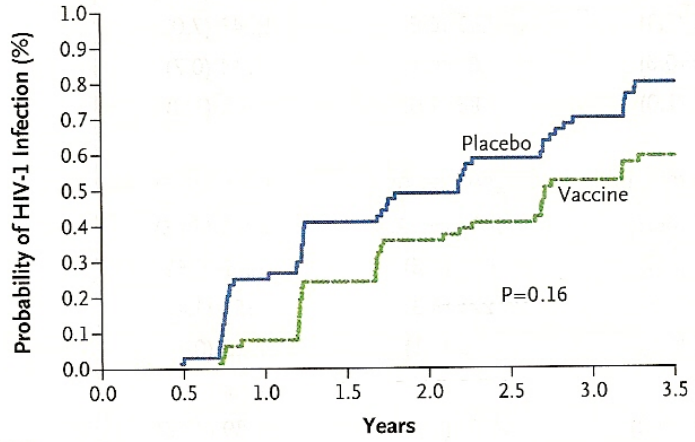
* STD denotes sexually transmitted disease.

A Intention-to-Treat Analysis



No. at Risk					
Placebo	8200	7775	7643	7441	7325
Vaccine	8202	7797	7665	7471	7347
Cumulative No. of Infections					
Placebo		32	52	67	76
Vaccine		17	37	50	56

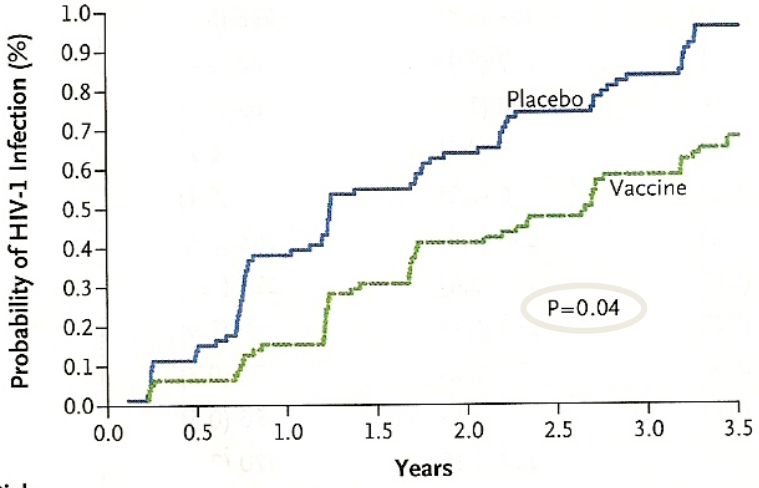
B Per-Protocol Analysis



No. at Risk					
Placebo	6366	6283	6220	6089	6002
Vaccine	6176	6140	6068	5958	5874
Cumulative No. of Infections					
Placebo		16	31	44	50
Vaccine		5	22	32	36

Vaccine		5	22	32	36

C Modified Intention-to-Treat Analysis



No. at Risk					
Placebo	8198	7775	7643	7441	7325
Vaccine	8197	7797	7665	7471	7347
Cumulative No. of Infections					
Placebo		30	50	65	74
Vaccine		12	32	45	51

Table 2. Rate of HIV Infection and Vaccine Efficacy, According to Selected Baseline Variables (Modified Intention-to-Treat Population).

Variable	Vaccine (N=8197)				Placebo (N=8198)				Vaccine Efficacy
	No. Evaluated	No. with Infection	No. of Person-Years	Rate	No. Evaluated	No. with Infection	No. of Person-Years	Rate	
				no./person-yr				*no./person-yr*	*% (95% CI)*
All subjects	7960	51	26,507	0.192	7988	74	26,478	0.279	31.2 (1.7 to 51.8)
Sex									
Male	4875	32	16,221	0.197	4885	43	16,179	0.266	25.8 (–17.3 to 53.0)
Female	3085	19	10,286	0.185	3103	31	10,300	0.301	38.6 (–8.6 to 65.3)
Age group									
≤20 yr	2228	12	7,358	0.163	2185	11	7,216	0.152	7.1 (–143.0 to 52.7)
21–25 yr	3517	20	11,713	0.171	3610	40	11,946	0.335	49 (12.8 to 70.2)
≥26 yr	2215	19	7,437	0.255	2193	23	7,316	0.314	18.7 (–49.3 to 55.7)
Living with partner									
Yes	4017	19	13,466	0.141	4083	34	13,612	0.25	43.5 (1.0 to 67.8)
No	3943	32	13,041	0.245	3905	40	12,866	0.311	21 (–25.7 to 50.4)
Risk group									
Low	3767	17	12,565	0.135	3837	29	12,798	0.227	40.4 (–8.5 to 67.2)
Medium	2297	12	7,642	0.157	2222	22	7,353	0.299	47.6 (–6.0 to 74.0)
High	1896	22	6,300	0.349	1929	23	6,327	0.364	3.7 (–72.7 to 46.3)

cination did not affect the degree of viremia or the CD4+ T-cell count in subjects in whom HIV-1 infection was subsequently diagnosed.

CONCLUSIONS

This ALVAC-HIV and AIDSVAX B/E vaccine regimen may reduce the risk of HIV infection in a community-based population with largely heterosexual risk. Vaccination did not affect the viral load or CD4+ count in subjects with HIV infection. Although the results show only a modest benefit, they offer insight for future research. (ClinicalTrials.gov number, NCT00223080.)

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N Engl J

Els resultats obtinguts mostren un modest efecte protector de la vacuna i no han trobat diferències significatives en la CV i CD4 postinfecció entre els dos grups.

L'estudi no te poder suficient per contestar dues preguntes importants

- **L'eficàcia de la vacuna es redueix després del primer any?**
- **L'eficàcia es més alta en persones amb menys risc de infectar-se?**

Editorial

- **L'eficàcia es moderada i no es pot considerar com una mesura sanitària per el control del VIH**
- **A l'estudi no es pot determinar el temps de protecció, els resultats son a 3 anys, però els autors suggereixen que la major part d'eficàcia es durant el primer any**

