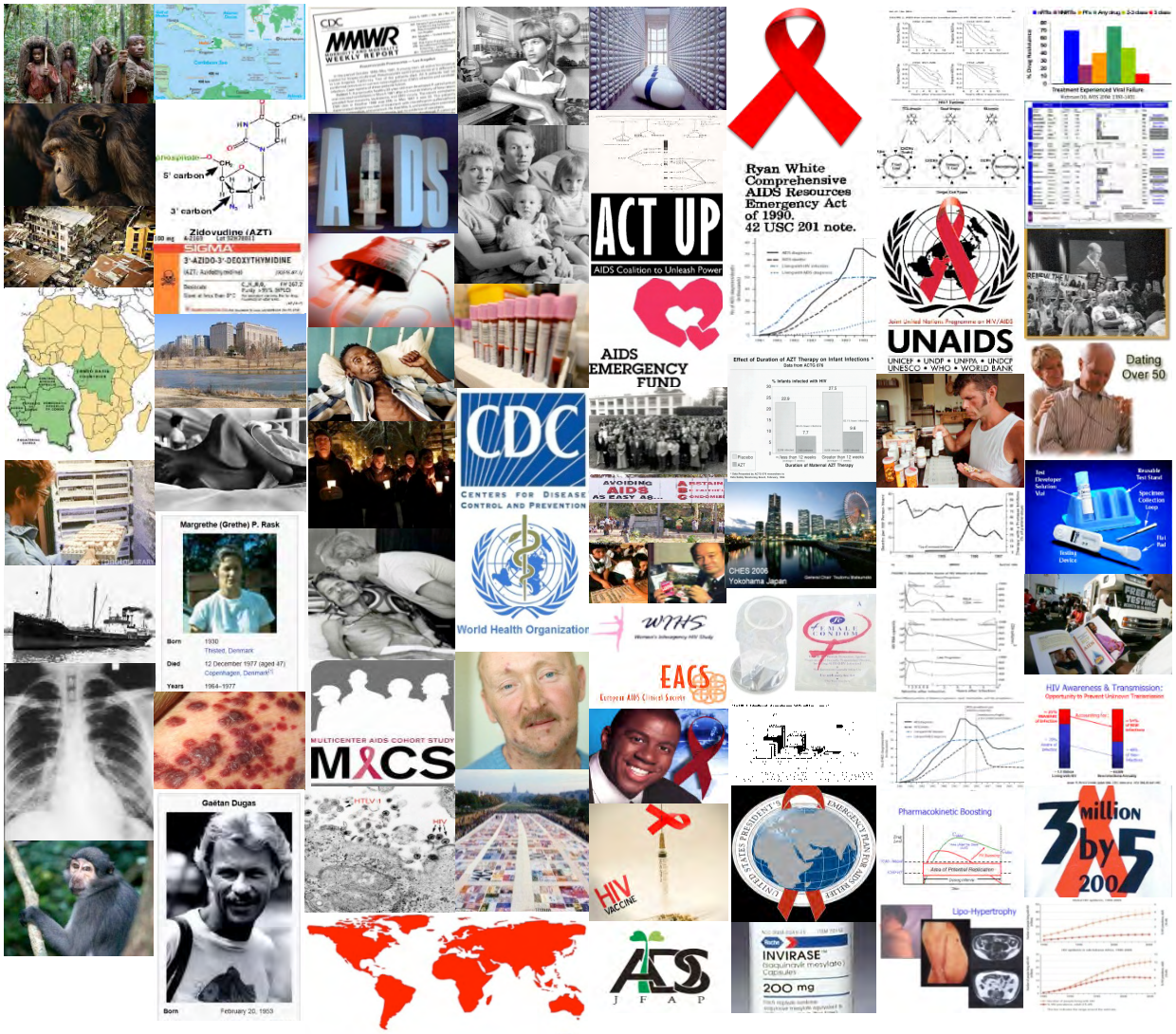
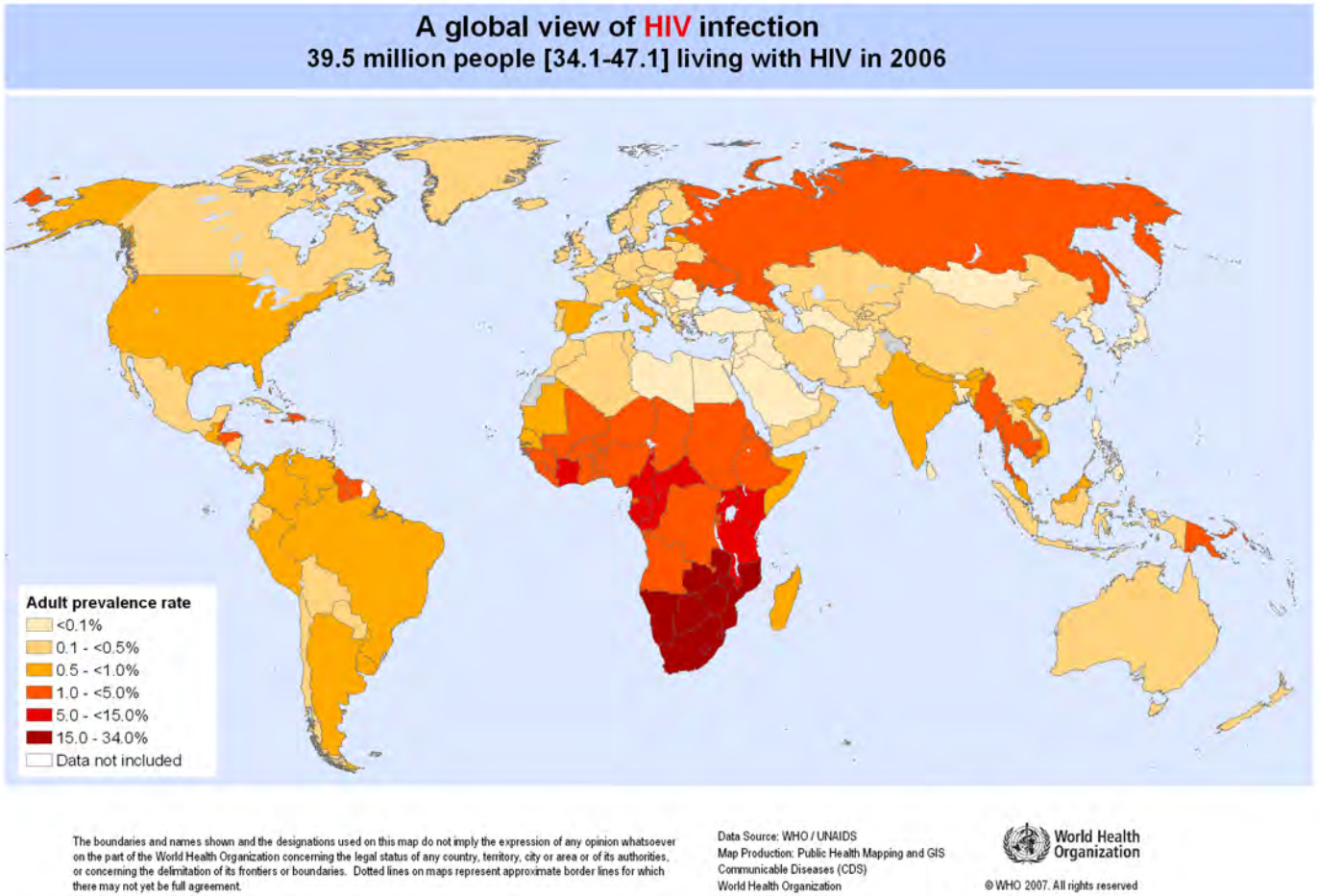
The Eras of the HIV Epidemic

1930-1980 | 1981-1986 | 1987-1995 | 1996-2005 | 2nd Gen. HAART | 2006-2011



Second Generation HAART Era: 2006-2011

2006: Disproportionate distribution of HIV



Second Generation HAART Era: 2006-2011

2006: Gates and Clinton at International AIDS conference announce increased funding and in-country work

Second Generation HAART Era: 2006-2011

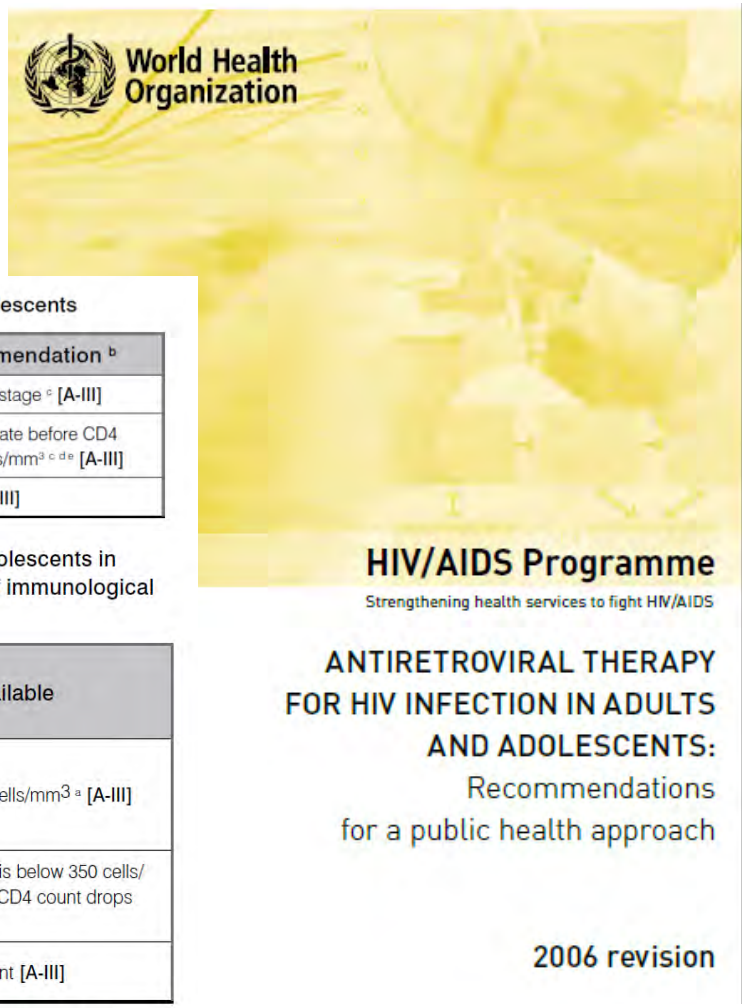
2006: WHO revision of ART Guidelines

Table 3. CD4 criteria for the initiation of ART in adults and adolescents

CD4 (cells/mm³) [a]	Treatment recommendation [b]
<200	Treat irrespective of clinical stage [c] [A-III]
200–350	Consider treatment and initiate before CD4 count drops below 200 cells/mm³ [c d e] [A-III]
>350	Do not initiate treatment [A-III]

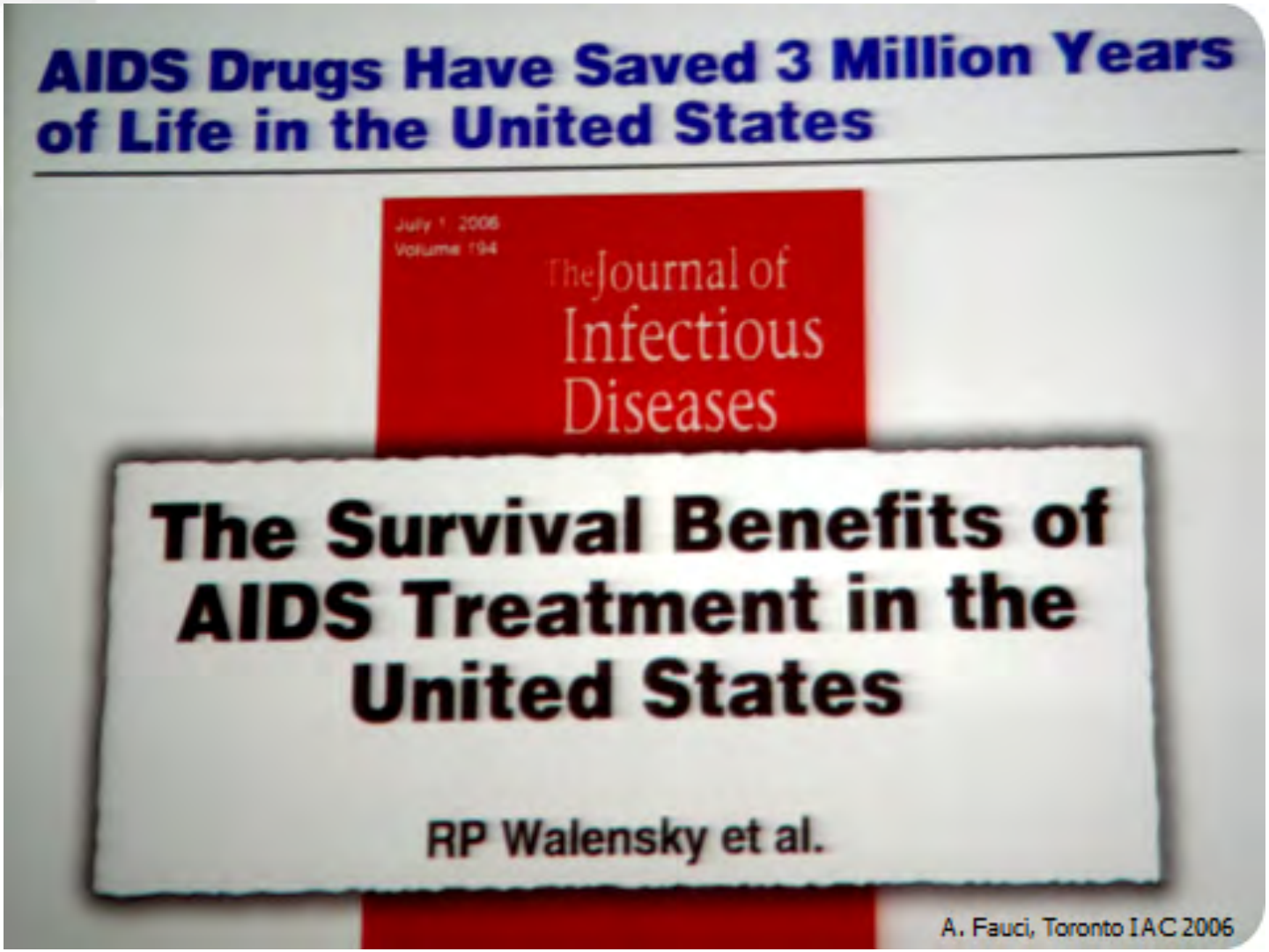
Table 4. Recommendations for initiating ART in adults and adolescents in accordance with clinical stages and the availability of immunological markers

WHO clinical staging	CD4 testing not available	CD4 testing available
1	Do not treat [A-III]	Treat if CD4 count is below 200 cells/mm3 [a] [A-III]
2	Do not treat [b] [B-III]	
3	Treat [A-III]	Consider treatment if CD4 count is below 350 cells/mm3 [a c d] and initiate ART before CD4 count drops below 200 cells/mm3 [e] [B-III]
4	Treat [A-III]	Treat irrespective of CD4 cell count [A-III]



Second Generation HAART Era: 2006-2011

2006: Benefit of treatment in developed nations



Second Generation HAART Era: 2006-2011

2006: CDC recommends routine opt-out HIV testing

Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings

For patients in all health-care settings

- *HIV screening is recommended for patients in all health-care settings after the patient is notified that testing will be performed unless the patient declines (opt-out screening).*
- *Persons at high risk for HIV infection should be screened for HIV at least annually.*
- *Separate written consent for HIV testing should not be required; general consent for medical care should be considered sufficient to encompass consent for HIV testing.*
- *Prevention counseling should not be required with HIV diagnostic testing or as part of HIV screening programs in health-care settings.*

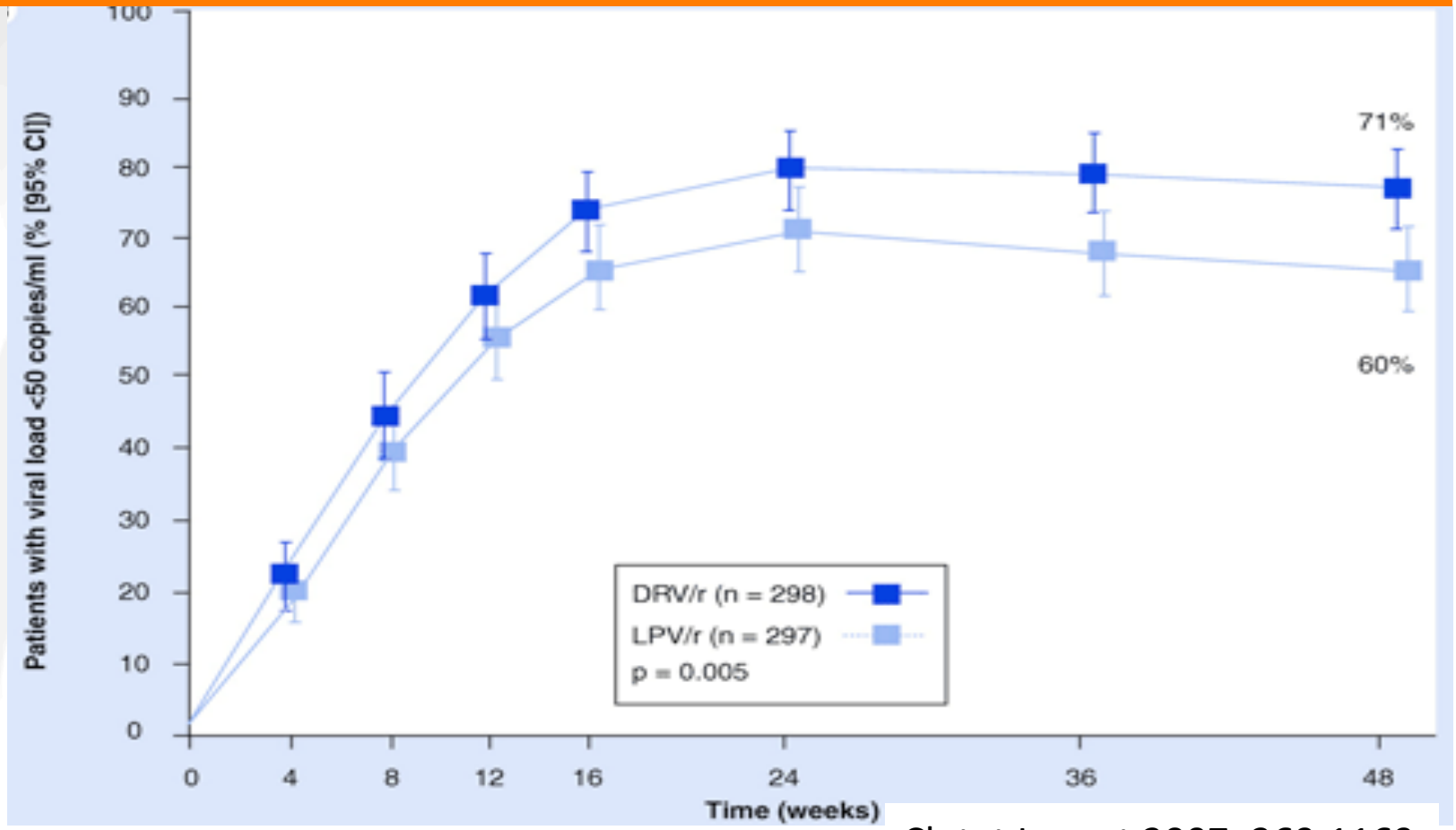
Second Generation HAART Era: 2006-2011

2006: 1st 2-Class STR (Single Tablet Regimen)
Atripla: 1st significant reduction in pill burden

Second Generation HAART Era: 2006-2011

2006: 10th PI Darunavir approved.