Microbicides

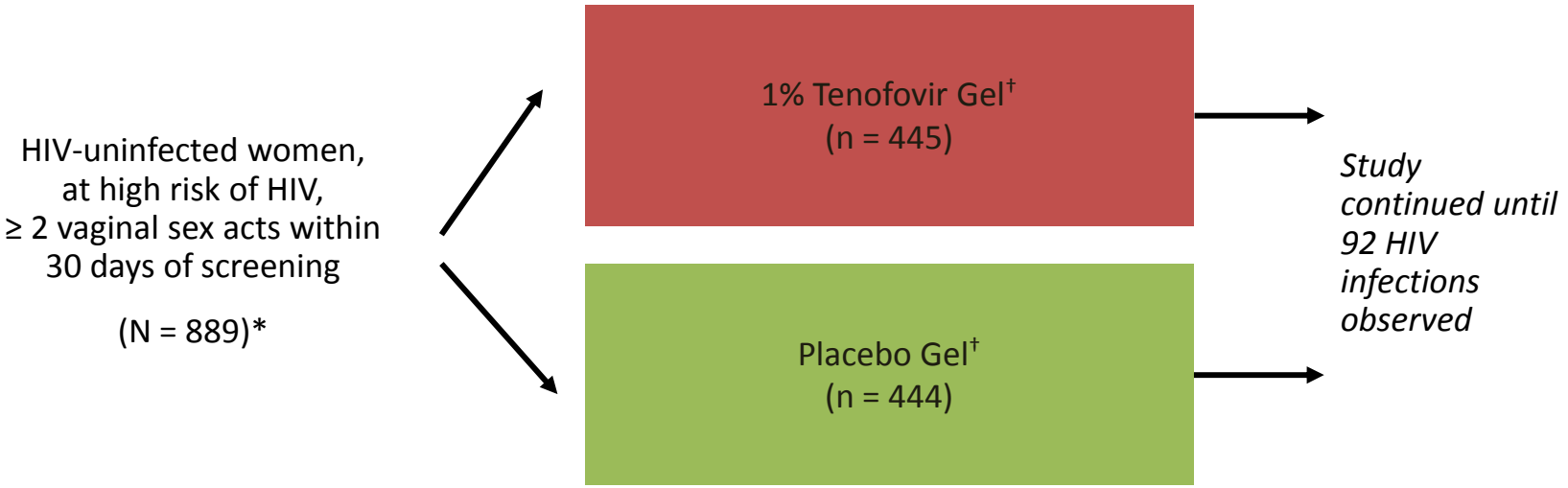
- L'espermicida Nonoxynol-9. A l'assaig la incidència de seroconversions va ser més alta en el grup que l'utilitzava
  - Van Damme L et al. Lancet 2002
- Surfactants que destrueixen la membrana del virus. L'assaig amb Savvy es va suspendre a l'anàlisi intermedi al veure que era poc probable que aportés evidències convincents
  - Feldblum P et al. Microbicides 2006 Conference
- Fins a un total de 6 gels candidats han fracassat en 11 estudis

ESTUDI CAPRISA 004
Microbicida amb TDF al 1%

- **Estudi presentat per investigadors de la Universitat de Columbia, NYC i la Universitat KwaZulu-Natal de Durban**
- **El primer microbicida capaç de reduir la incidència d'infecció un 50% si l'adherència es bona**
- **Bona tolerància**
- **També és van reduir de manera significativa les noves infeccions per VHS-2**
- **Els aplaudiments van interrompre 3 vegades la presentació dels resultats**

CAPRISA 004: 1% Tenofovir Microbicide Gel for Prevention of HIV in Women

- Randomized, placebo-controlled, double-blind, proof-of-concept study conducted at 2 sites in South Africa



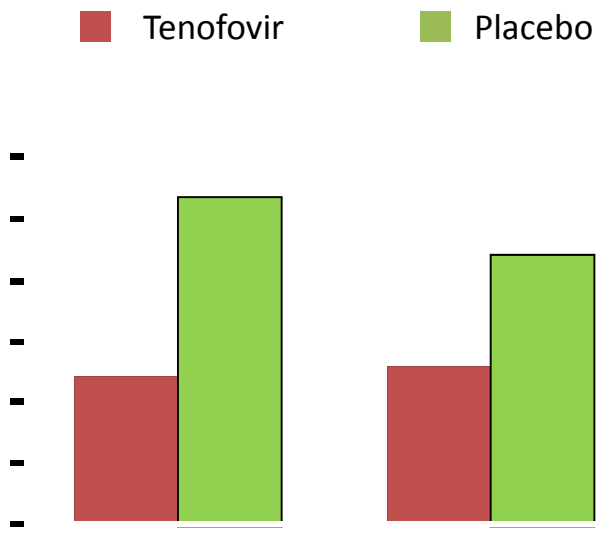
*N = 889 enrolled and eligible subjects from screened population of 2160 subjects. Common causes of exclusion included HIV infection (n = 536), failure to return for further evaluation (n = 142), no sexual activity (n = 132), coenrollment in a separate study (n = 135), pregnancy (n = 51).

†Gel applied using "BAT 24" regimen: 1 gel dose up to 12 hrs before sex; 1 gel dose as soon after sex as possible within 12 hrs after sex; maximum of 2 doses to be used within 24-hr period.

Abdool Karim Q, et al. Science DOI: 10.1126/science.1193748.
Abdool Karim Q, et al. AIDS 2010. Abstract TUSS0202.

CAPRISA: Reduced HIV Incidence With Tenofovir vs Placebo Gel

- Tenofovir gel associated with decrease in HIV incidence[1]
  - 50% decrease at 12 mos
  - 39% decrease at 30 mos



Tenofovir Efficacy vs Levels of Adherence			
Adherence Level, %	**n**	**No. of Infections**	**Efficacy, %**
> 80	336	36	54
50-80	181	20	38
< 50	367	41	28

- ↑ cervicovaginal fluid tenofovir concentrations associated with ↓ HIV seroconversion[2]
- No HIV resistance to tenofovir in patients infected while using gel
- Use of tenofovir gel also associated with 51% decrease in HSV-2 infection[3]

1. Abdool Karim Q, et al. Science DOI: 10.1126/science.1193748. 2. Kashuba A, et al. AIDS 2010. Abstract TUSS0203.
3. Abdool Karim S, et al. AIDS 2010. Abstract TUSS0204.

ESTUDI **CAPRISA 004**
Microbicida amb TDF al 1%

- **CONCLUSIÓ: L'ús del gel de tenofovir en relació al acte sexual sembla segur i efectiu per prevenir la infecció pel VIH. Una vegada corroborats aquests prometedors resultats, aquest microbicida antirretroviral podria omplir un important buit en la prevenció de la infecció pel VIH, *especialment en dones que no poden negociar de mutu acord la monogàmia o l'ús de preservatiu***