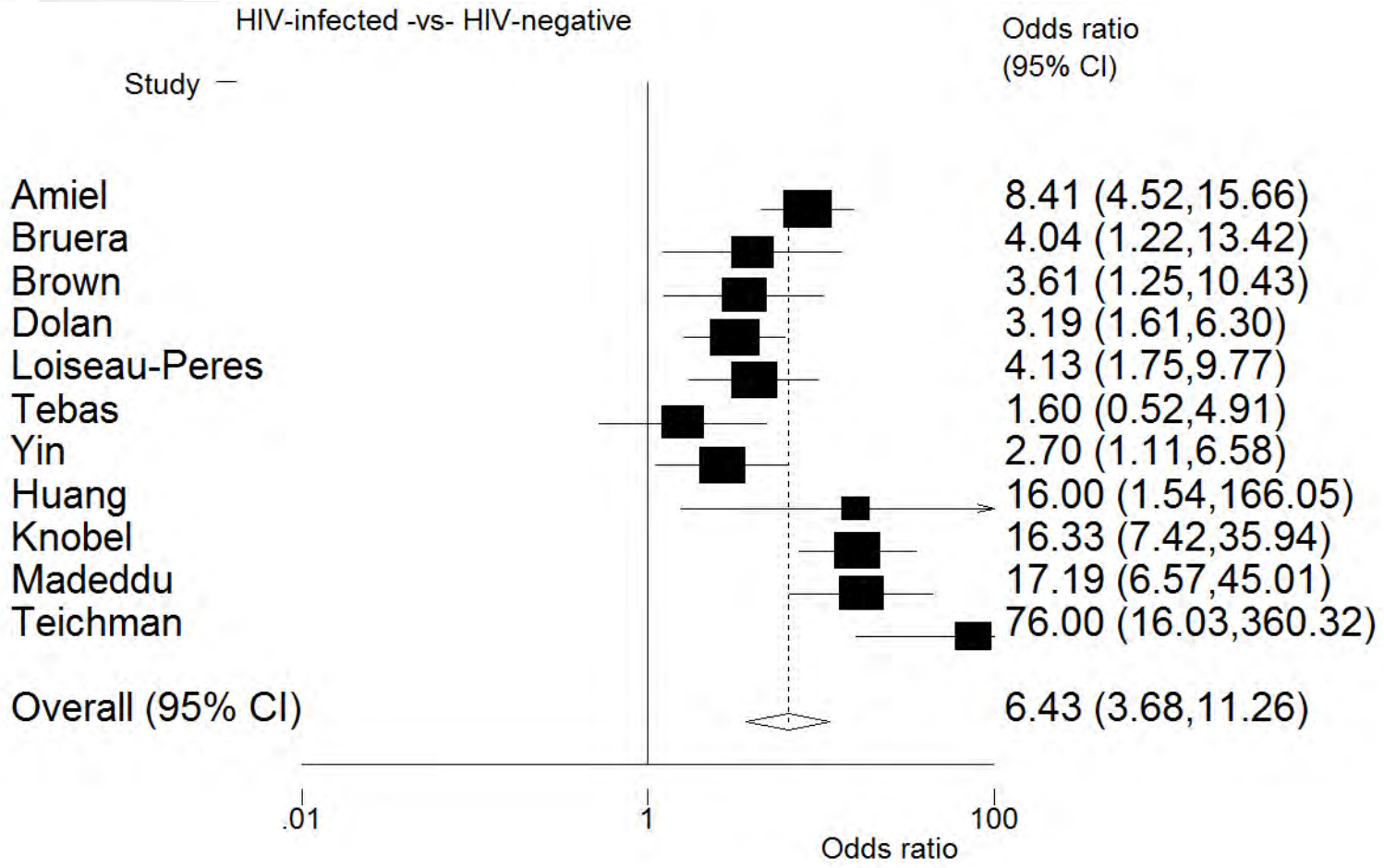
New Standard = high efficacy in treatment experienced patients



Clotet Lancet 2007; 369:1169

Second Generation HAART Era: 2006-2011

2006: Increased risk of osteoporosis



T. Brown. Lipodystrophy meeting. Dublin 2005

T. Brown, R. Qaqish: AIDS 2006; 20: 2165–2174

Second Generation HAART Era: 2006-2011

2006: Immune activation from microbial translocation

Nature Medicine **12**, 1365 - 1371 (2006)
Published online: 19 November 2006 | doi:10.1038/nm1511

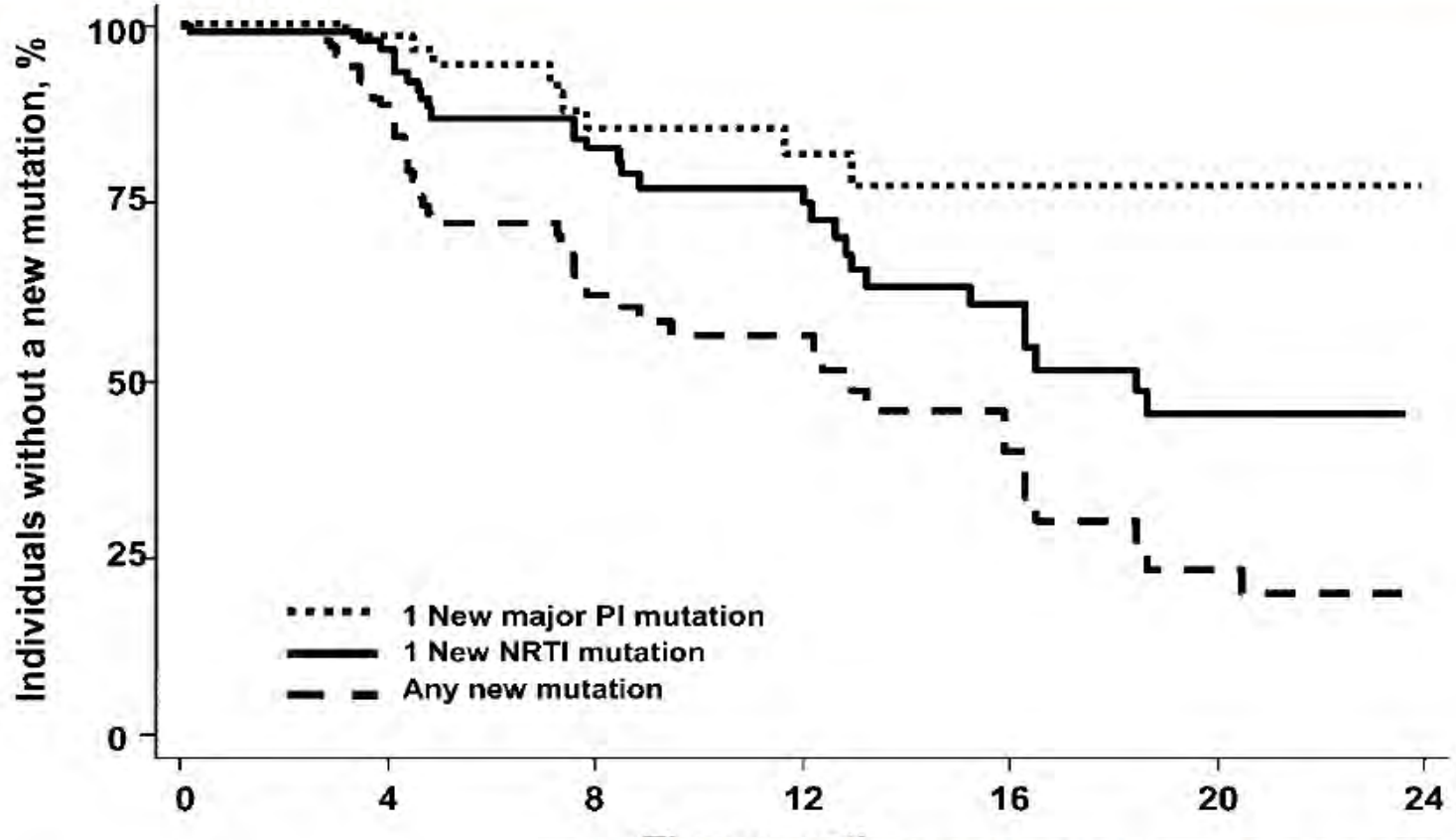
Microbial translocation is a cause of systemic immune activation in chronic HIV infection

Jason M Brenchley[1], David A Price[1], Timothy W Schacker[2], Tedi E Asher[1], Guido Silvestri[3], Srinivas Rao[4], Zachary Kazzaz[1], Ethan Bornstein[1], Olivier Lambotte[5], Daniel Altmann[6], Bruce R Blazar[7], Benigno Rodriguez[8], Leia Teixeira-Johnson[8], Alan Landay[9], Jeffrey N Martin[10], Frederick M Hecht[10], Louis J Picker[11], Michael M Lederman[8], Steven G Deeks[10] & Daniel C Douek[1]

Chronic activation of the immune system is a hallmark of progressive HIV infection and better predicts disease outcome than plasma viral load, yet its etiology remains obscure. Here we show that circulating microbial products, probably derived from the gastrointestinal tract, are a cause of HIV-related systemic immune activation. Circulating lipopolysaccharide, which we used as an indicator of microbial translocation, was significantly increased in chronically HIV-infected individuals and in simian

Second Generation HAART Era: 2006-2011

2006: Accumulation of resistance mutations with continuation of partially suppressive ARV regimen



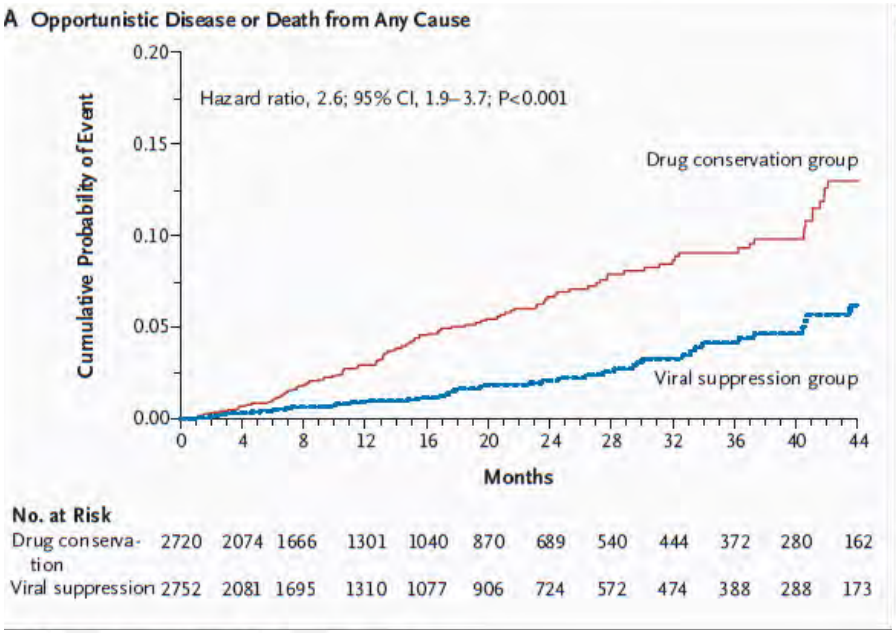
HIV/AIDS • CID 2006:43 (15 November) • 1329

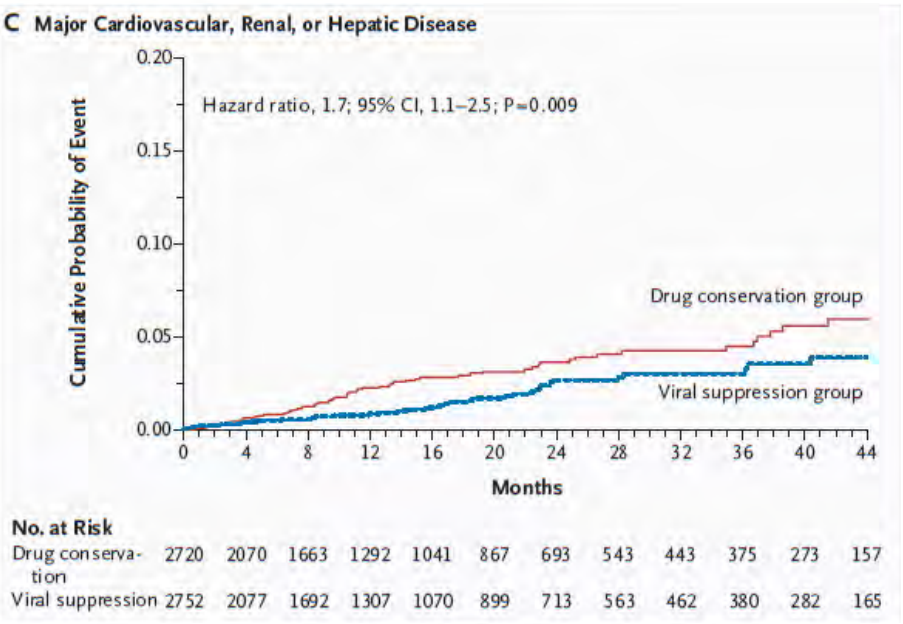
Second Generation HAART Era: 2006-2011

2006: Treatment interruptions increase death and disease

CD4+ Count–Guided Interruption of Antiretroviral Treatment

The Strategies for Management of Antiretroviral Therapy (SMART) Study Group*





N ENGL J MED 355;22 WWW.NEJM.ORG NOVEMBER 30, 2006

Second Generation HAART Era: 2006-2011

2006: Immune restoration determines disease progression

Disease progression in patients with virological suppression in response to HAART is associated with the degree of immunological response

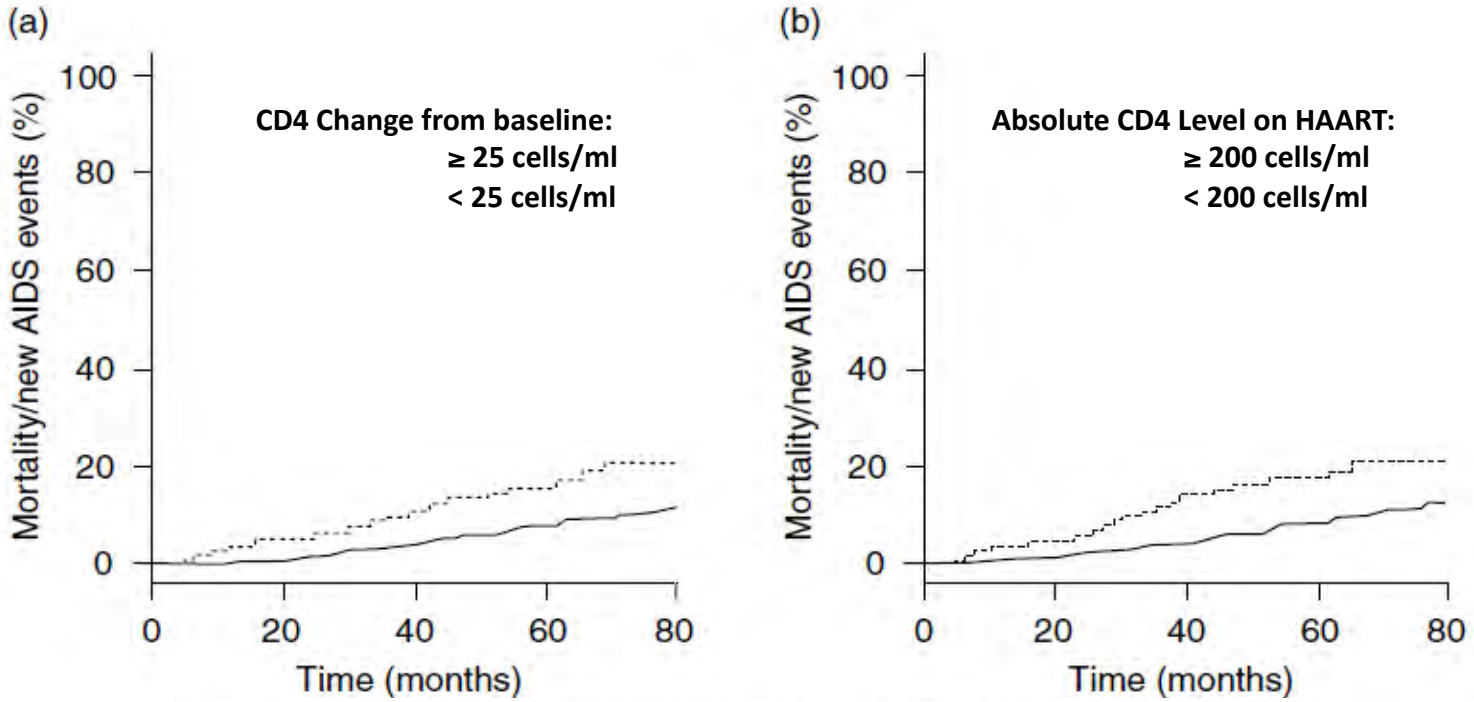


Fig. 1. Kaplan–Meier curves of non-accidental mortality or new AIDS events associated with immunological responses in 1084 individuals with viral load < 500 copies/ml at 3 to 9 months after initiating HAART. (a) Response defined by change in baseline CD4 cell counts: increase ≥ 25 cells/μl (—) and < 25 cells/μl (- - -); log rank $P < 0.001$. (b) Response defined by absolute CD4 cell count: ≥ 200 cells/μl (—) and < 200 cells/μl (- - -); log rank $P < 0.001$.

AIDS 2006, **20**:371–377

Second Generation HAART Era: 2006-2011

2006 2007 2008 2009 2010 2011

Second Generation HAART Era: 2006-2011

2007: 1500 international delegates convene to discuss prevention and treatment in the field

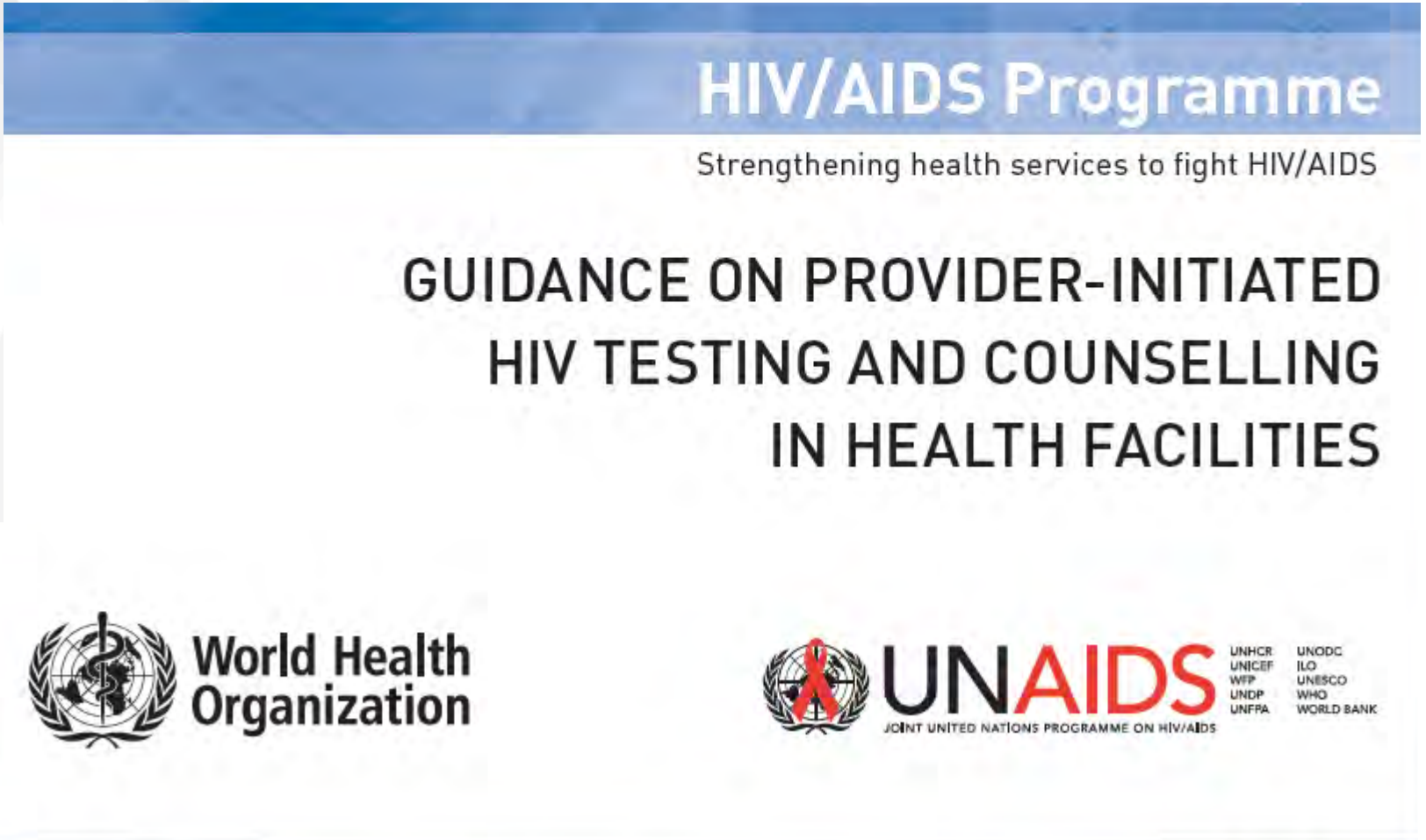
2007 HIV/AIDS Implementers' Meeting

Kigali, Rwanda – June 16–19, 2007

2008 HIV/AIDS Implementers' Meeting: June 2008, Kampala, Uganda

Second Generation HAART Era: 2006-2011

2007: Provider-initiated routine HIV testing recommended internationally



Second Generation HAART Era: 2006-2011

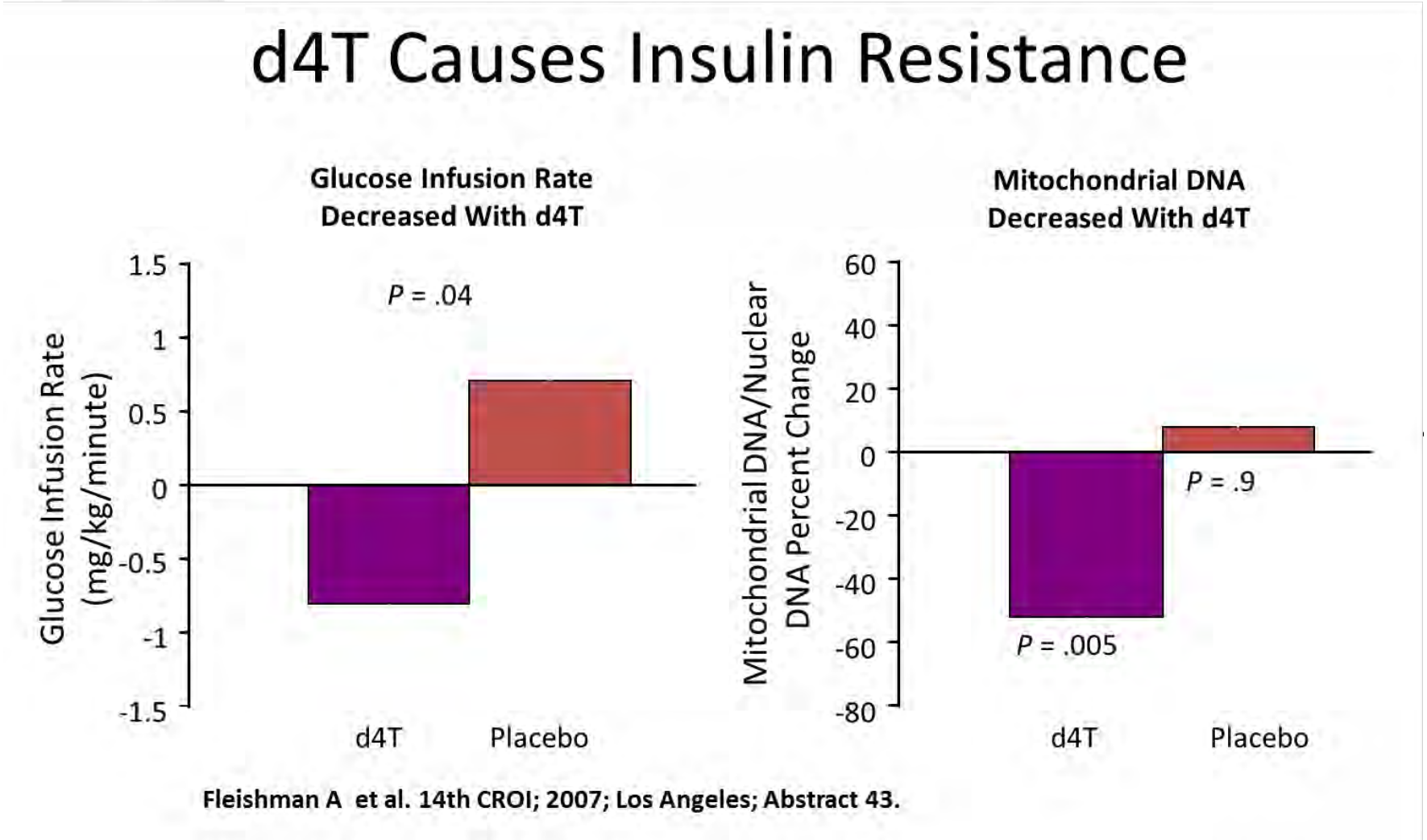
2007: International leaders revise pledge for ARV treatment of 5 million by 2010