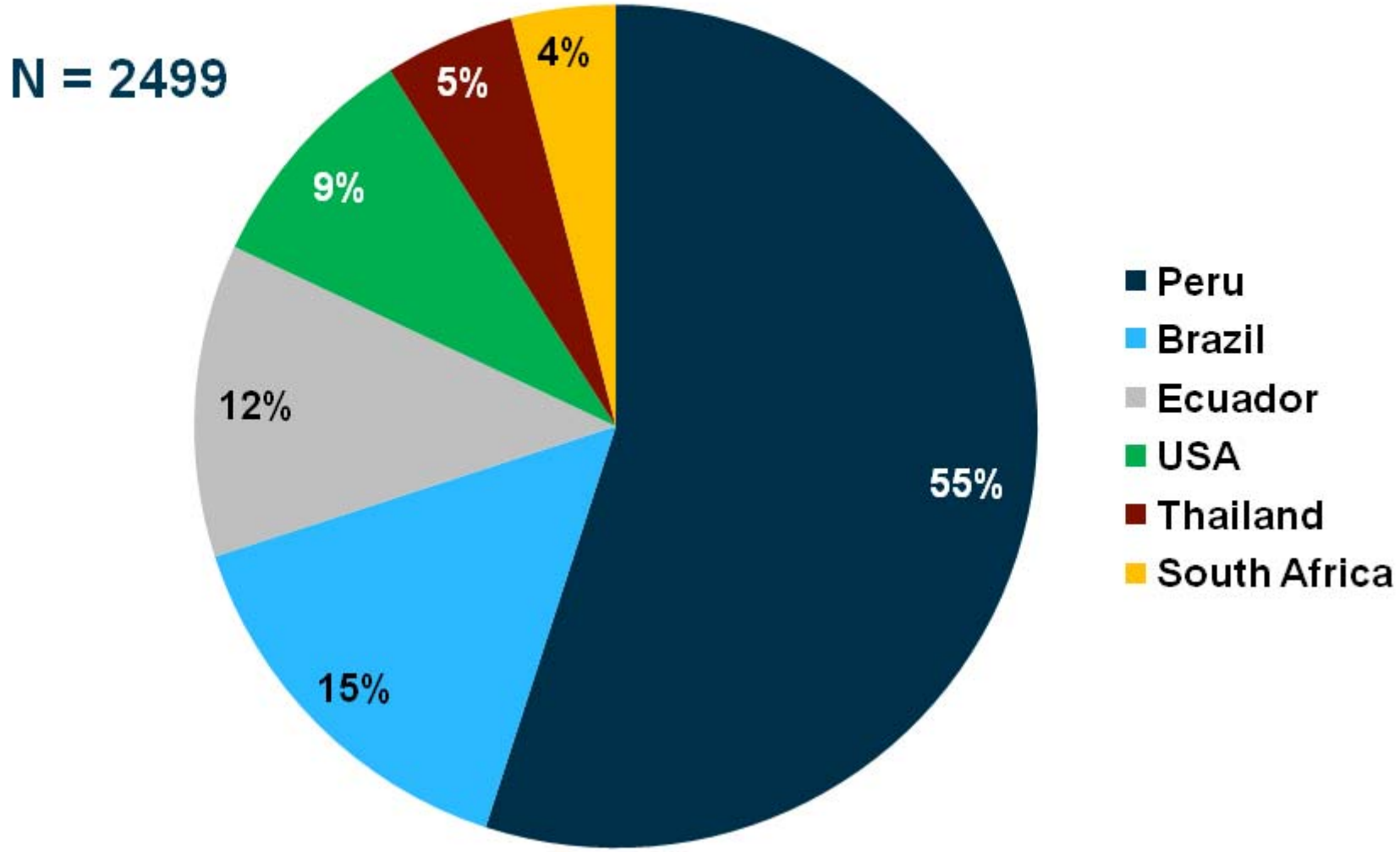
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 30, 2010 VOL. 363 NO. 27

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 McMahan, B.S., Albert Y. Liu, M.D., M.P.H., Lorena Vargas, Pedro Goicochea, M.Sc., Martín Casapía, 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 Fernández, M.D., Valdilea G. Veloso, M.D., Ph.D., Susan P. Buchbinder, M.D., Suwat Chariyalertsak, 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 Defechereux, 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*

iPrEx: Study Population



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

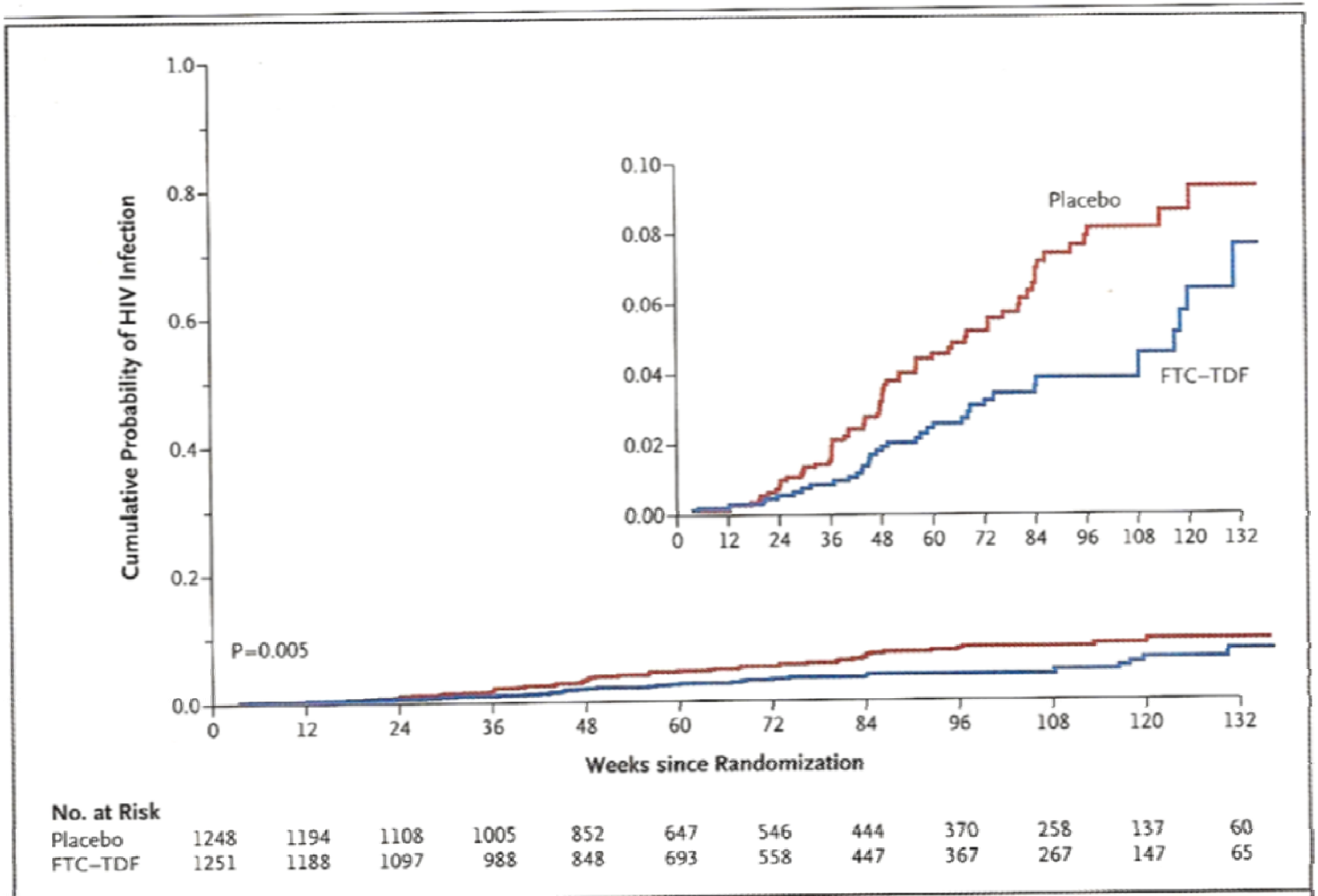
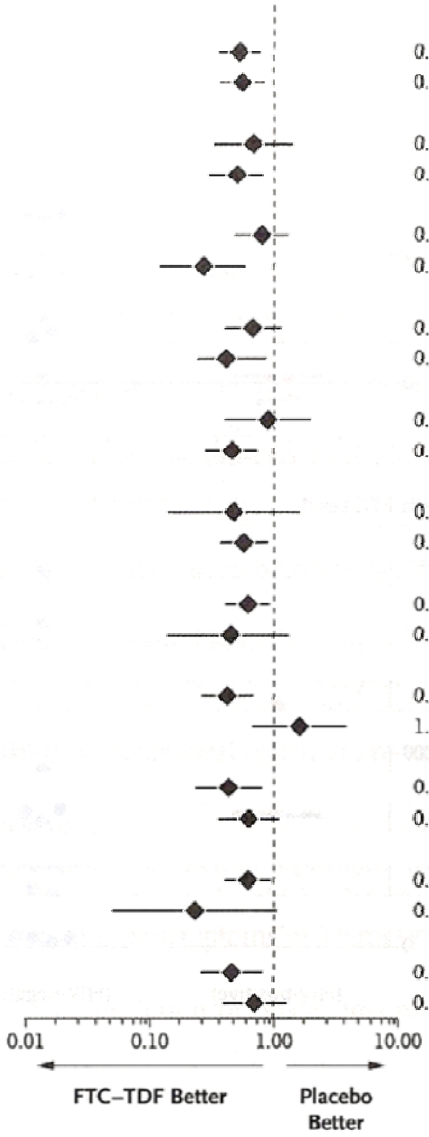