Second Generation HAART Era: 2006-2011

2007: International vaginal micobicide trial halted for lack of efficacy

Second Generation HAART Era: 2006-2011

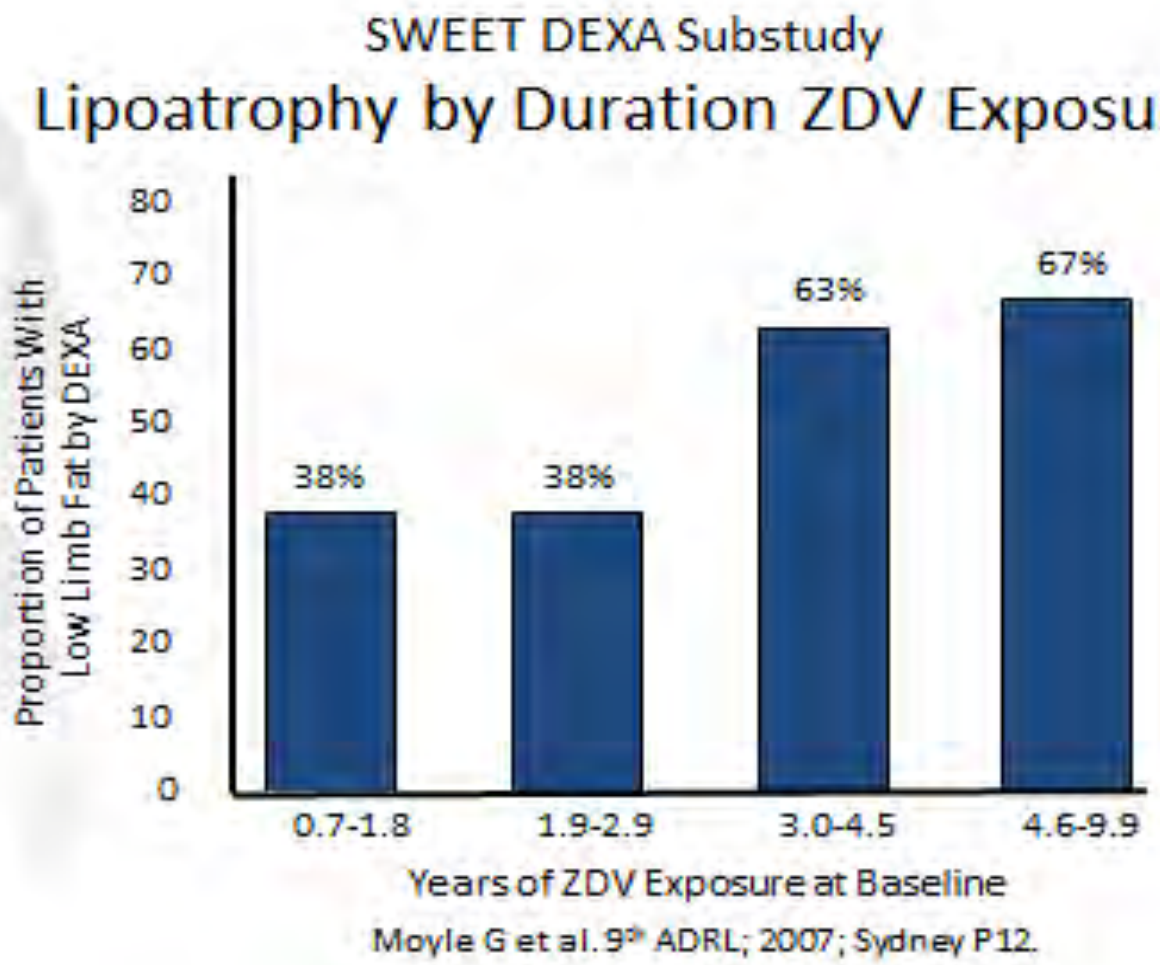
2007: Insulin resistance accompanies mitochondrial toxicity



Fleishman A et al. 14th CROI; 2007; Los Angeles; Abstract 43.

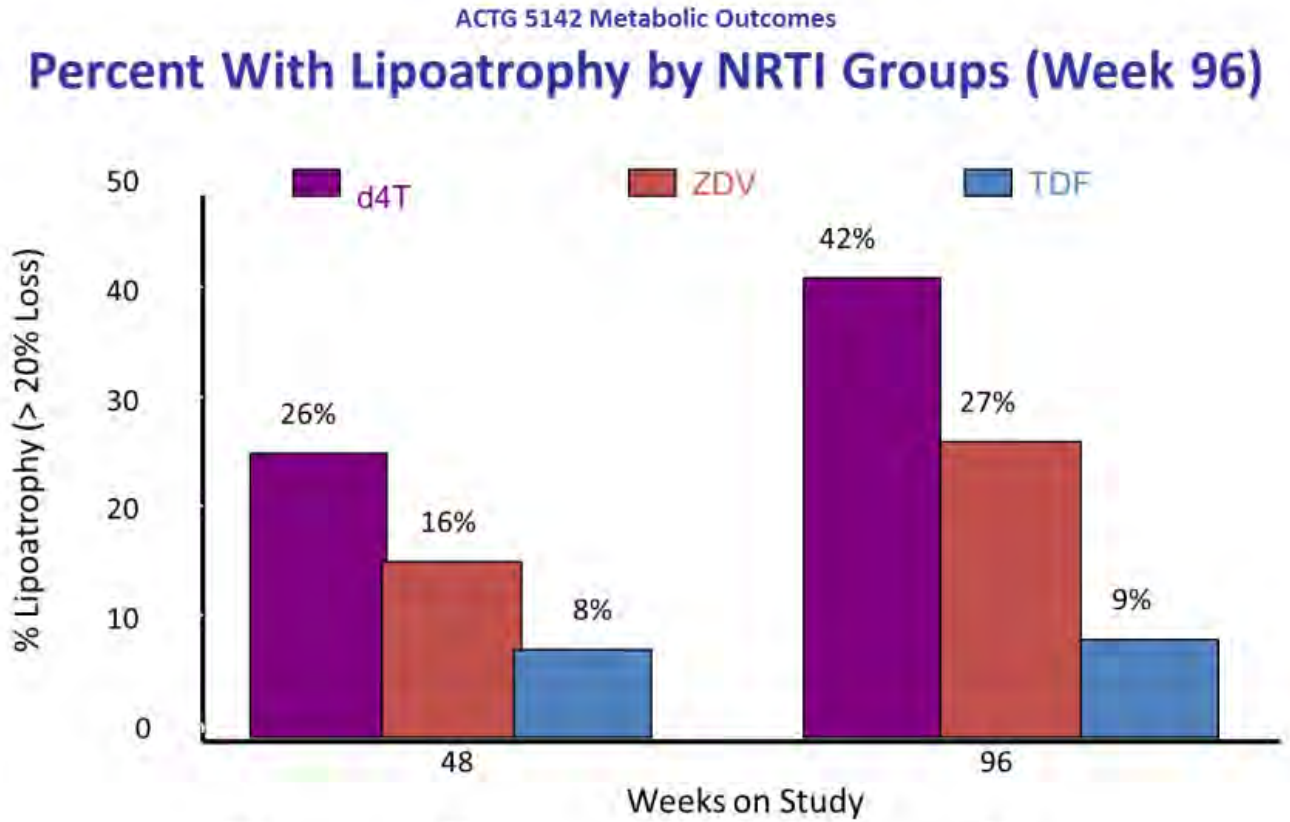
Second Generation HAART Era: 2006-2011

2007: Lipoatrophy increases after ≥3 years zidovudine



Second Generation HAART Era: 2006-2011

2007: Lipoatrophy worse with certain NRTIs

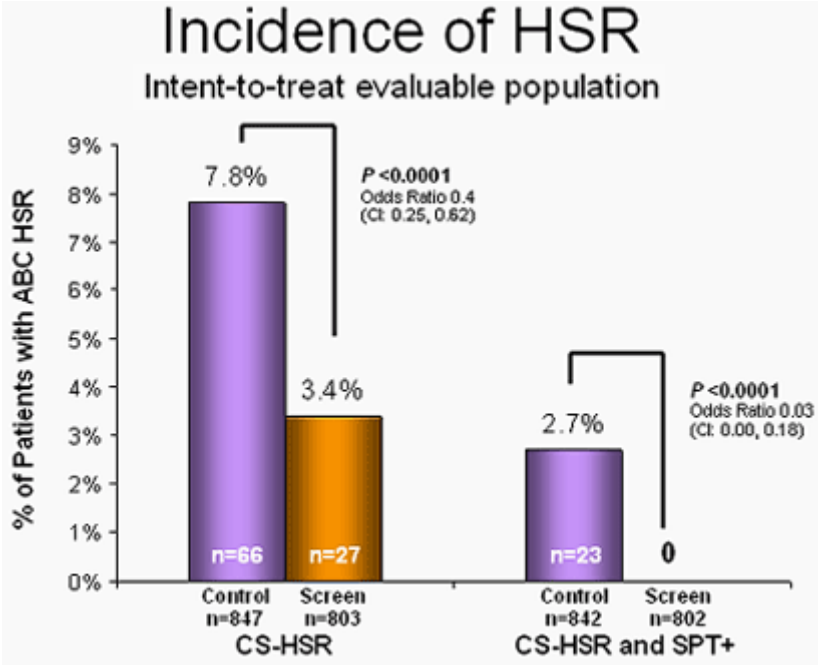


Haubrich R et al. 14th CROI; 2007; Los Angeles. Abstract 38.

Second Generation HAART Era: 2006-2011

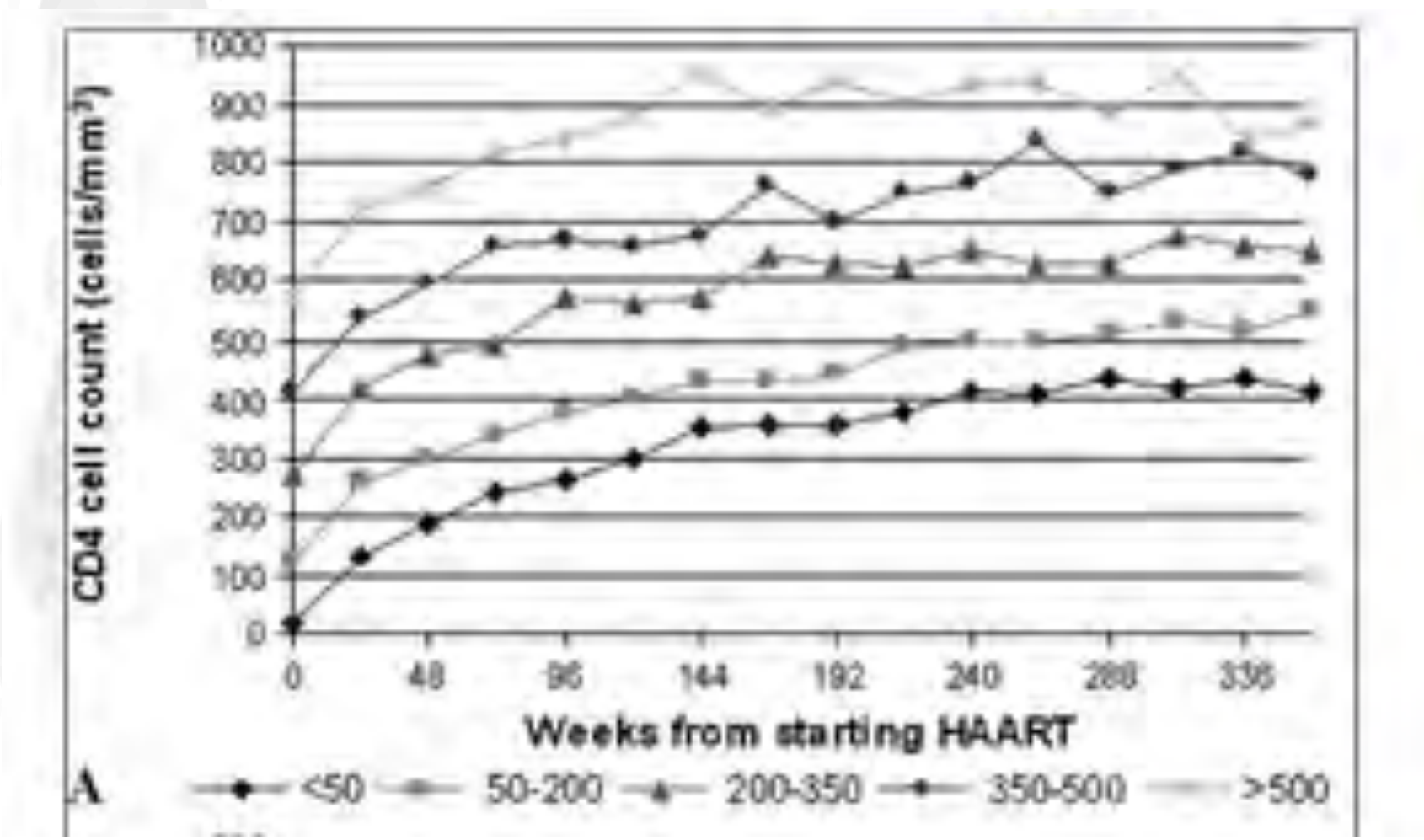
2007: PREDICT 1 Study confirms HLA-B*5701 association with ABC hypersensitivity reaction

Mallal S et al.4th IAS; 2007; Sydney. Abstract WESS101.



Second Generation HAART Era: 2006-2011

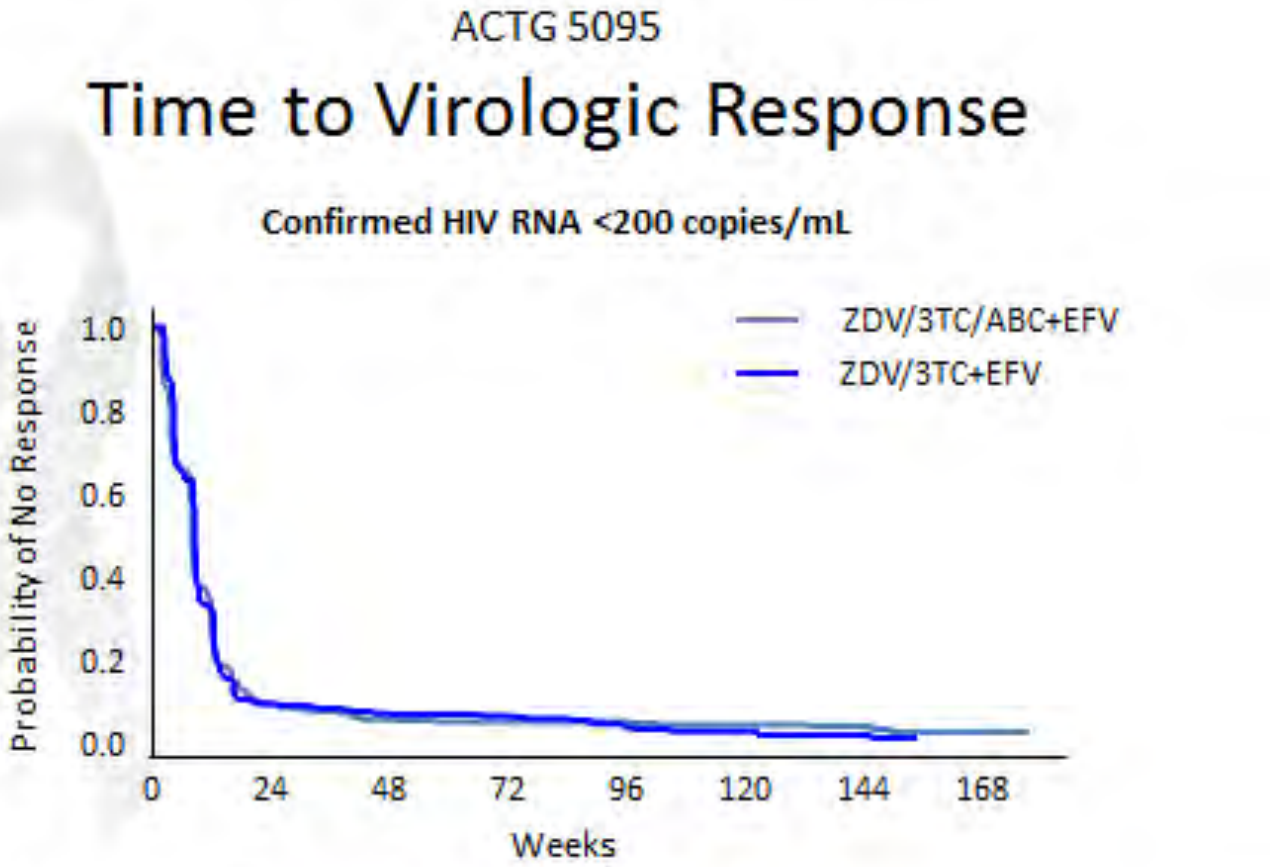
2007: CD4 ≥800 after 7 years if ART initiated at CD4 ≥350



Gras JAIDS 2007 45:183-192

Second Generation HAART Era: 2006-2011

2007: 4 drugs no better than 3

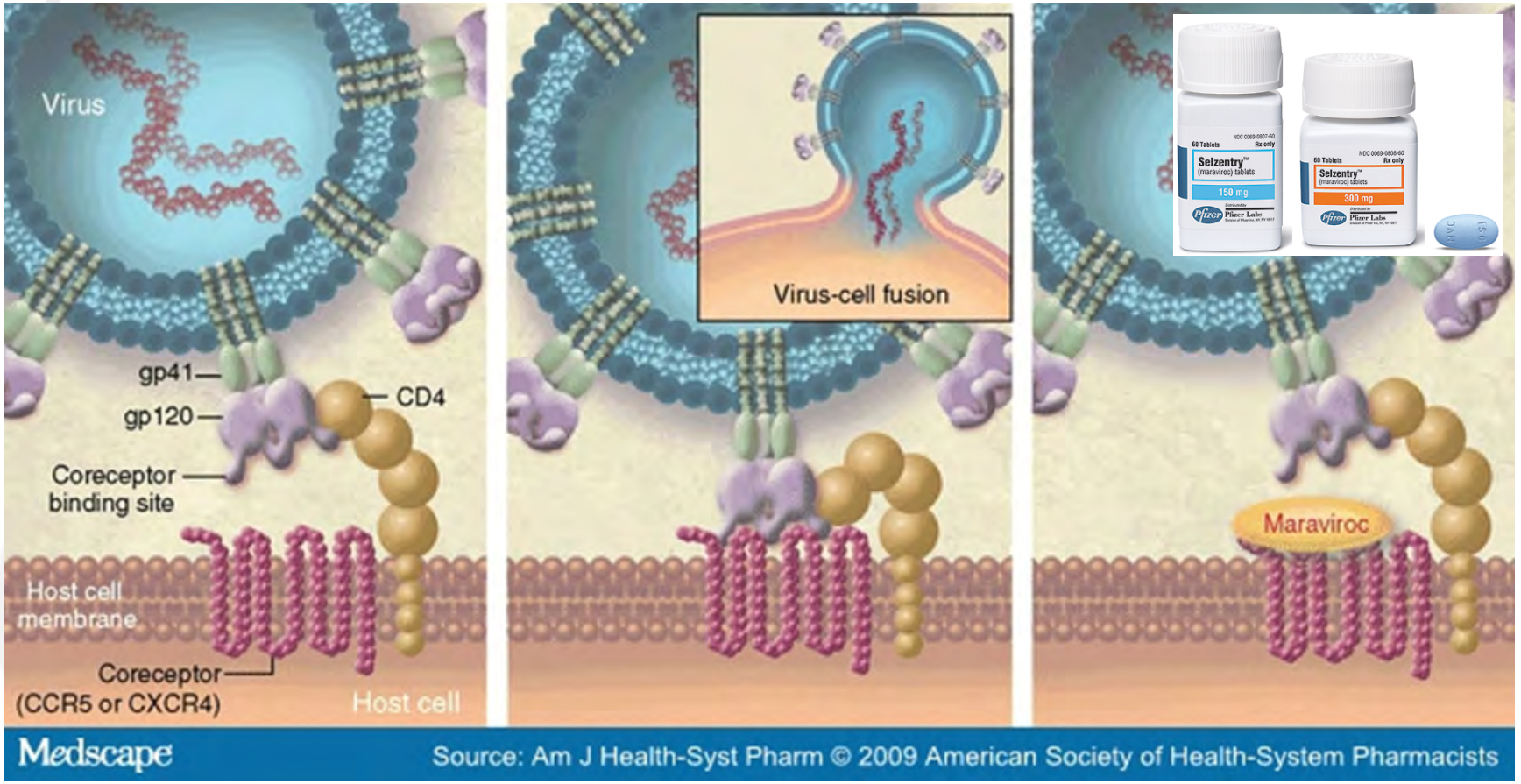


No difference in probability of not failing among patients with HIV RNA >100,000 copies/mL

Gulick R et al. JAMA. 2006;296:769-781.