Figure 2. Kaplan–Meier Estimates of Time to HIV Infection (Modified Intention-to-Treat Population).

The cumulative probability of HIV acquisition is shown for the two study groups. The efficacy of preexposure prophylaxis with emtricitabine and tenofovir disoproxil fumarate (FTC–TDF) was 44%, as compared with placebo (P=0.005). The inset graph shows a more detailed version of the overall graph up to a probability of 0.10.

Subgroup	FTC–TDF	Placebo	FTC–TDF	Placebo	Hazard Ratio (95% CI)	P Value
	no. of patients		*no. of events*			
Analysis						
Intention-to-treat	1251	1248	38	72	0.53 (0.36–0.78)	0.001
Modified intention-to-treat	1251	1248	36	64	0.56 (0.37–0.85)	0.005
As treated						0.48
<50% Pill use	NA	NA	13	17	0.68 (0.33–1.41)	
≥50% Pill use	NA	NA	23	47	0.50 (0.30–0.82)	
Pill use						0.02
<90% Pill use	NA	NA	28	34	0.79 (0.48–1.31)	
≥90% Pill use	NA	NA	8	30	0.27 (0.12–0.59)	
Age						0.36
<25 yr	591	662	22	37	0.67 (0.40–1.14)	
≥25 yr	660	586	14	27	0.41 (0.24–0.87)	
Education						0.16
<Secondary education	279	244	12	12	0.89 (0.40–1.98)	
≥Secondary education	955	992	23	52	0.46 (0.28–0.74)	
Ethnic group						0.79
Non-Hispanic	351	342	4	8	0.48 (0.14–1.60)	
Hispanic	900	906	32	56	0.57 (0.37–0.89)	
Region						0.62
Andean	850	850	32	55	0.59 (0.38–0.91)	
Non-Andean	401	398	4	9	0.43 (0.13–1.39)	
Risk at screening						0.01
URAI	732	753	23	56	0.42 (0.26–0.68)	
No URAI	519	495	13	8	1.59 (0.66–3.84)	
Daily alcohol use						0.38
0–4 Drinks	554	529	15	32	0.43 (0.23–0.80)	
≥5 Drinks	666	687	19	32	0.63 (0.36–1.11)	
Circumcised						0.22
No	1085	1074	34	55	0.62 (0.40–0.95)	
Yes	162	170	2	9	0.23 (0.05–1.06)	
HSV-2 at screening						0.32
Negative or indeterminate	783	813	17	38	0.46 (0.26–0.82)	
Positive	458	430	19	26	0.70 (0.39–1.2)	



Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report

Weekly / Vol. 60 / No. 3 January 28, 2011

Interim Guidance: Preexposure Prophylaxis for the Prevention of HIV Infection in Men Who Have Sex with Men

An estimated 56,000 human immunodeficiency virus (HIV) infections occur each year in the United States (*1*). Men who have sex with men (MSM) account for 53% of the estimated incident infections, and surveillance data suggest that the annual number of new HIV infections among MSM has been rising since the mid-1990s (*1*). Strategies for reducing acquisition of HIV infection by MSM have included 1) expanded HIV testing so that infected persons can be treated and their risk for trans-

Enrolled participants were randomized to receive either daily doses of TDF/FTC or a placebo pill. Participants were seen every 4 weeks for an interview, HIV testing, risk-reduction and PrEP medication adherence counseling, pill count, and dispensing of pills and condoms. Every 3 months, participants received physical examinations with collection of blood and urine samples for evaluation of renal and liver function, and were tested for sexually transmitted infections and treated as

BOX. CDC interim guidance for health-care providers electing to provide preexposure prophylaxis (PrEP) for the prevention of HIV infection in adult men who have sex with men and who are at high risk for sexual acquisition of HIV

Before initiating PrEP

Determine eligibility

- Document negative HIV antibody test(s) immediately before starting PrEP medication.
- Test for acute HIV infection if patient has symptoms consistent with acute HIV infection.
- Confirm that patient is at substantial, ongoing, high risk for acquiring HIV infection.
- Confirm that calculated creatinine clearance is ≥60 mL per minute (via Cockcroft-Gault formula).

Other recommended actions

- Screen for hepatitis B infection; vaccinate against hepatitis B if susceptible, or treat if active infection exists, regardless of decision about prescribing PrEP.
- Screen and treat as needed for STIs.

Beginning PrEP medication regimen

- Prescribe 1 tablet of Truvada* (TDF [300 mg] plus FTC [200 mg]) daily.
- In general, prescribe no more than a 90-day supply, renewable only after HIV testing confirms that patient remains HIV-uninfected.
- If active hepatitis B infection is diagnosed, consider using TDF/FTC for both treatment of active hepatitis B infection and HIV prevention.
- Provide risk-reduction and PrEP medication adherence counseling and condoms.

Follow-up while PrEP medication is being taken

- Every 2–3 months, perform an HIV antibody test; document negative result.
- Evaluate and support PrEP medication adherence at each follow-up visit, more often if inconsistent adherence is identified.
- Every 2–3 months, assess risk behaviors and provide risk-reduction counseling and condoms. Assess STI symptoms and, if present, test and treat for STI as needed.
- Every 6 months, test for STI even if patient is asymptomatic, and treat as needed.
- 3 months after initiation, then yearly while on PrEP medication, check blood urea nitrogen and serum creatinine.

On discontinuing PrEP (at patient request, for safety concerns, or if HIV infection is acquired)

- Perform HIV test(s) to confirm whether HIV infection has occurred.
- If HIV positive, order and document results of resistance testing and establish linkage to HIV care.
- If HIV negative, establish linkage to risk-reduction support services as indicated.
- If active hepatitis B is diagnosed at initiation of PrEP, consider appropriate medication for continued treatment of hepatitis B.

Partners PrEP: Both PrEP Strategies Significantly Reduce HIV Acquisition

Primary Efficacy Outcome, mITT* Analysis	TDF (n = 1584)	TDF/FTC (n = 1579)	Placebo (n = 1584)
HIV acquisitions, n	18	13	47
HIV incidence/100 PY	0.74	0.53	1.92
Efficacy vs placebo, % (95% CI)	62 (34-78)	73 (49-85)	--
▪ *P* value	.0003	< .0001	--

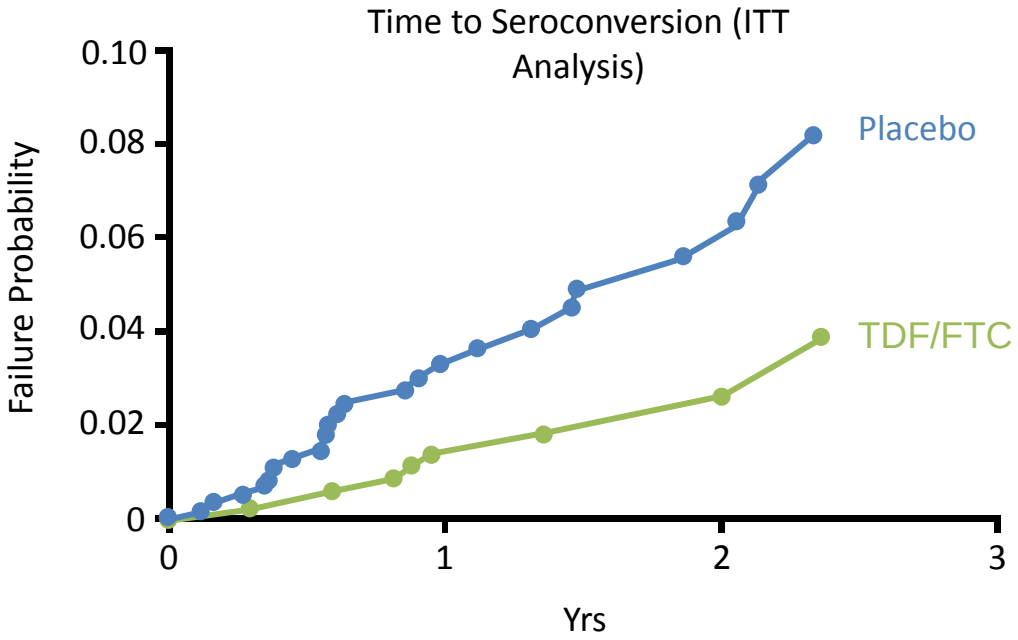
*mITT analysis includes HIV acquisitions not detected at enrollment.

- **No difference in efficacy of TDF vs TDF/FTC in reducing HIV acquisition (*P* = .18)**
- **Both PrEP strategies associated with significant reduction in HIV transmission vs placebo in both men and women**
  - **TDF efficacy: 68% in women, 55% in men**
  - **TDF/FTC efficacy: 62% in women, 83% in men**

Baeten J, et al. IAS 2011. Abstract MOAX0106.

TDF2: PrEP With TDF/FTC Significantly Reduces HIV Acquisition

- **9 vs 24 patients seroconverted in TDF/FTC vs placebo arms, respectively**
- **Overall protective efficacy of TDF/FTC: 62.6% (95% CI: 21.5-83.4; *P* = .0133)**



Thigpen MC, et al. IAS 2011. Abstract WELBC01.

FEM-PrEP: TDF/FTC in Heterosexual African Women

- **HIV-uninfected women at high risk of HIV infection randomized to TDF/FTC vs placebo (n = 1951)**
- **Preliminary results reported in April 2011**
  - **28 infections in TDF/FTC arm and 28 in placebo arms**
    - **New infection rate: ~ 5%/yr**
  - **Adherence ~ 95% when product available**
  - **Increased pregnancy rate in TDF/FTC group**
  - **TDF/FTC associated with known adverse effects**

Orderly closure of study recommended due to futility

FHI360. FHI Statement on the FEM-PrEP HIV Prevention Study. Available at: http://www.fhi.org/en/AboutFHI/Media/Releases/FEM-PrEP_statement041811.htm. These data are available in press release format only, have not been peer reviewed, may be incomplete, and we await presentation or publication in a peer-reviewed format before conclusions should be made from these data.

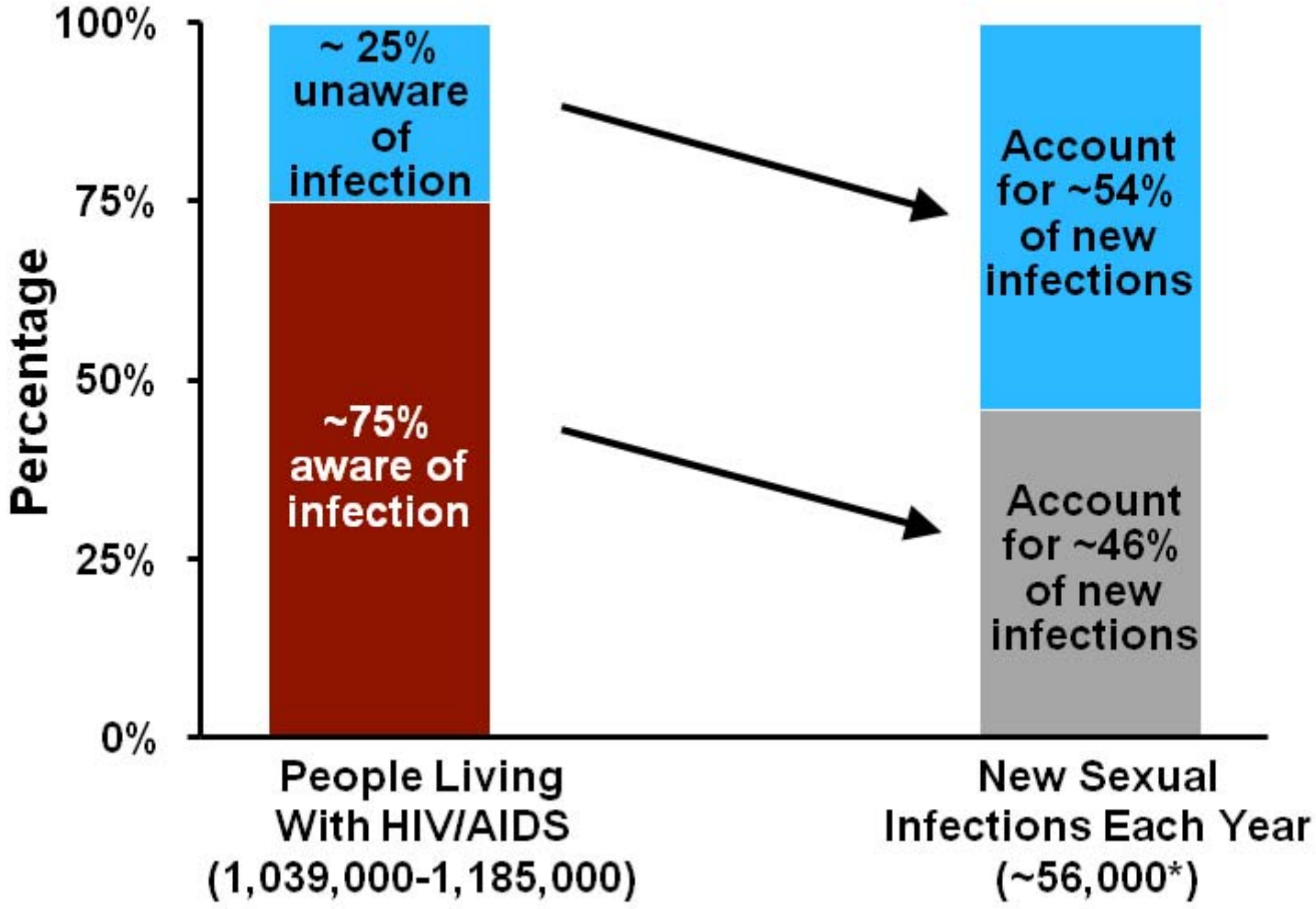
Prevenció de la infecció

- Informació i Educació per modificar hàbits de conducta
- Control MTS
- Vacunes
- Circumcisió
- Gels vaginals amb activitat microbicida
- Profilaxi post-exposició (PPE)
- Profilaxi pre-exposició (PrEx)
- **Prevenció de la transmissió mare-fill**
- **Diagnòstic i tractament precoç**