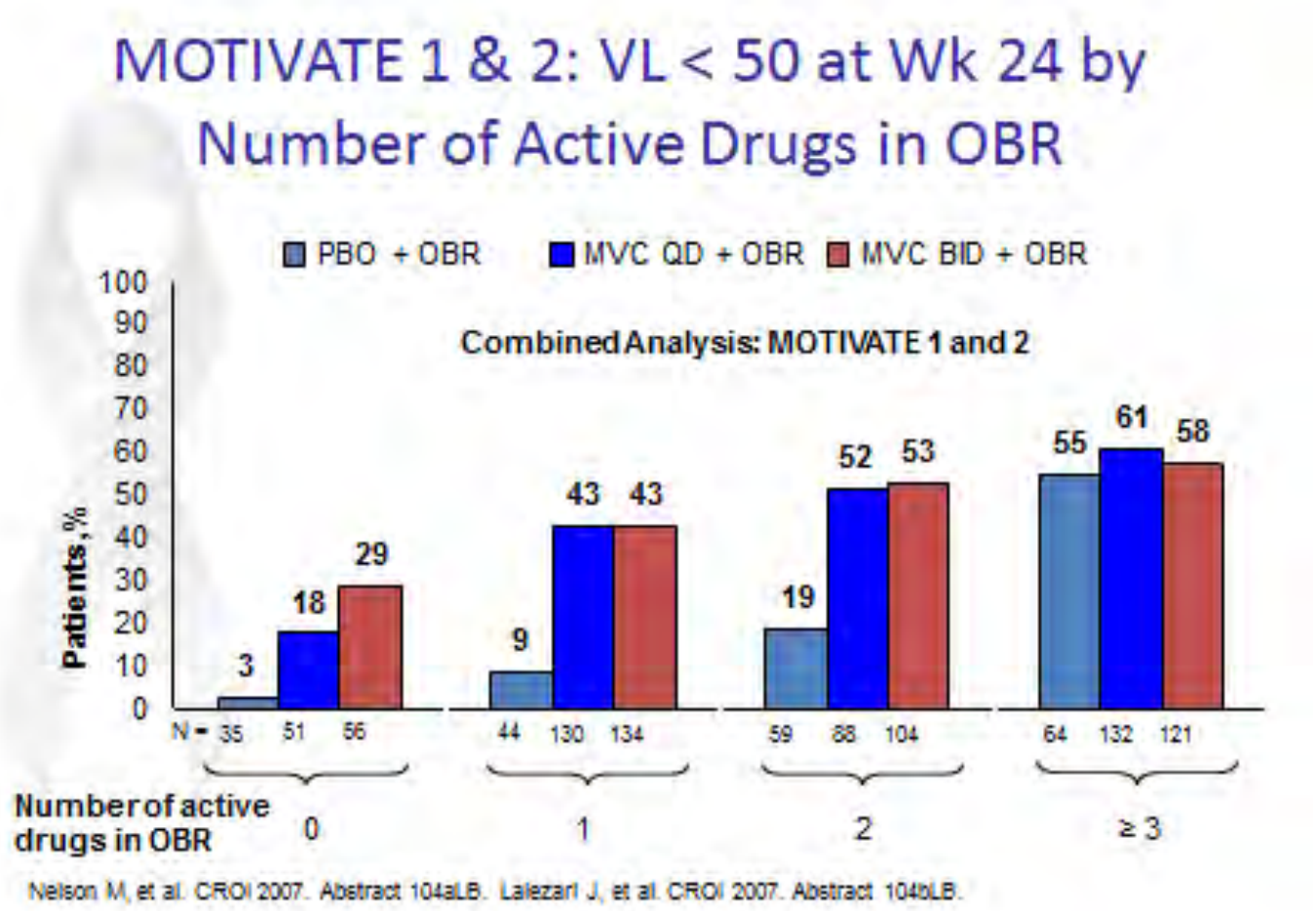
Second Generation HAART Era: 2006-2011

2007: 1st CCR5 Inhibitor Maraviroc



Second Generation HAART Era: 2006-2011

2007: VL suppression related to number of active ARV agents

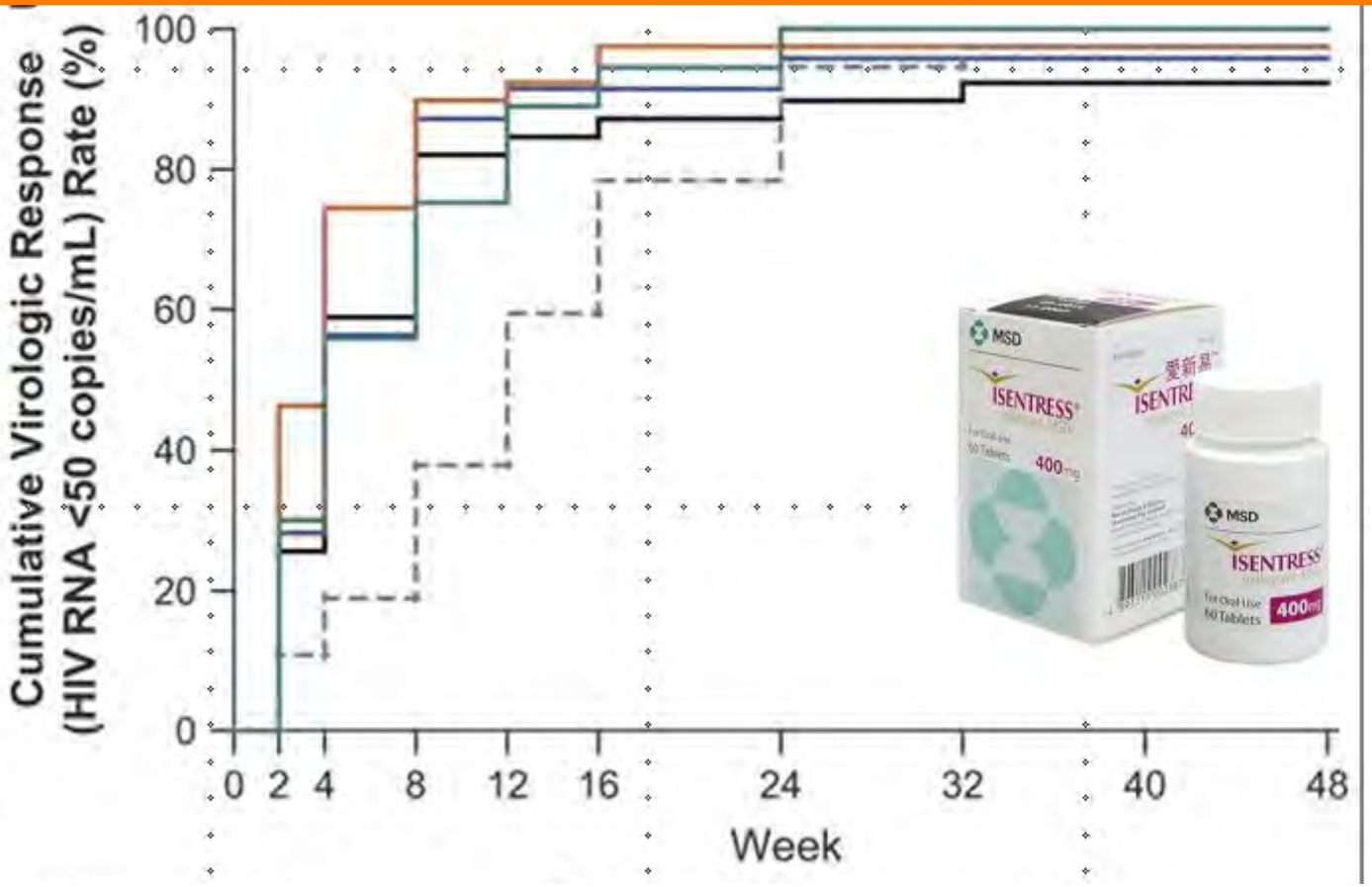


Nelson M, et al. CROI 2007. Abstract 104aLB. Lalezari J, et al. CROI 2007. Abstract 104bLB.

Second Generation HAART Era: 2006-2011

2007: 1st INSTI Raltegravir: Rapid VL Suppression

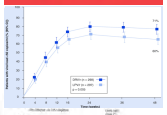
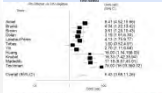
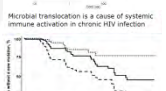
Fully suppressive "Salvage" regimens available again

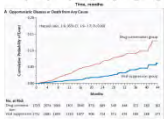
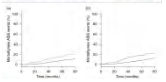


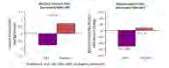
JAIDS 2007 Oct 1;46(2):125-33.

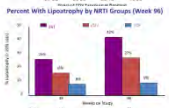
Second Generation HAART Era: 2006-2011

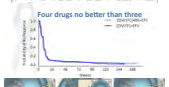
2006 2007 2008 2009 2010 2011

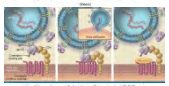
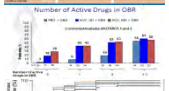





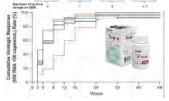





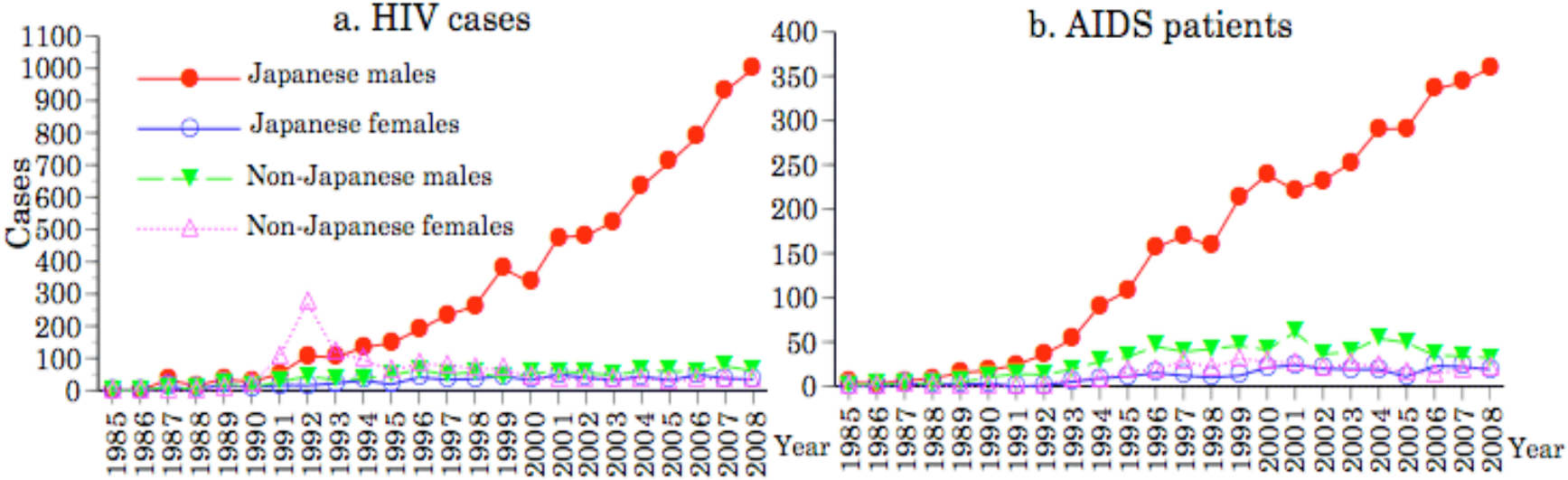





Second Generation HAART Era: 2006-2011

2008: HIV and AIDS continue to rise in Japan

Figure 2. Nationality and gender of HIV cases and AIDS patients, 1985-2008, Japan



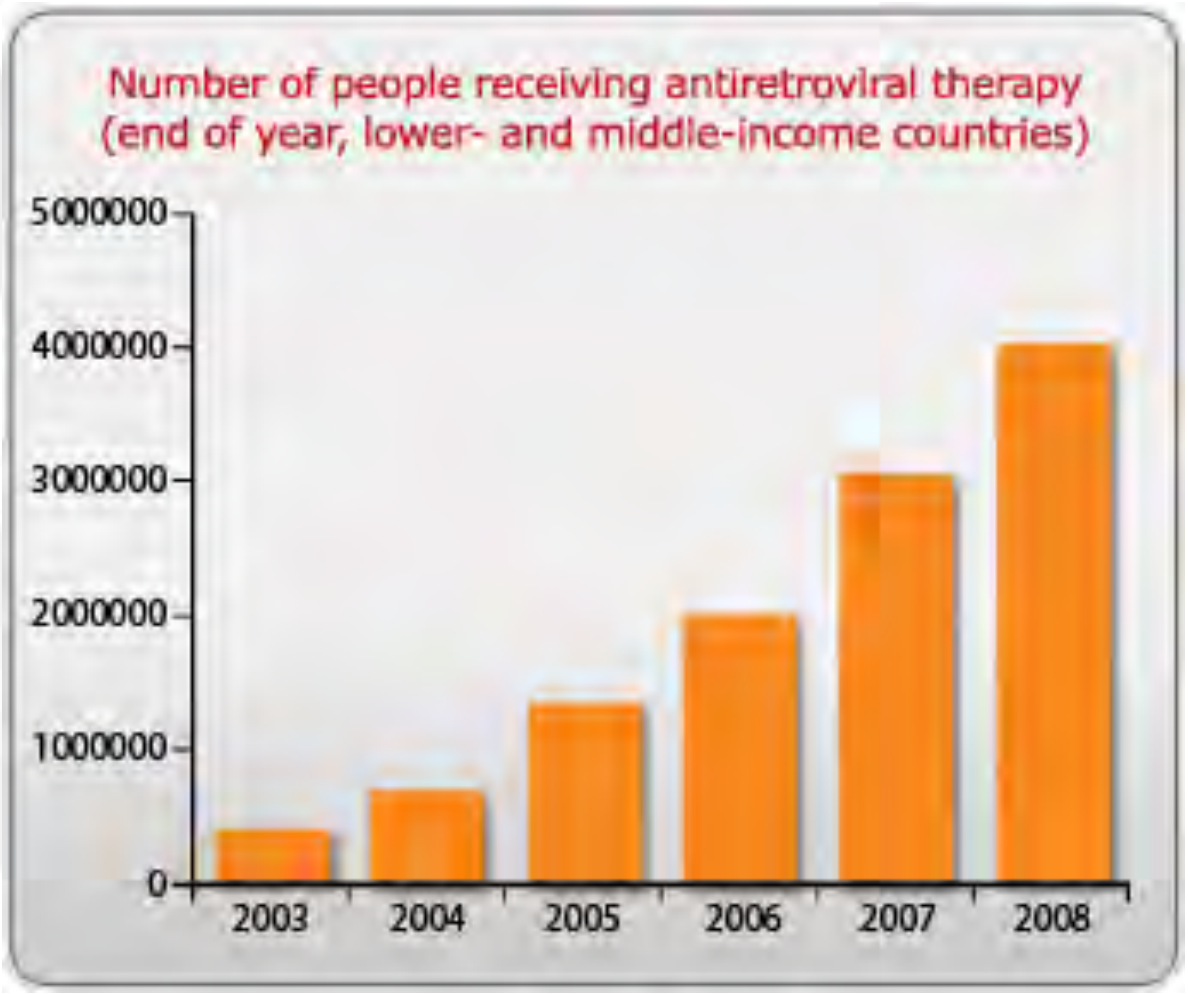
(The 2008 Annual Report on HIV/AIDS Surveillance in Japan, the National AIDS Surveillance Committee, Ministry of Health, Labour and Welfare)