Determinació de rutina de serologia del VIH

- **Tot i les millores en el tractament i maneig de la infecció pel VIH, encara *el diagnòstic dels nous casos es fa amb el mateix retard* que fa dos dècades**
- **S'han *triplicat els contactes heterosexuals com factor de risc* en el període 2003-06, disminuint els casos en ADVP i MSM**
- **La pràctica sistemàtica de la serologia pel VIH durant la gestació ha fet que es detecti la infecció abans en les dones embarassades que en la resta de la població**
- **La detecció de rutina del VIH en els Centres de Salut, permetria el diagnòstic precoç i l'entrada dels infectats en el circuit de cures mèdiques, millorar el pronòstic i potencialment disminuir el risc de transmissió**
    - **M Goicoechea, D Smith. CID 2007**

Awareness of Serostatus Among People With HIV and Estimates of Transmission



Marks G, et al. *AIDS*. 2006;20:1447-1450.
Hall HI, et al. *JAMA*. 2008;300:520-529.

Determinació de rutina de serologia del VIH i TAR precoç

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

Lancet 2009; 373: 48–57

Published Online November 26, 2008 DOI:10.1016/S0140-6736(08)61697-9

See Comment pages 7 and 9

Department of HIV/AIDS (R M Granich MD, Prof C F Gilks DPhil, Prof K M De Cock MD) **and Stop TB Department** (Prof C Dye DPhil, B G Williams PhD), **WHO, Geneva, Switzerland**

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Summary

Background Roughly 3 million people worldwide were receiving antiretroviral therapy (ART) at the end of 2007, but an estimated 6·7 million were still in need of treatment and a further 2·7 million became infected with HIV in 2007. Prevention efforts might reduce HIV incidence but are unlikely to eliminate this disease. We investigated a theoretical strategy of universal voluntary HIV testing and immediate treatment with ART, and examined the conditions under which the HIV epidemic could be driven towards elimination.

Methods We used mathematical models to explore the effect on the case reproduction number (stochastic model) and long-term dynamics of the HIV epidemic (deterministic transmission model) of testing all people in our test-case community (aged 15 years and older) for HIV every year and starting people on ART immediately after they are diagnosed HIV positive. We used data from South Africa as the test case for a generalised epidemic, and assumed that all HIV transmission was heterosexual.

Findings The studied strategy could greatly accelerate the transition from the present endemic phase, in which most adults living with HIV are not receiving ART, to an elimination phase, in which most are on ART, within 5 years. It could reduce HIV incidence and mortality to less than one case per 1000 people per year by 2016, or within 10 years of full implementation of the strategy, and reduce the prevalence of HIV to less than 1% within 50 years. We estimate that in 2032, the yearly cost of the present strategy and the theoretical strategy would both be US$1·7 billion; however, after this time, the cost of the present strategy would continue to increase whereas that of the theoretical strategy would decrease.

Interpretation Universal voluntary HIV testing and immediate ART, combined with present prevention approaches, could have a major effect on severe generalised HIV/AIDS epidemics. This approach merits further mathematical modelling, research, and broad consultation.

Determinació de rutina de serologia del VIH i TAR precoç

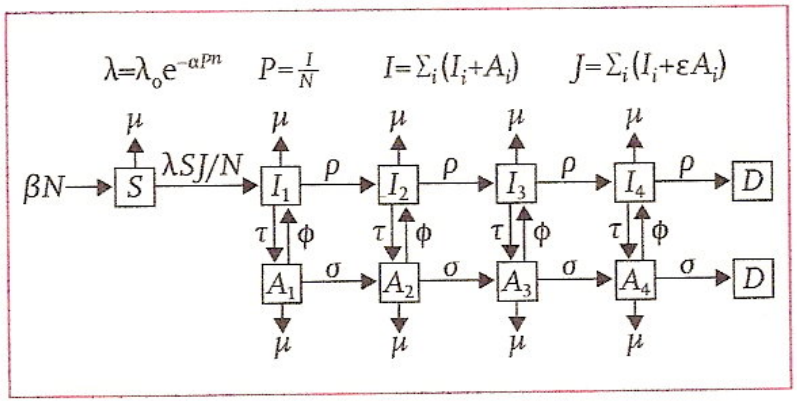

Figure 2: **Transmission model for HIV infection and antiretroviral therapy (ART) provision**

N represents population aged 15 years and above. People enter into the susceptible class (*S*) at a rate βN, become infected at a rate $\lambda SJ/N$, progress through four stages of HIV (I_i, i=1–4) at a rate ρ between each stage, and then die (D). The background mortality rate is μ and people are tested at a rate τ. If they are tested and put onto ART, they move to the corresponding ART box A_i (i=1–4), where they progress through four stages at a rate σ and then die. The term governing transmission contains the factor J α ($I_i+\varepsilon A_i$) where ε allows for the fact that people receiving ART are less infectious than are those who are not. They might also stop treatment or the treatment might become ineffective, in which case they return to the corresponding non-ART state at a rate φ. To allow for heterogeneity in sexual behaviour and for the observed steady state prevalence of HIV, we let the transmission decrease with the prevalence, *P*. If n=1, the decrease is exponential; if n=∞, the decrease is a step function. Both have been used in previous models.[5,29]

For more on **both models** see http://www.who.int/hiv/topics/treatmentasprevention

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"Test & Treat"

Universal Voluntary HIV Testing and Immediate ART

- Universal testing of all people in the "community" annually
- ART immediately upon HIV diagnosis (CD4 ~900/μL)
- Could decrease HIV incidence to < 1/1000/year by 2016 (or within 10 years)
- Could decrease HIV prevalence to < 1% in 50 years
- Cost neutral in 2032, cost saving thereafter

Granich RM, et al. *Lancet.* 2009;373:48-57.

HIV/AIDS BRIEF REPORT

The Effect of Expanded Antiretroviral Treatment Strategies on the HIV Epidemic Among Men Who Have Sex With Men in San Francisco

Edwin D. Charlebois,[1,2] Moupali Das,[1,3] Travis C. Porco,[4] and Diane V. Havlir[1]

[1]HIV/AIDS Division, Department of Medicine, San Francisco General Hospital, California; [2]Center for AIDS Prevention Studies, Department of Medicine, University of California; [3]San Francisco Department of Public Health, California; [4]Francis I. Proctor Foundation for Research in Ophthalmology, Department of Epidemiology and Biostatistics, University of California, San Francisco, California

(See editorial commentary by DeGruttola and Schooley, on pages 1050–1052.)