IASR

Infectious Agents Surveillance Report

Second Generation HAART Era: 2006-2011

2008: International gains in ART: Steady but below target



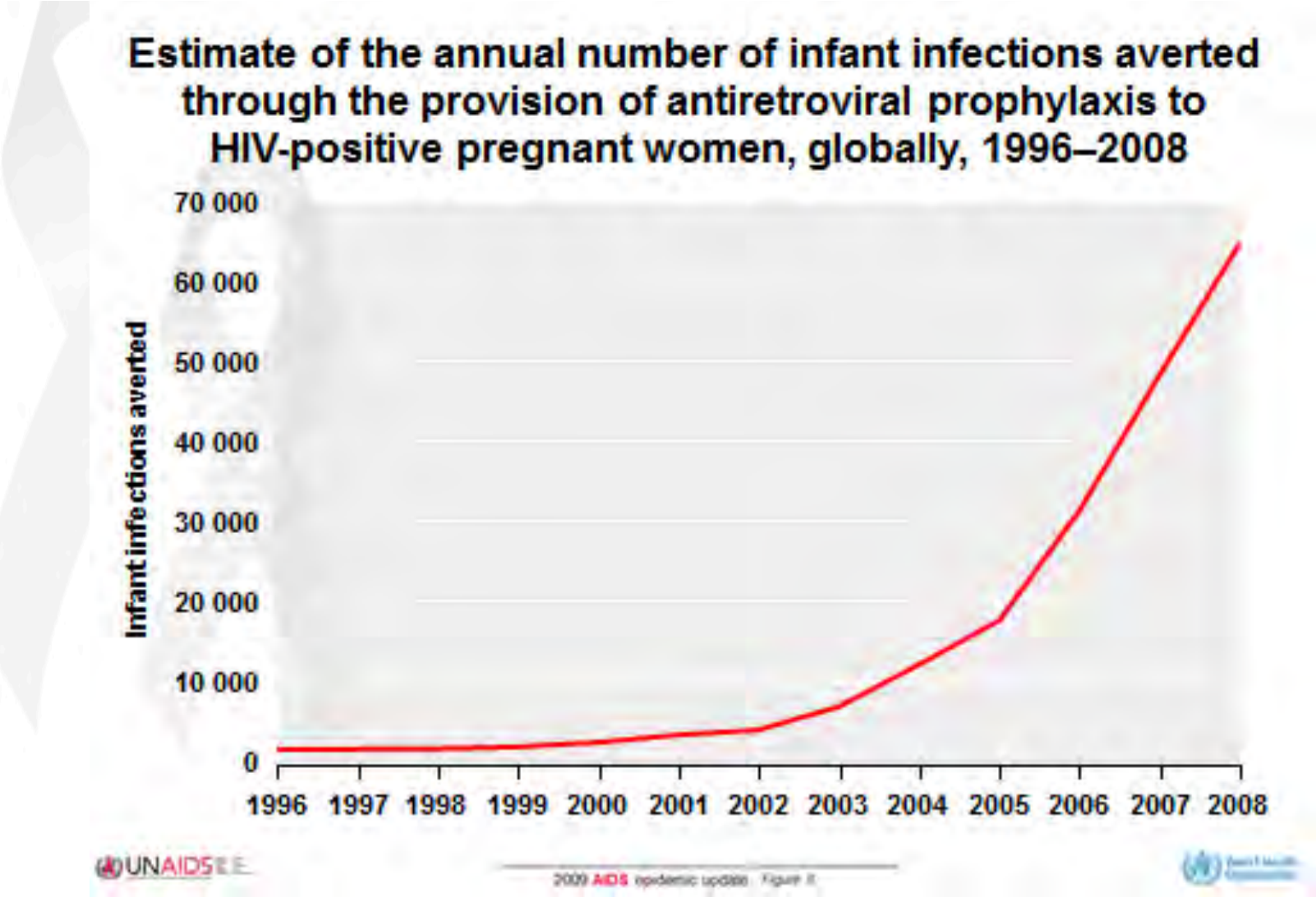
Second Generation HAART Era: 2006-2011

2008: International AIDS conference: Focus on community involvement

AIDS 2008
XVII INTERNATIONAL AIDS CONFERENCE
Mexico City, 3 - 8 August

Second Generation HAART Era: 2006-2011

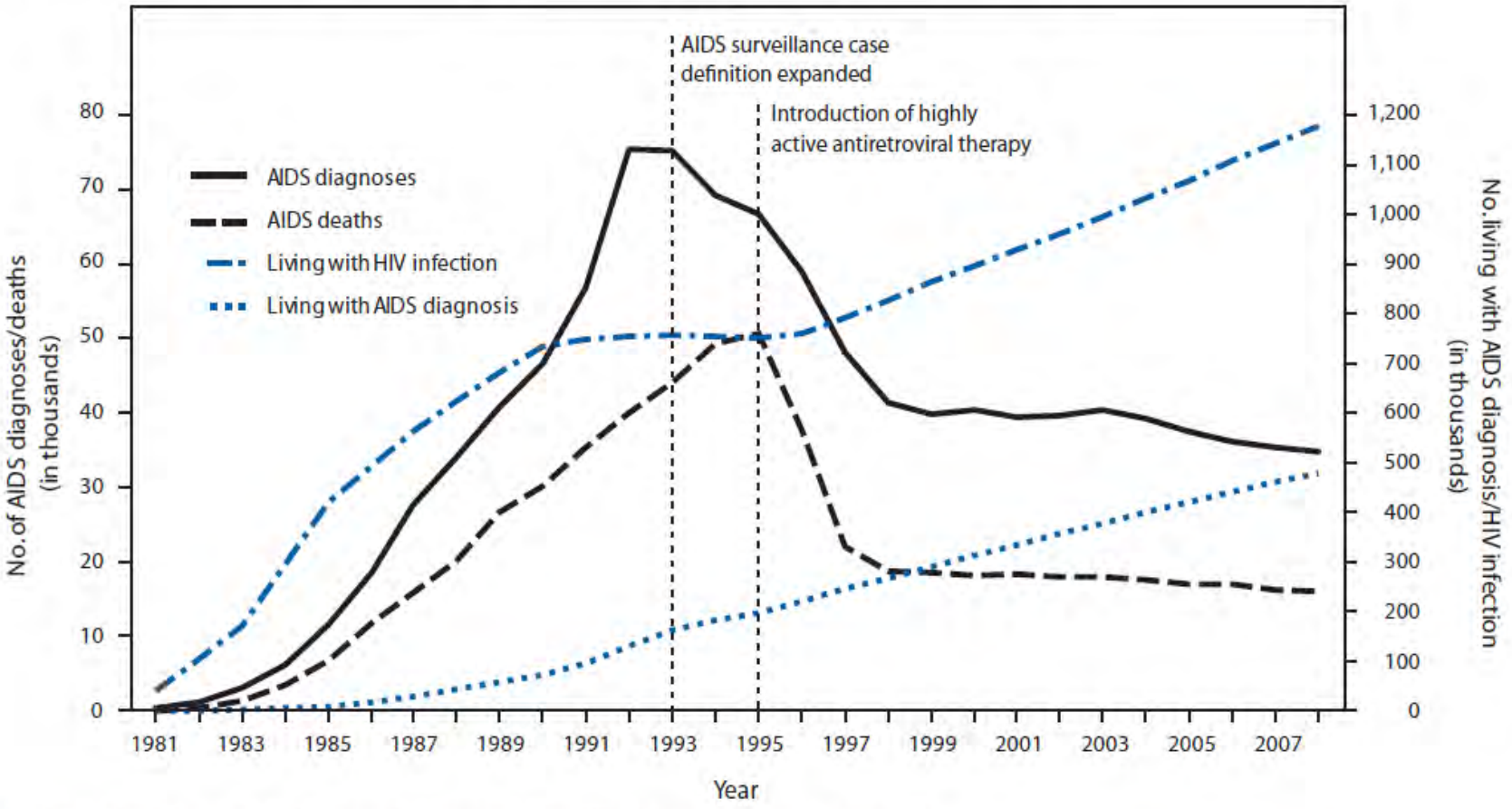
2008: Increasing global perinatal transmission prevention



Second Generation HAART Era: 2006-2011

2008: Persistent increase in US HIV "incidence": 54,000 new infections annually

FIGURE. Estimated number of AIDS diagnoses and deaths and estimated number of persons living with AIDS diagnosis* and living with diagnosed or undiagnosed HIV infection† among persons aged ≥13 years — United States, 1981–2008



Second Generation HAART Era: 2006-2011

2008: National HIV care quality measures approved

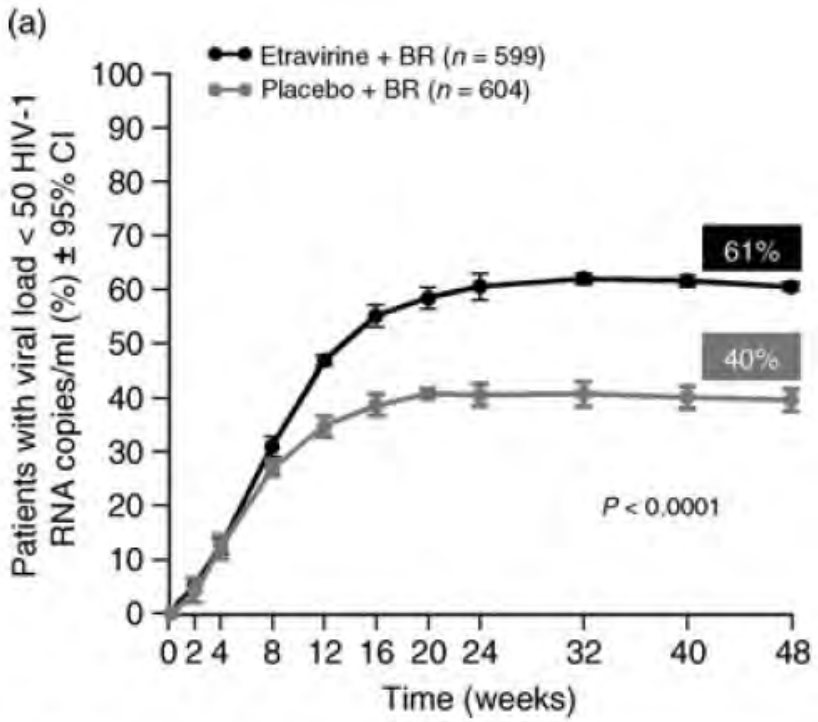
Second Generation HAART Era: 2006-2011

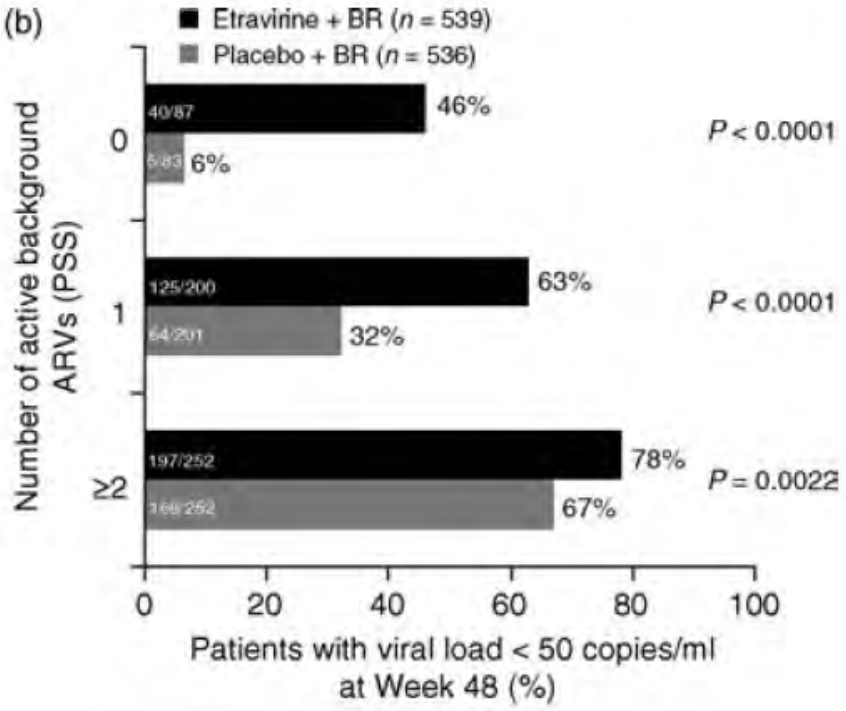
2008: National HIV care quality measures approved

1.	Retention in care	two visits/year
2.	CD4 measurement	twice/year
3.	GC / CT screening	once/year
4.	Syphilis screening	once/year
5.	Injection drug use screening	once/year
6.	High-risk sex screening	once/year
7.	Tuberculosis screening	once/year
8.	Hepatitis B screening	once ever
9.	Hepatitis C screening	once ever
10.	Influenza immunization	annually
11.	Pneumococcal immunization	once
12.	Hepatitis B vaccination	ordered
13.	Hepatitis B vaccination	completed
14.	PCP prophylaxis	if CD4 <200
15.	ART prescribed	if appropriate
16.	Viral suppression	system level
17.	Viral suppression	provider level

Second Generation HAART Era: 2006-2011

2008: 4th NNRTI: Etravirine: High VL suppression rate in DUET trial





Katlama AIDS 2009; 23:2299

Second Generation HAART Era: 2006-2011

2008: Evaluating number of baseline mutations becomes new standard in treatment experienced

ETR and DRV Mutations

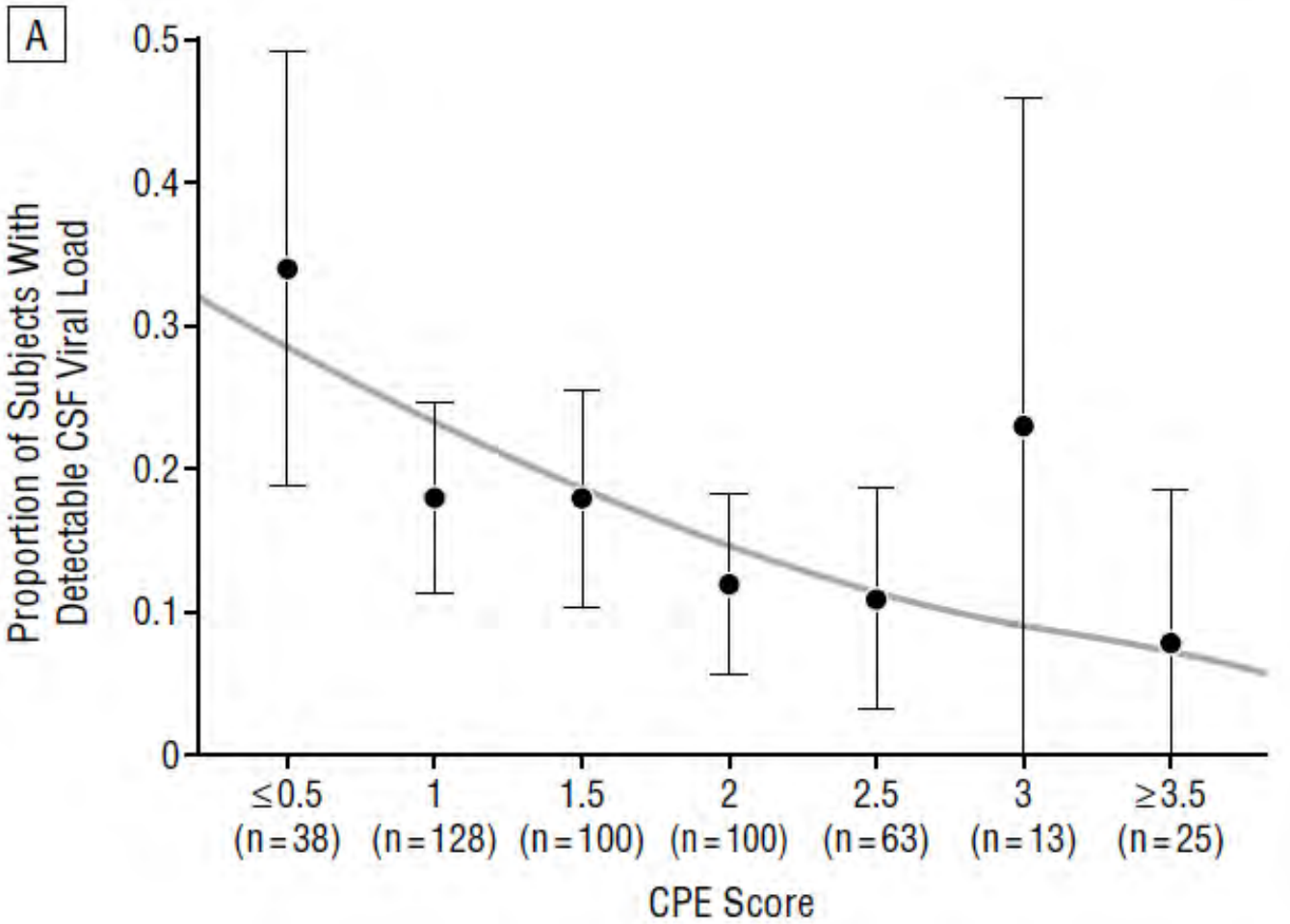
- High response rates in pts with ≤ 3 combined ETR + DRV mutations at Wk 24

		ETR mutations, n				
VL< 50 c/mL, % (n/N)		0	1	2	3	> 3
Darunavir Mutations, n	0	78 (7/9)	67 (8/12)	100 (3/3)	67 (2/3)	0 (0/1)
	1	83 (36/44)	71 (27/38)	93 (13/14)	57 (4/7)	40 (2/5)
	2	73 (30/41)	75 (18/24)	56 (9/16)	29 (2/7)	17 (1/6)
	3	78 (31/40)	50 (12/24)	45 (9/20)	60 (3/5)	30 (3/10)
	> 3	63 (17/27)	35 (8/23)	27 (3/11)	27 (3/11)	0 (0/5)

Haubrich R, et al. IAC 2008. Abstract TUPE0048.

Second Generation HAART Era: 2006-2011

2008: ARV CHARTER score correlates with CNS VL



Letendre. (2008). *Archives of Neurology, 65(1)*, 65-70.

Second Generation HAART Era: 2006-2011

2008: HIV persistence in GALT

Persistence of HIV in Gut-Associated Lymphoid Tissue despite Long-Term Antiretroviral Therapy

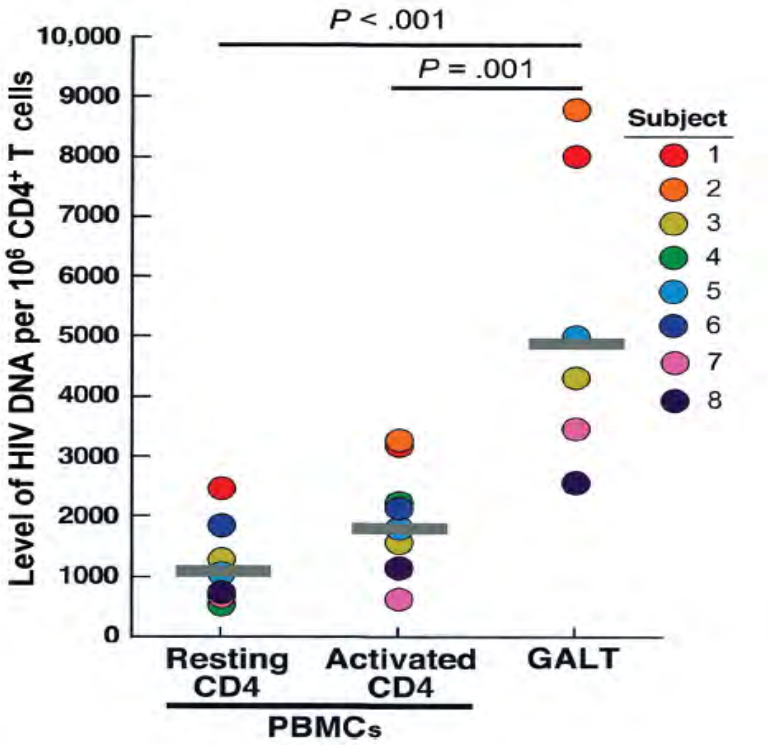


Figure 2. Frequency of HIV proviral DNA in resting and activated CD4+ T cells sorted by fluorescence-activated cell sorter analysis (FACS) and CD8-depleted single cell suspensions from gut-associated lymphoid tissue (GALT) (term

Second Generation HAART Era: 2006-2011

2008: Durable persistence of viremia on

Low-level viremia persists for at least 7 years in patients on suppressive antiretroviral therapy

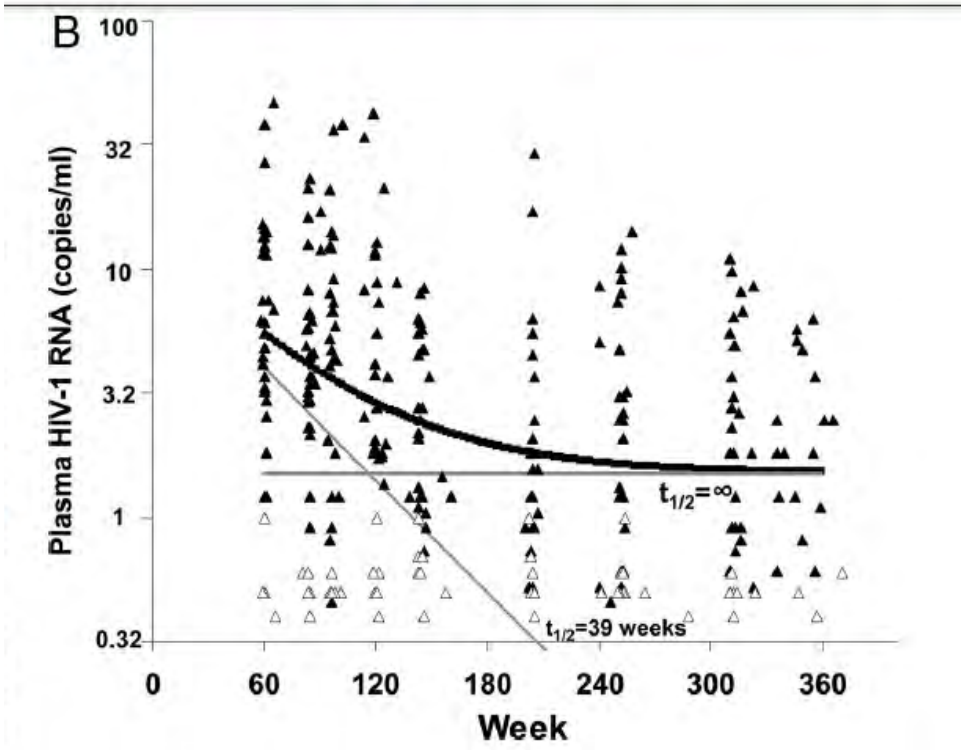
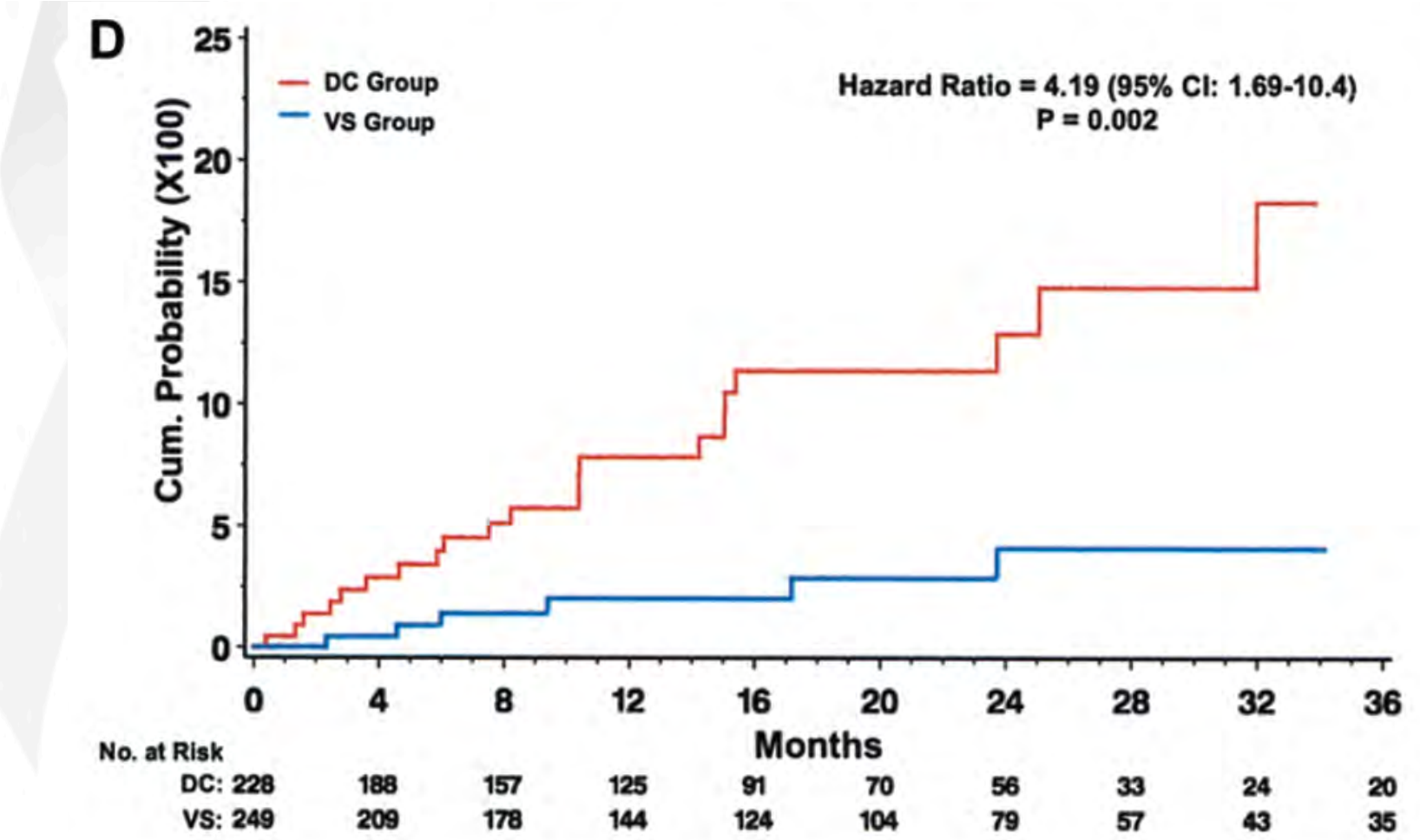