Modeling of expanding antiretroviral treatment to all HIV-infected adults already in care in San Francisco predicts reductions in new HIV infection at 5 years of 59% among men who have sex with men. Addition of annual HIV testing for men who have sex with men to universal treatment decreases new infections by 76%.

Table 1. Model Results

Year	Prevalence of HIV infection, %			
	Baseline CD4 cell count <350 cells/mm^3	ART initiation, CD4 cell count <500 cells/mm^3	Treat all in care	Test-and-treat all
2009	24.7	24.7	24.7	24.7
2014	25.1	22.9	21.9	20.9
2019	25.5	21.7	19.4	17.5
2029	26.2	21.8	17.1	12.8
New HIV infections since 2009	Baseline (CD4<350)	ART start CD4<500	Treat all in care	Test-and-treat all
2014	3703	2149	1534	893
2019	7446	4344	2896	1406
2029	14,960	10,020	6739	2771
HIV Infections Averted*		ART start CD4<500	Treat all in care	Test-and-treat all
2014	Reference	1554	2169	2810
2019	Reference	3102	4550	6040
2029	Reference	4940	8221	12,189
Percent reduction in new HIV infections[a]	Reference	ART start CD4<500	Treat all in care	Test-and-treat all
2014	Reference	42	59	76
2019	Reference	42	61	81
2029	Reference	33	55	81

[a] HIV infections averted and percent reduction in new infections are relative to 2009 model estimates. Expansion of ART treatment strategies are assumed to start in 2009.

Determinació de rutina de serologia del VIH i TAR precoç

- **Swiss Federal Comission on HIV/AIDS**
  - **Una persona infectada en TAR amb supressió del virus (<40 cps/ml) no transmet la infecció per via sexual**
- **Estudi prospectiu de 393 parelles serodicordants 0 transmissions**
  - **JAIDS 2005;40:96**
- **62 embarassos en parelles serodiscordants, no transmissió amb el pare amb CV indetectable**
  - **JAIDS 2006;43:324**
- **2993 parelles, sense tractament risc de infecció 3.4%, amb tractament risc de infecció 0.7%**
  - **Abst 52bLB CROI 2009.**

The NEW ENGLAND JOURNAL of MEDICINE

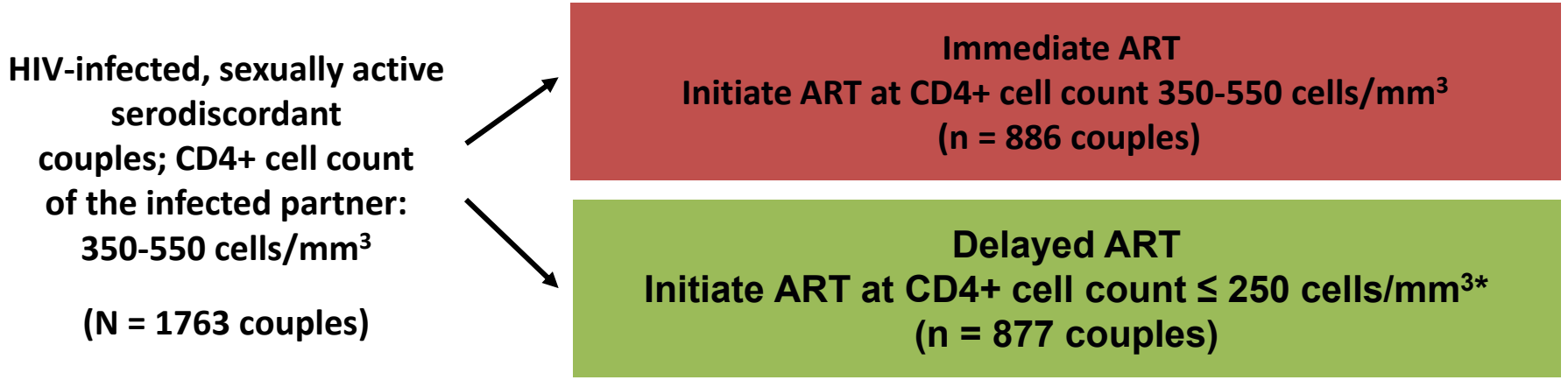
ESTABLISHED IN 1812 AUGUST 11, 2011 VOL. 365 NO. 6

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 Ribaudo, 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*

HPTN 052: Immediate vs Delayed ART in Serodiscordant Couples

Àfrica, Brasil, India, Thailandia, USA



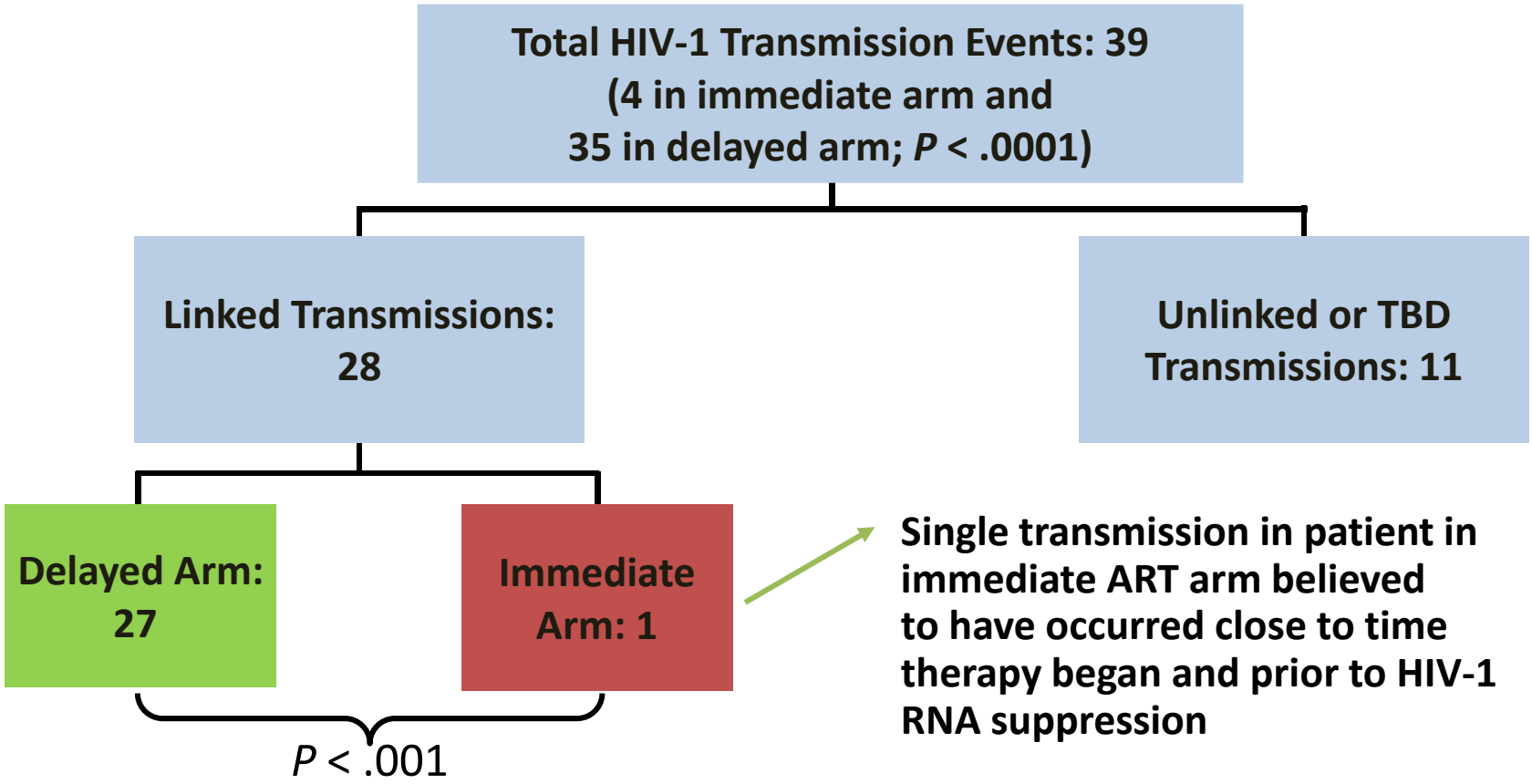
*Based on 2 consecutive values ≤ 250 cells/mm^3.