Fig. 2. Decline in persistent viremia over 7 years of treatment. (*A*) Initial two-phase decline in viremia after the initiation of treatment for the 720 patients included in this study, as assayed by Amplicor. (*B*) Individual HIV-1 RNA values determined by SC^ starting at week 60 (open symbols indicate

PNAS | March 11, 2008 | vol. 105 | no. 10 | 3879–3884

Second Generation HAART Era: 2006-2011

2008: SMART: Continuous ART superior to interrupted ART



Emery J Inf Dis 2008;197:1133-1144; Gill CID 2010;50:98-105

Second Generation HAART Era: 2006-2011

2008: Elite controller patient characteristics further elucidated

Genetic and Immunologic Heterogeneity among Persons Who Control HIV Infection in the Absence of Therapy

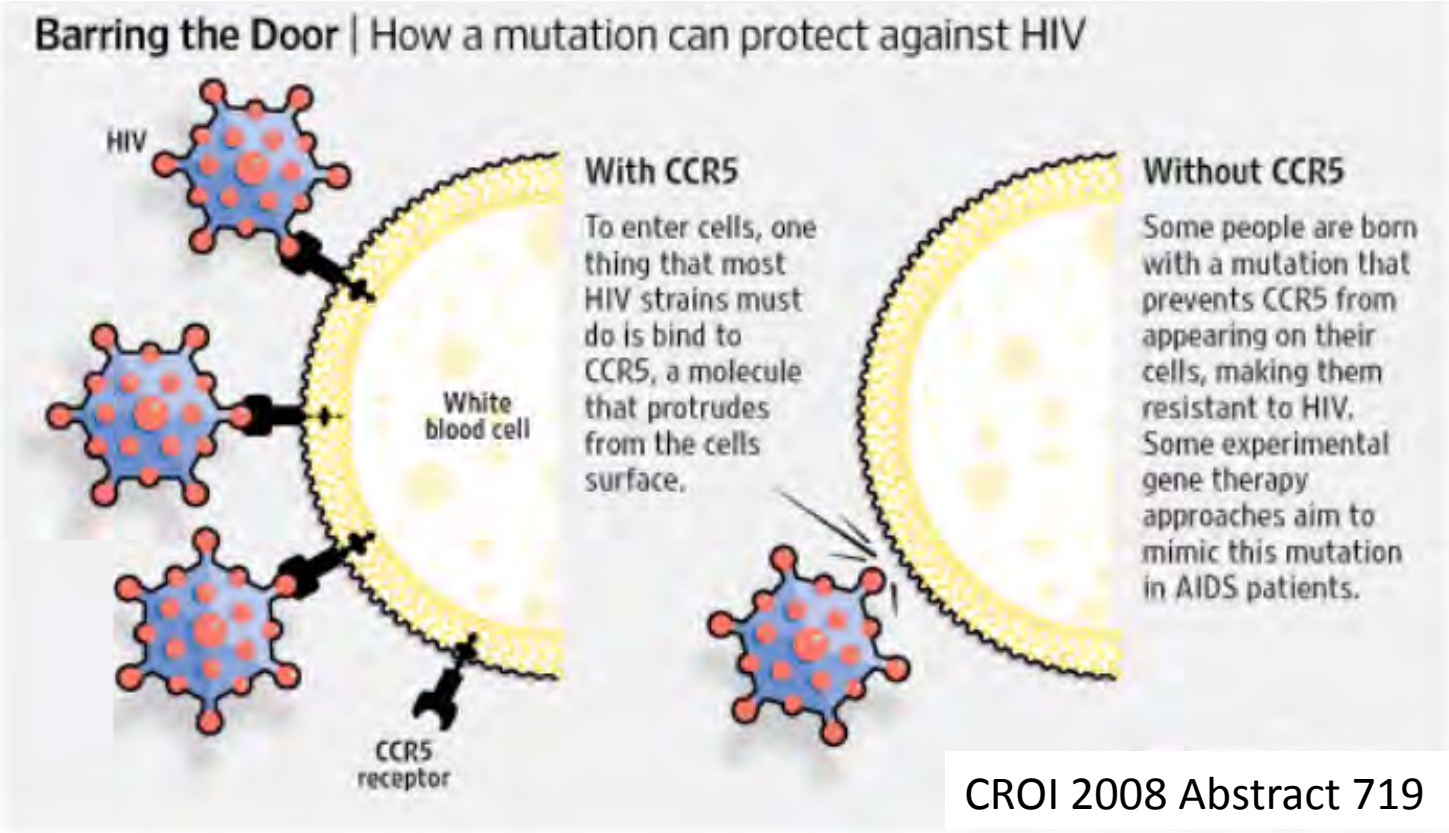
Conclusions. Elite controllers are a distinct group, even when compared to persons with low level viremia, but they exhibit marked genetic and immunologic heterogeneity. Even low-level viremia among HIV controllers was associated with measurable T cell dysfunction, which has implications for current prophylactic vaccine strategies.

Second Generation HAART Era: 2006-2011

2008: Berlin patient "functionally cured" of HIV

Treatment of HIV-1 Infection by Allogeneic CCR5-Δ32/Δ32 Stem Cell Transplantation: A Promising Approach.

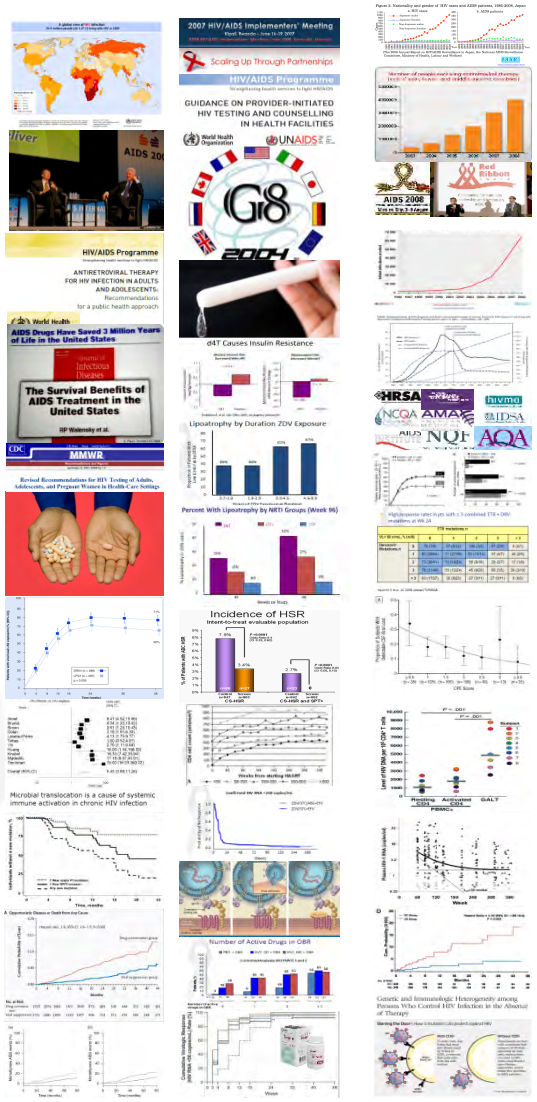
G. Hütter, D. Nowak, M. Mossner, S. Ganepola, K. Allers, T. Schneider, J. Hofmann, I.W. Blau, W.K. Hofmann, E. Thiel
From the Charité – Medical University of Berlin, Germany



CROI 2008 Abstract 719

Second Generation HAART Era: 2006-2011

2006 2007 2008 2009 2010 2011



Second Generation HAART Era: 2006-2011

2009: Pope warns against condom use: WHO states Pope's comments "dangerous"

World Health Organization

Second Generation HAART Era: 2006-2011

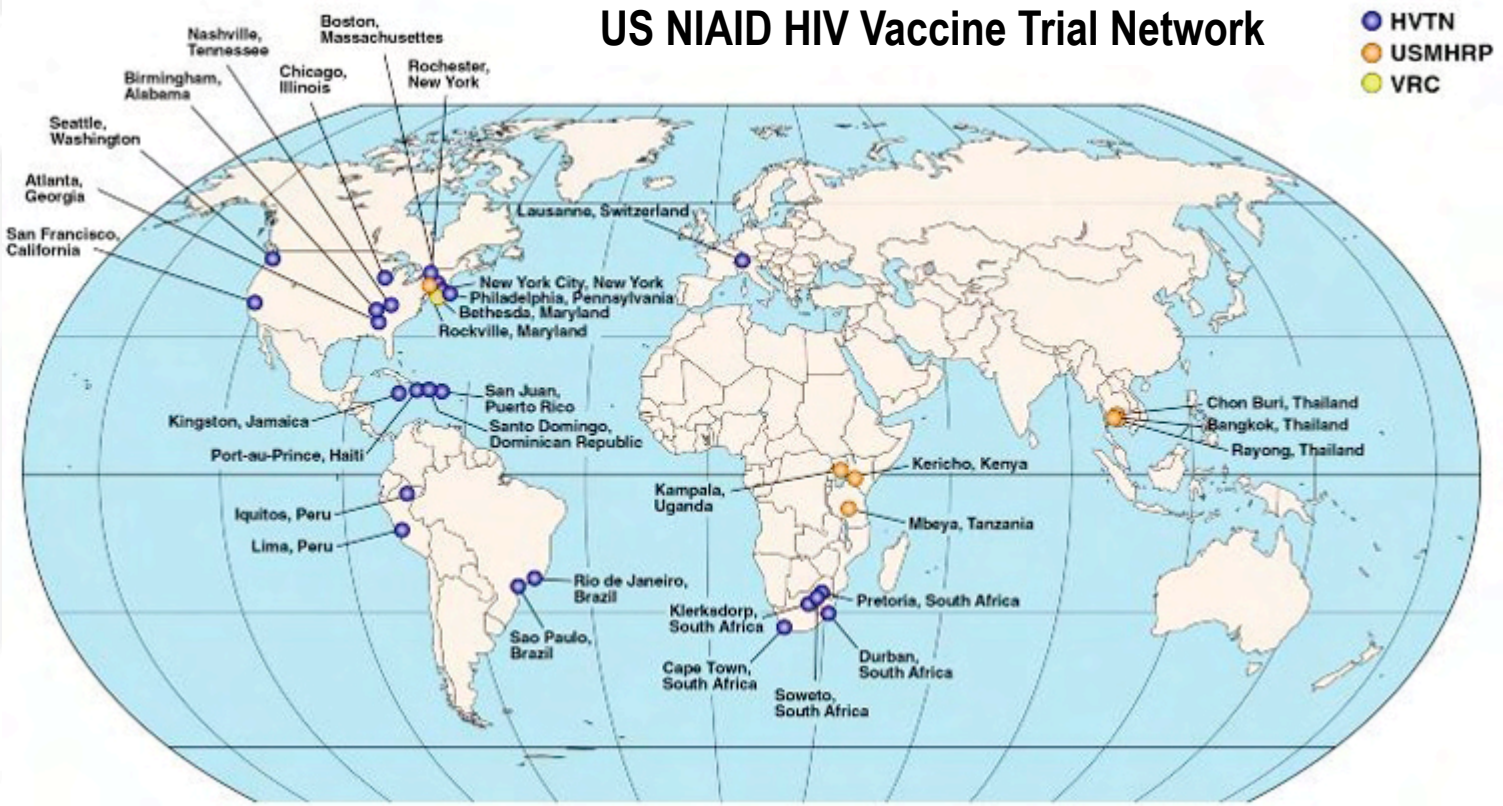
2009: India lifts ban against homosexutality

Second Generation HAART Era: 2006-2011

2009: US allows government funding of needle exchange programs

Second Generation HAART Era: 2006-2011

2009: HIV Vaccine still elusive



Second Generation HAART Era: 2006-2011

2009: Early ART beneficial during acute OIs

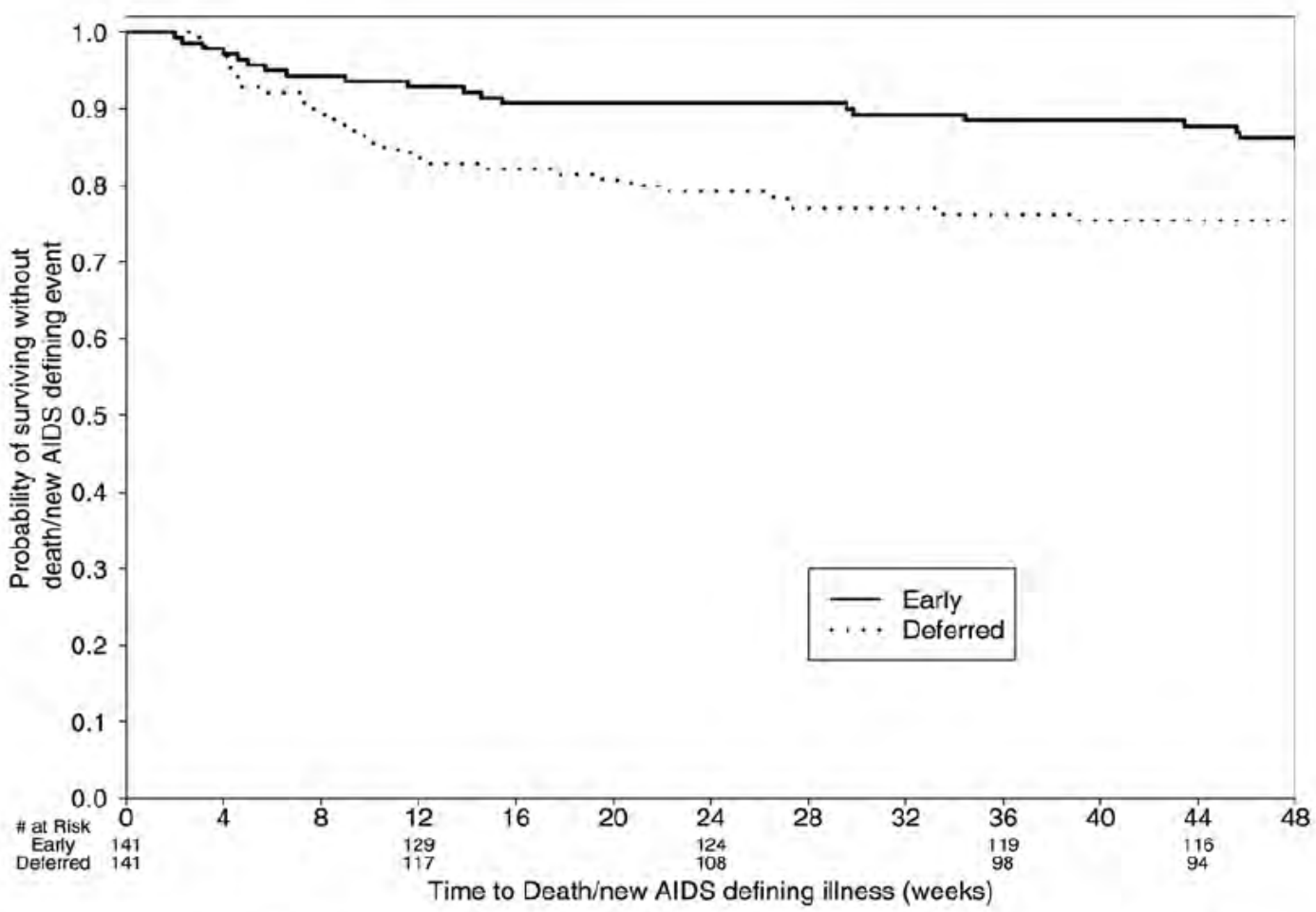


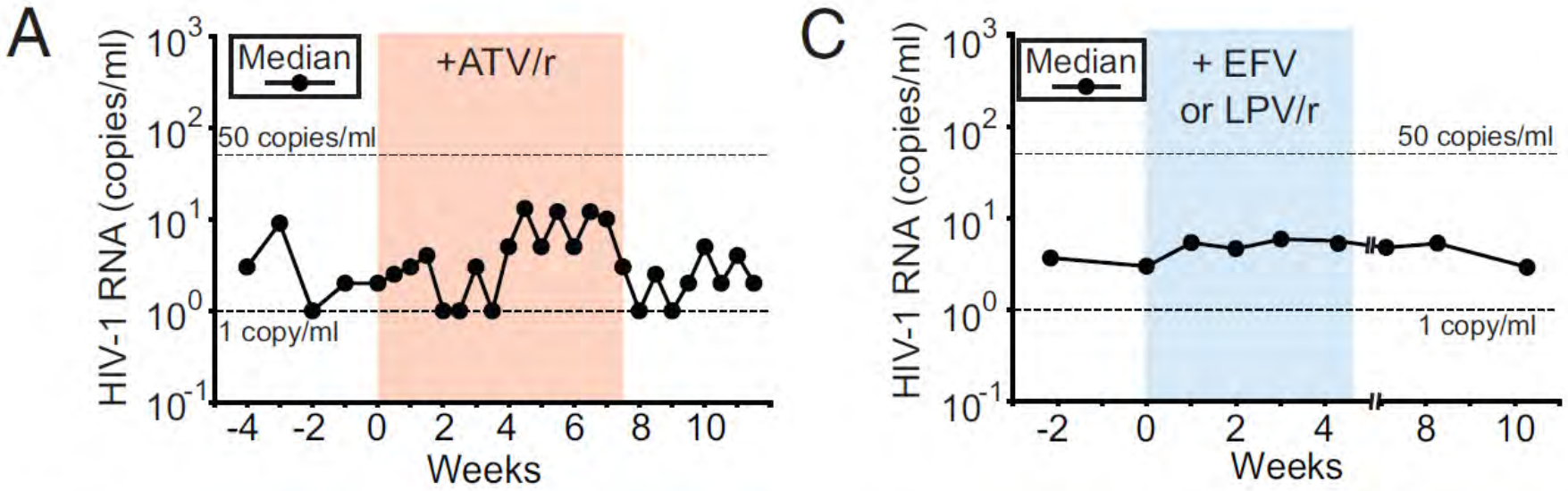
Figure 3. Time to AIDS progression or death. HR=0.53 Early versus Deferred ART [95%CI 0.30–0.92 p=0.023].

Zolopa PLoS One 2009;4:e5575

Second Generation HAART Era: 2006-2011

2009: Residual viremia not reducible with current ARVs

Treatment intensification does not reduce residual HIV-1 viremia in patients on highly active antiretroviral therapy



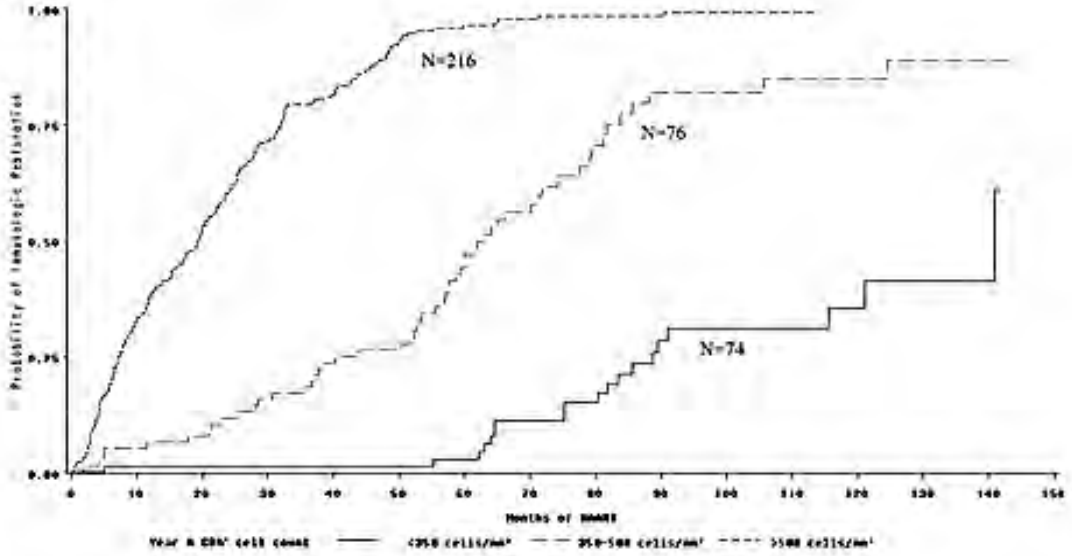
PNAS June 9, 2009 vol. 106 no. 23 9403-9408

Second Generation HAART Era: 2006-2011

2009: CD4 restoration better with earlier ARV treatment

Incomplete Peripheral CD4$^+$ Cell Count Restoration in HIV-Infected Patients Receiving Long-Term Antiretroviral Treatment

The time from initiation of HAART to achievement of a CD4+ cell count >500 cells/mm3, estimated using Kaplan-Meier techniques.



Kelley C F et al. Clin Infect Dis. 2009;48:787-794

Clinical Infectious Diseases

Second Generation HAART Era: 2006-2011

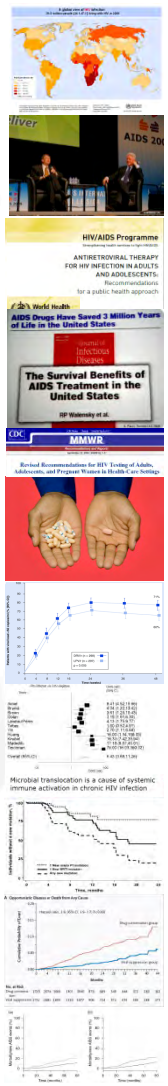
2009: Survival benefit when ART started at CD4 >500

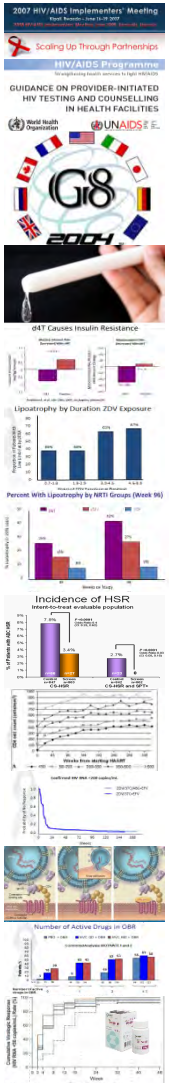
	CD4 350 – 500		CD4 >500	
	RR of Death (95% CI)	P Value	RR of Death (95% CI)	P Value
Deferred ART	1.69 (1.26-2.26)	<0.001	1.94 (1.37-2.79)	<0.001

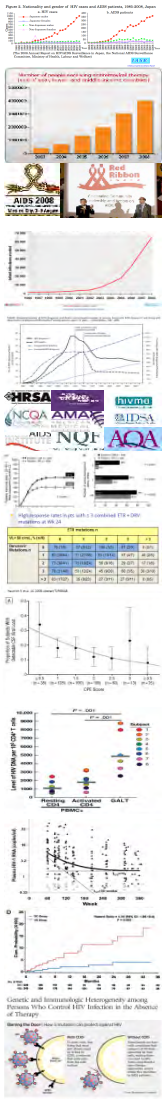
NA-ACCORD, Kitahata NEJM 2009;360:1815-1826

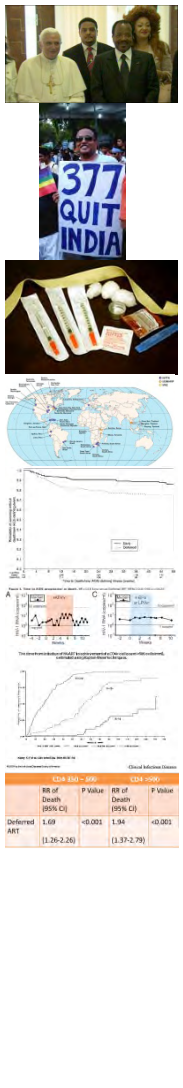
Second Generation HAART Era: 2006-2011

2006 2007 2008 2009 2010 2011





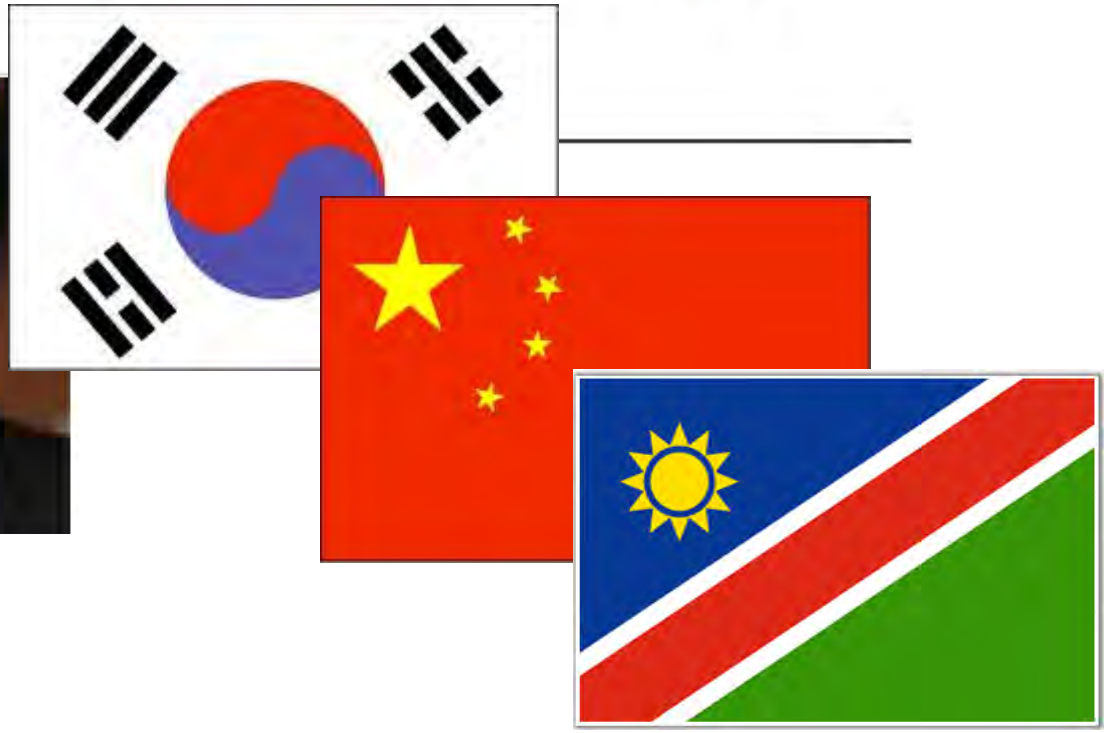




Second Generation HAART Era: 2006-2011

2010: US lifts 22 year HIV travel ban
Followed by South Korea, China and Namibia

HIV Travel Ban Lifted By President Obama



Second Generation HAART Era: 2006-2011

2010: Treatment guidelines focus on co-morbid factors

Antiretroviral Treatment of Adult HIV Infection

2010 Recommendations of the International AIDS Society–USA Panel

Table 1. Recommendations for Initiating Antiretroviral Therapy (ART) in Treatment-Naive Adults With HIV-1 Infection Who Are Ready to Begin Therapy[a]

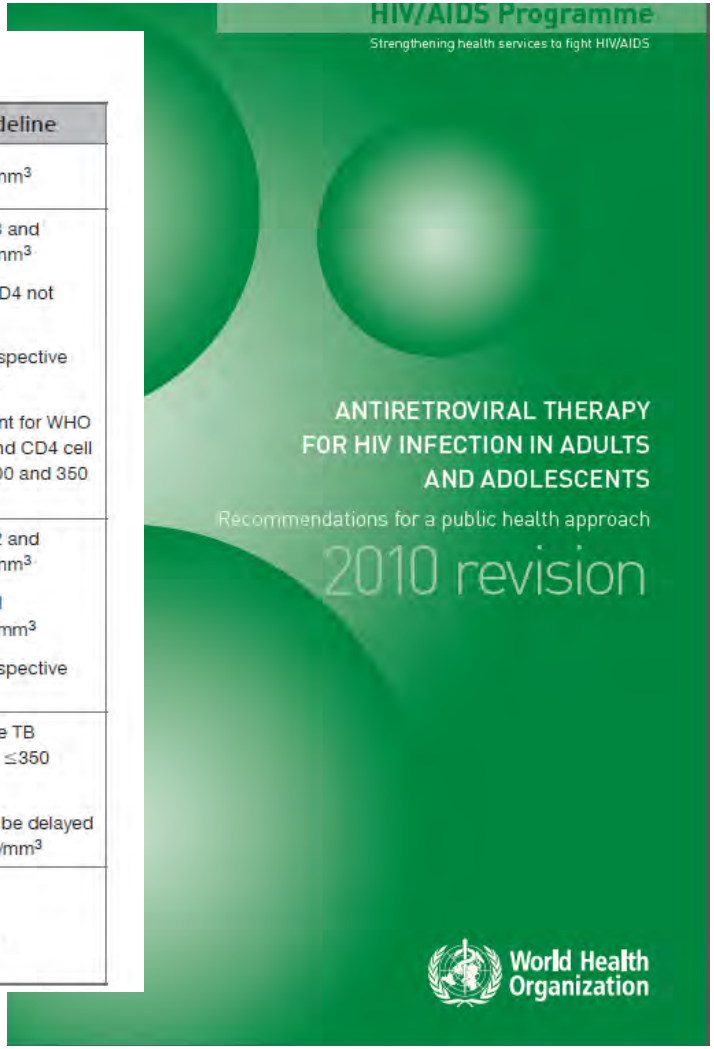
Measure	Recommendation	Rating
Specific conditions	ART is recommended regardless of CD4 cell count	
Symptomatic HIV disease		AIa
Pregnant women		AIa
HIV-1 RNA >100 000 copies/mL		AIIa
Rapid decline in CD4 cell count, >100/μL per year		AIIa
Active hepatitis B or C virus coinfection		BIIa, AIIa
Active or high risk for cardiovascular disease		BIIa
HIV-associated nephropathy		BIIa
Symptomatic primary HIV infection		BIIa
Risk for secondary HIV transmission is high, eg, serodiscordant couples		BIIa
Asymptomatic, CD4 cell count ≤500/μL	ART is recommended	
CD4 cell count <350/μL		AIa
CD4 cell count 350-500/μL		AIIa
Asymptomatic, CD4 cell count >500/μL	ART should be considered, unless patient is an elite controller (HIV-1 RNA <50 copies/mL) or has stable CD4 cell count and low-level viremia in the absence of ART	CIII

Second Generation HAART Era: 2006-2011

2010: WHO guidelines closer to US guidelines

Table 5. When to start antiretroviral therapy

Target population	2010 ART guideline	2006 ART guideline
HIV+ asymptomatic ARV-naive individuals	CD4 ≤350 cells/mm^3	CD4 ≤200 cells/mm^3
HIV+ symptomatic ARV-naive individuals	WHO clinical stage 2 if CD4 ≤350 cells/mm^3 OR WHO clinical stage 3 or 4 irrespective of CD4 cell count	WHO stage 2 or 3 and CD4 ≤200 cells/mm^3 WHO stage 3 if CD4 not available WHO stage 4 irrespective of CD4 cell count Consider treatment for WHO clinical stage 3 and CD4 cell count between 200 and 350 cells/mm^3
HIV+ pregnant women	CD4 ≤350 cells/mm^3 irrespective of clinical symptoms OR WHO clinical stage 3 or 4 irrespective of CD4 cell count	WHO stage 1 or 2 and CD4 ≤200 cells/mm^3 WHO stage 3 and CD4 ≤350 cells/ mm^3 WHO stage 4 irrespective of CD4 count
HIV/TB coinfection ARV-naive individuals	Presence of active TB disease, irrespective of CD4 cell count	Presence of active TB disease and CD4 ≤350 cells/mm^3 ART Initiation can be delayed if CD4 ≥200 cells/mm^3
HIV/HBV coinfection ARV-naive individuals	Individuals who require treatment for their HBV infection*, irrespective of CD4 cell count	No specific recommendation

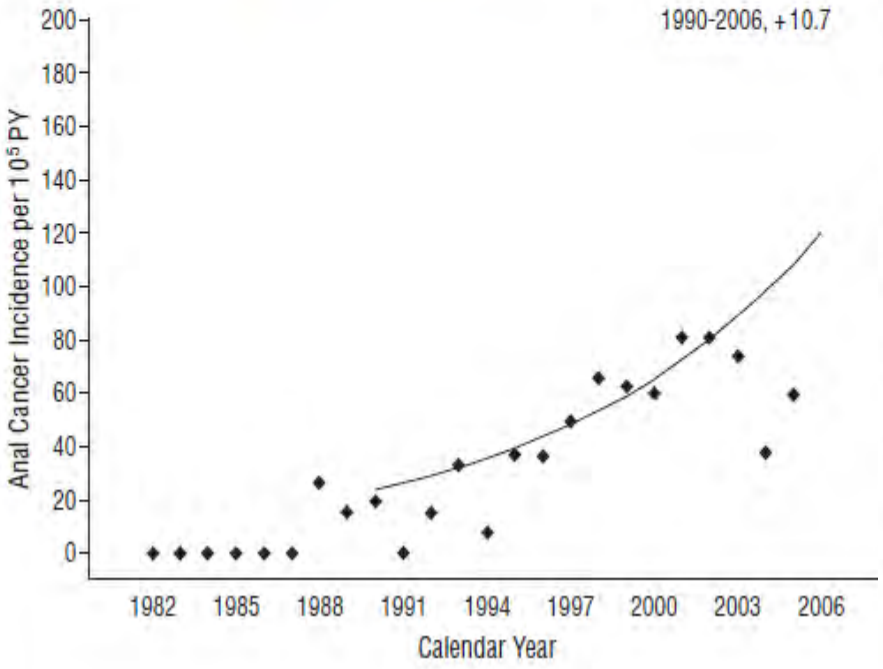


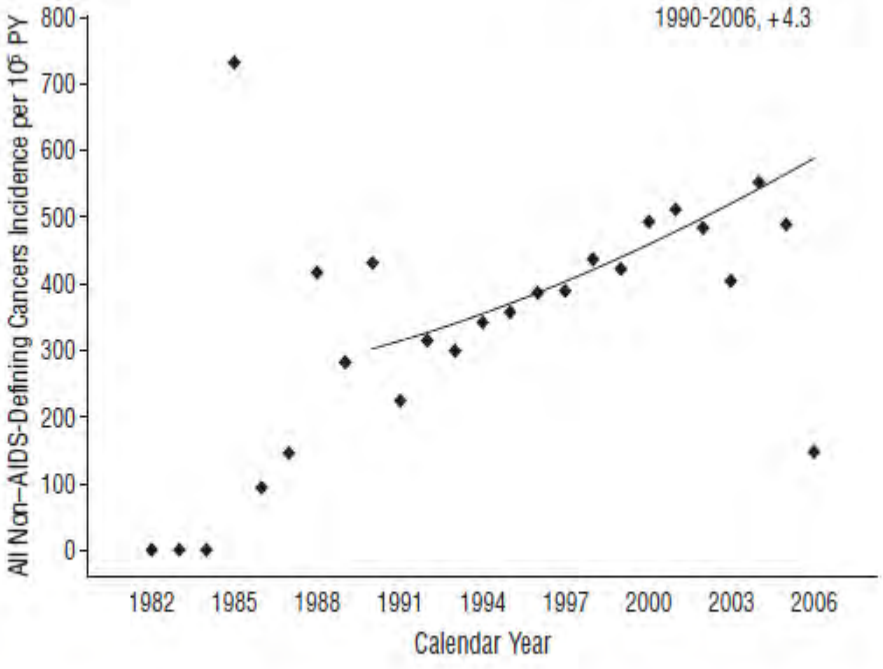
Second Generation HAART Era: 2006-2011

2010: increasing Non-AIDS cancers with prolonged survival

Conclusion: Among people who survived for several years or more after an AIDS diagnosis, we observed high risks of AIDS-defining cancers and increasing incidence of anal cancer and Hodgkin lymphoma.

Arch Intern Med. 2010;170(15):1337-1345

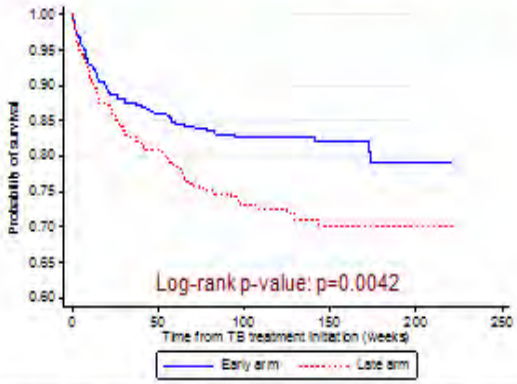




Second Generation HAART Era: 2006-2011

2010: Early ART during TB treatment increases survival and IRIS

Kaplan-Meier survival curves



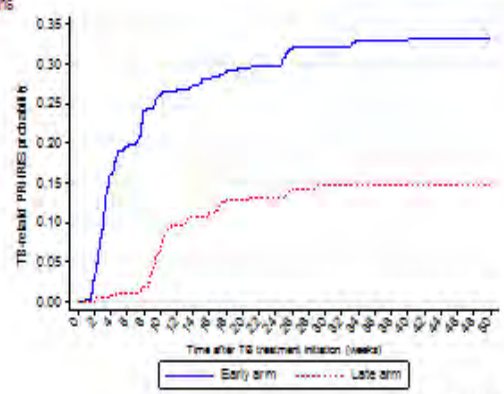
Survival probability (95% CI)	Early arm	Late arm	Log-rank *p*-value
Week 50	86.1 (81.8 – 89.4)	80.7 (76.0 – 84.6)	0.07
Week 100	82.6 (78.0 – 86.4)	73.0 (67.7 – 77.6)	0.006
Week150	82.0 (77.2 – 85.9)	70.2 (64.5 – 75.2)	0.002

ANRS 1295/12160 - CIPRA KH001/10425

IRIS significantly more frequent in the early arm

	N	PR/IRIS	Follow-up time*	Incidence** (95% CI)	*p*
Early arm	332	110	2 728.5	4.03 (3.34 – 4.86)	<0.0001
Late arm	329	48	3 333.5	1.44 (1.09 – 1.91)	

* expressed in person-months
** per 100 person-months

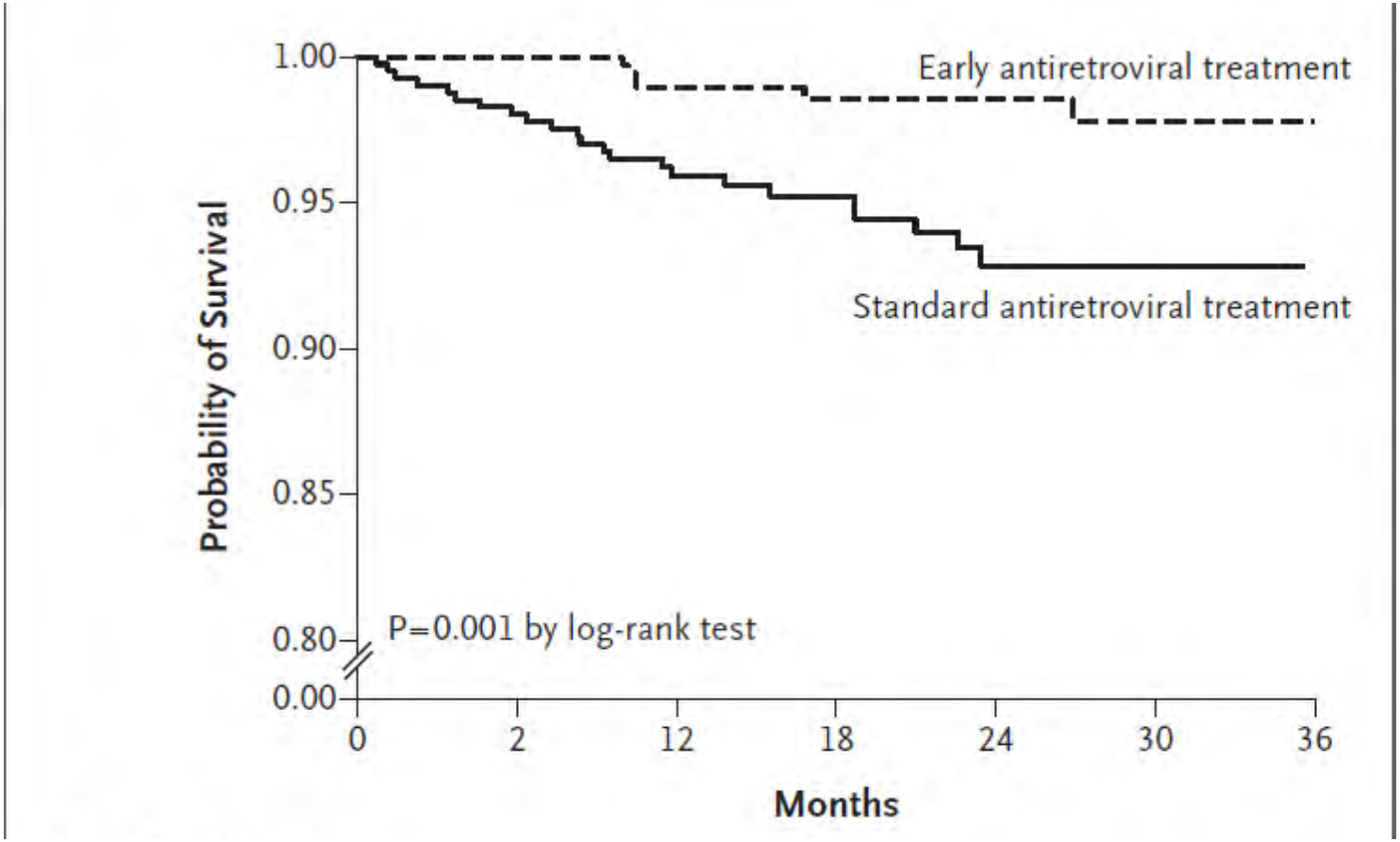


ANRS 1295/12160 - CIPRA KH001/10425 study

CAMELIA Study: Blanc, 18th IAC 2010, Abstract THLBB106.