- **Primary efficacy endpoint: virologically linked HIV transmission**
- Primary clinical endpoints: WHO stage 4 events, pulmonary TB, severe bacterial infection and/or death
- **Couples received intensive counseling on risk reduction and use of condoms**

DSMB recommended release of results as soon as possible following April 28, 2011, review; follow-up continues but all HIV-infected partners offered ART after release of results

Cohen MS, et al. IAS 2011. Abstract MOAX0102.
Cohen MS, et al. N Engl J Med. 2011; 365: 493-505

HPTN 052: HIV Transmission Reduced by 96% in Serodiscordant Couples



Cohen MS, et al. IAS 2011. Abstract MOAX0102.
Cohen MS, et al. N Engl J Med. 2011;365:493-505

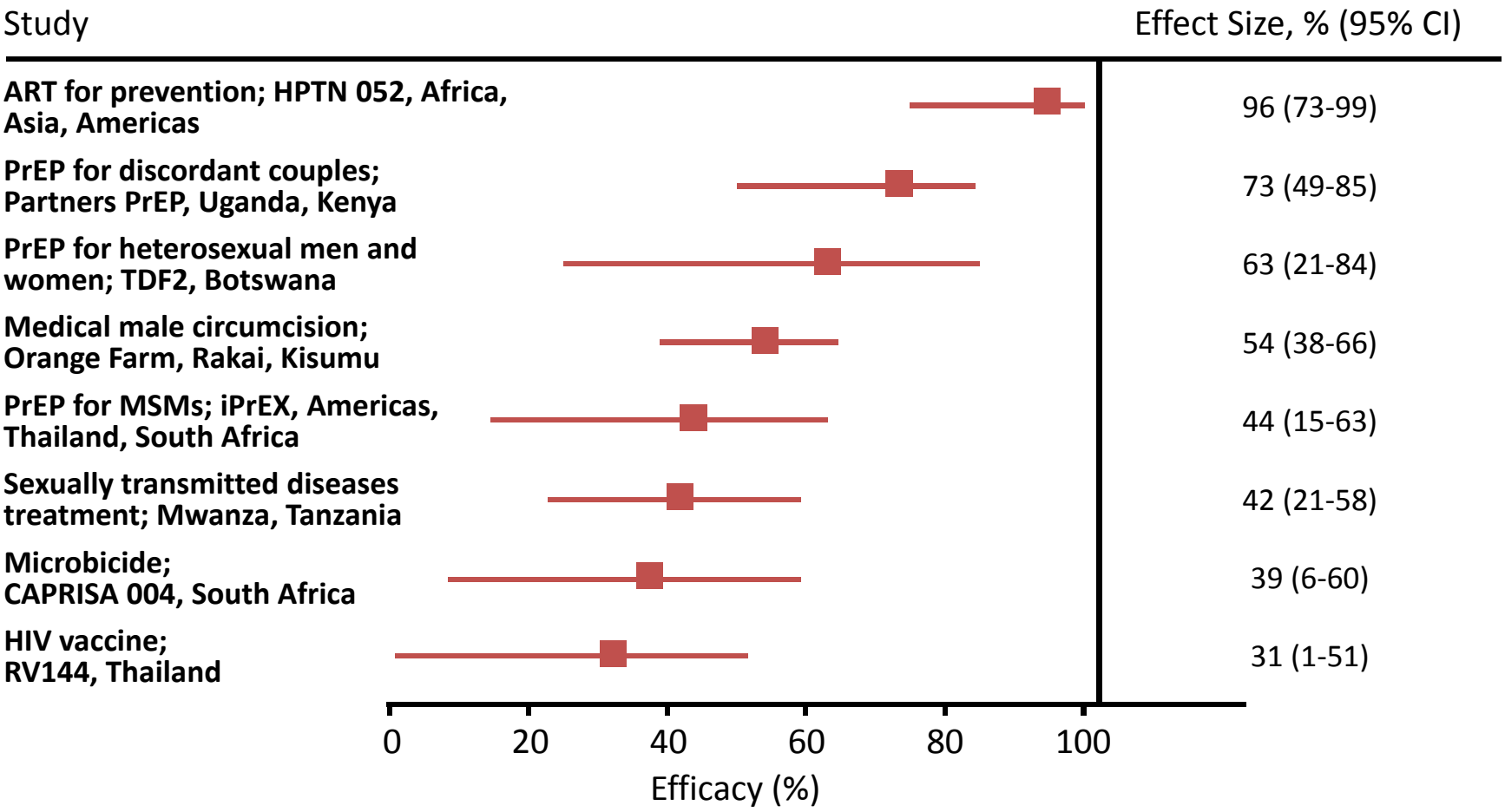
HPTN 052: Multivariate Analysis of Factors Associated With Linked Transmissions

Variable	HR	95% CI
Treatment, immediate vs delayed	**0.04**	0.01-0.28
Baseline CD4+ count, per 100 cells/mm^3 decrease	1.24	1.00-1.54
Baseline HIV-1 RNA, per 1 $\log_{10}$ copies/mL increase	2.85	1.51-5.41
Baseline condom use, 100% vs < 100%	**0.33**	0.12-0.91
Sex of infected partner, male vs female	0.73	0.33-1.65

- **61% of transmissions occurred from infected patient with CD4+ cell count > 350 cells/mm^3**
- **All transmissions occurred prior to starting ART**
- **82% of transmissions occurred in African patients**

Cohen MS, et al. IAS 2011. Abstract MOAX0102.
Cohen MS, et al. N Engl J Med. 2011;365:493-505

Efficacy of HIV Prevention Strategies From Randomized Clinical Trials



Abdool Karim SS, et al. Lancet. 2011;[Epub ahead of print].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la vostra atenció
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