Second Generation HAART Era: 2006-2011

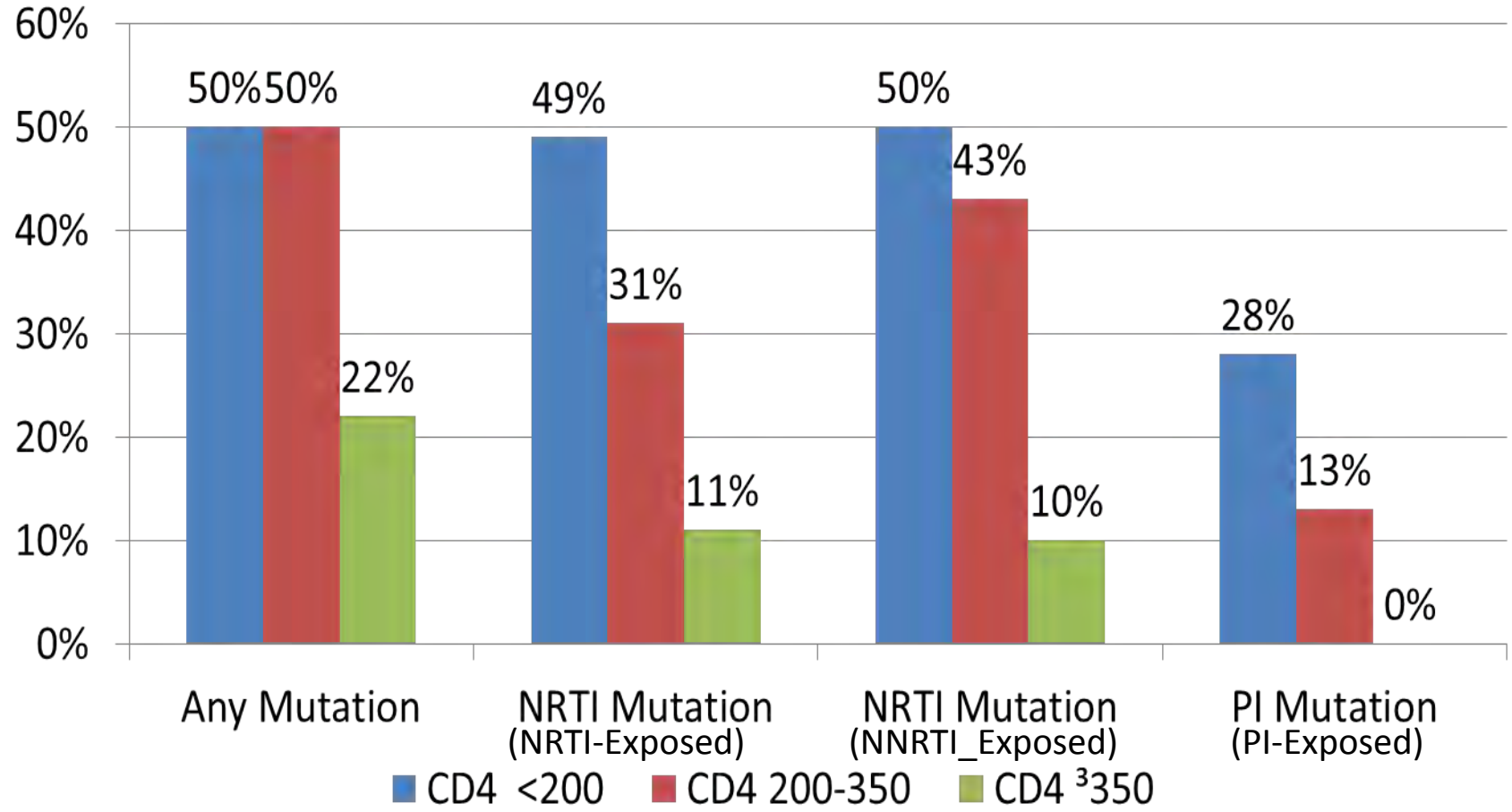
2010: Improved survival with earlier initiation even in resource limited settings



Severe NEJM 2010 363:257-265

Second Generation HAART Era: 2006-2011

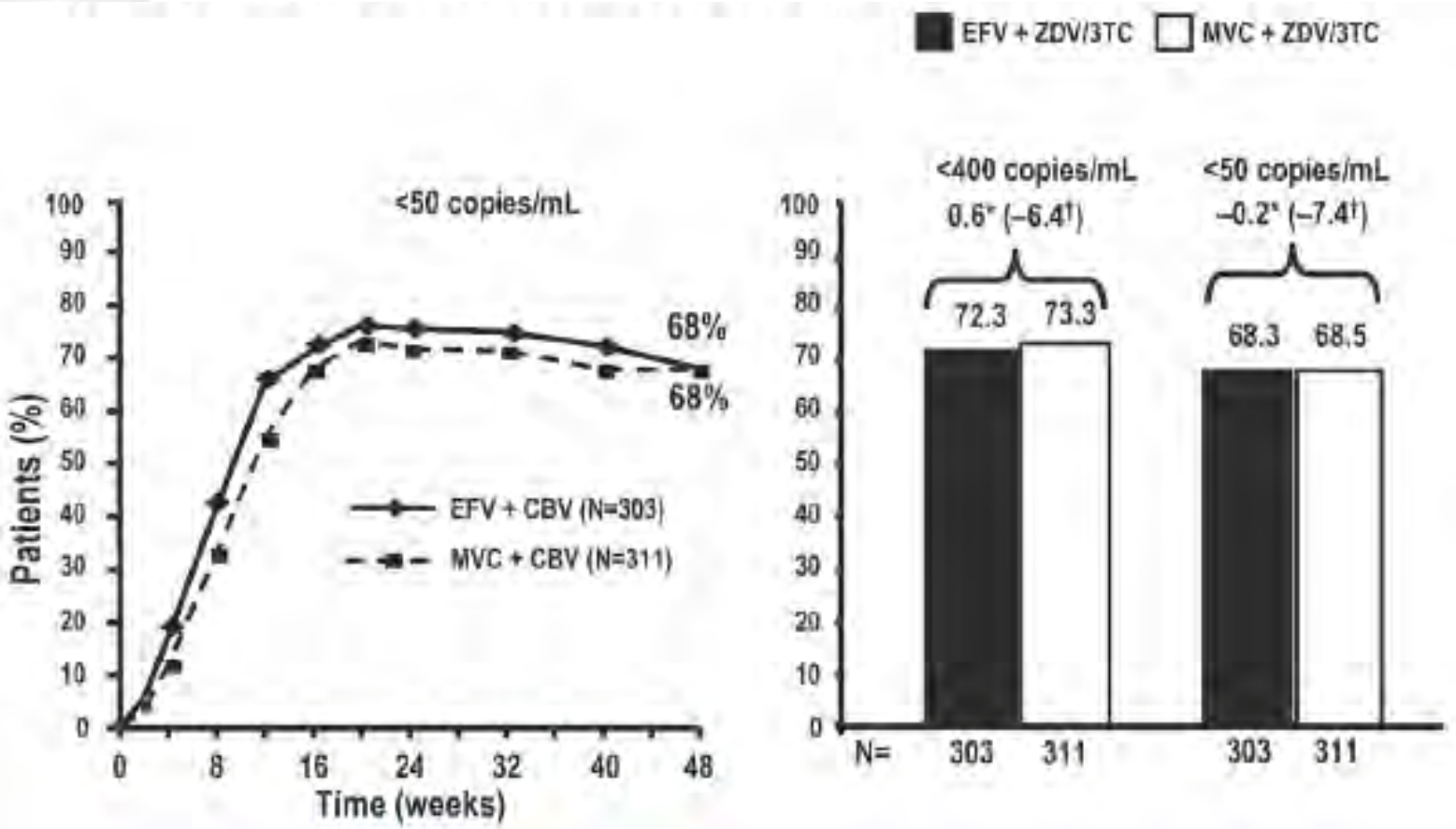
2010: Lower rate of resistance when ART started early



Uy, JAIDS 2009 51:450. Lodwick ArchIntMed 2010;170:410

Second Generation HAART Era: 2006-2011

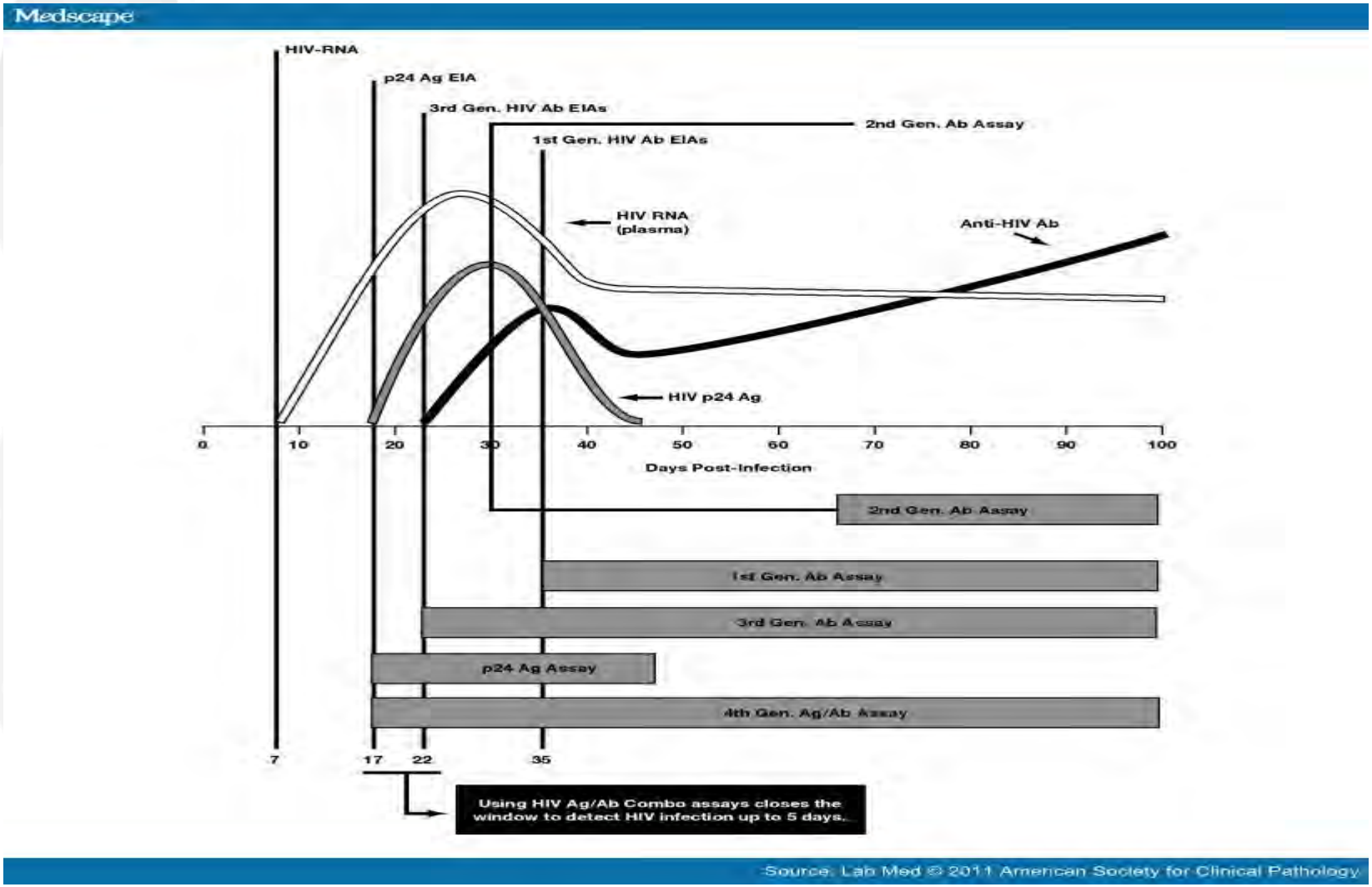
2010: CCR5 enhanced trofile for maraviroc use



Maraviroc versus Efavirenz in ARV-Naive Subjects • JID 2010:201 (15 March) • 803

Second Generation HAART Era: 2006-2011

2010: 4th Gen Ab/Ag test allows earlier HIV diagnosis



Second Generation HAART Era: 2006-2011

2010: INSTI intensification will not eradicate HIV

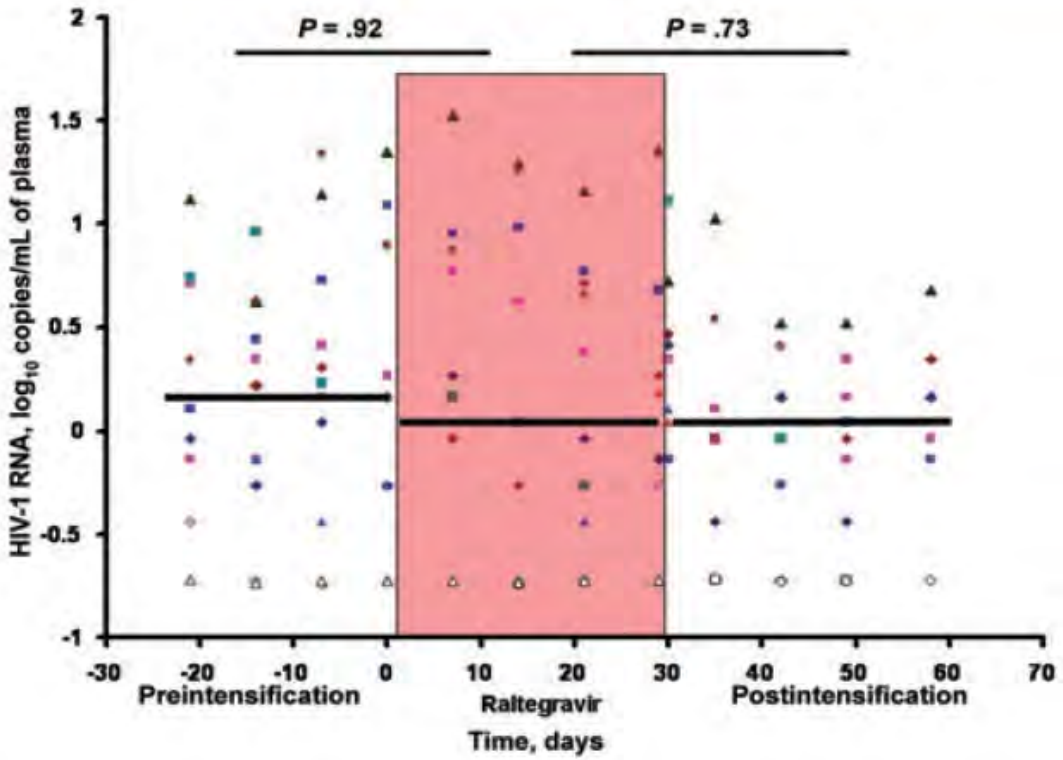


Figure 2. Human immunodeficiency virus type 1 (HIV-1) RNA levels for all time points for all 9 evaluable participants. Each set of colored symbols represents HIV-1 RNA values obtained for the indicated patient during

McMahon D, CID 2010, 50 (6): 912-919

Second Generation HAART Era: 2006-2011

2010: PrEP Reduces MSM HIV Acquisition

The NEW ENGLAND JOURNAL of MEDICINE

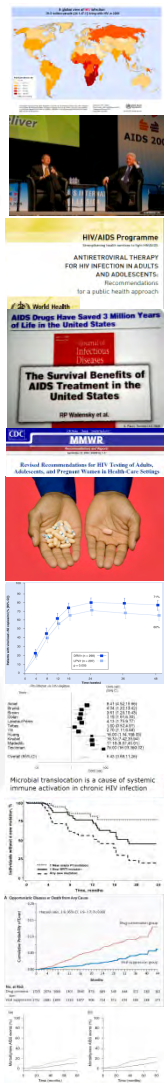
ESTABLISHED IN 1812 DECEMBER 30, 2010 VOL. 363 NO. 27

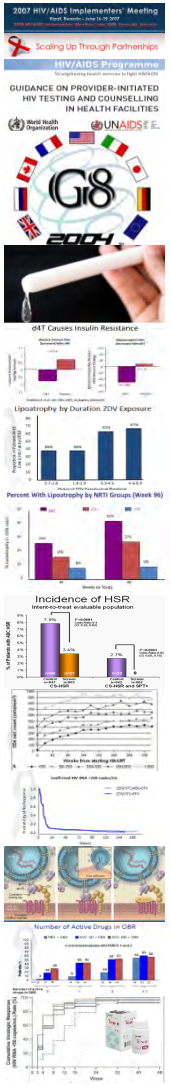
Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

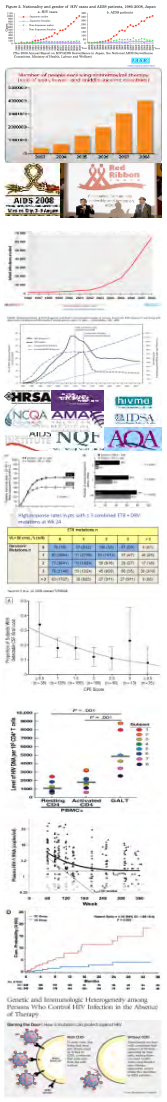
iPrEX study shows TDF-FTC reduces HIV infection rate by 44%

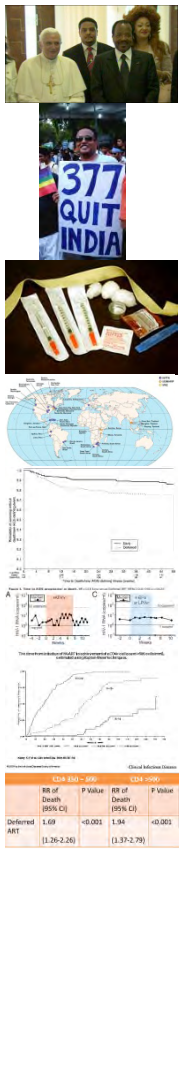
Second Generation HAART Era: 2006-2011

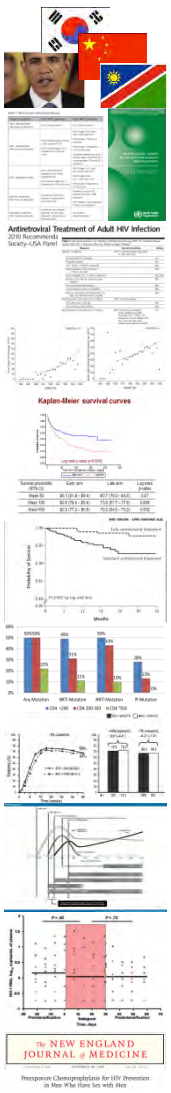
2006 2007 2008 2009 2010 2011











Second Generation HAART Era: 2006-2011

2011: cART Prevents Heterosexual HIV Transmission

HPTN 052

A Randomized Trial to Evaluate the Effectiveness of Antiretroviral Therapy Plus HIV Primary Care versus HIV Primary Care Alone to Prevent the Sexual Transmission of HIV-1 in Serodiscordant Couples

cART leads to 96% reduced risk of transmission to uninfected partners

Second Generation HAART Era: 2006-2011

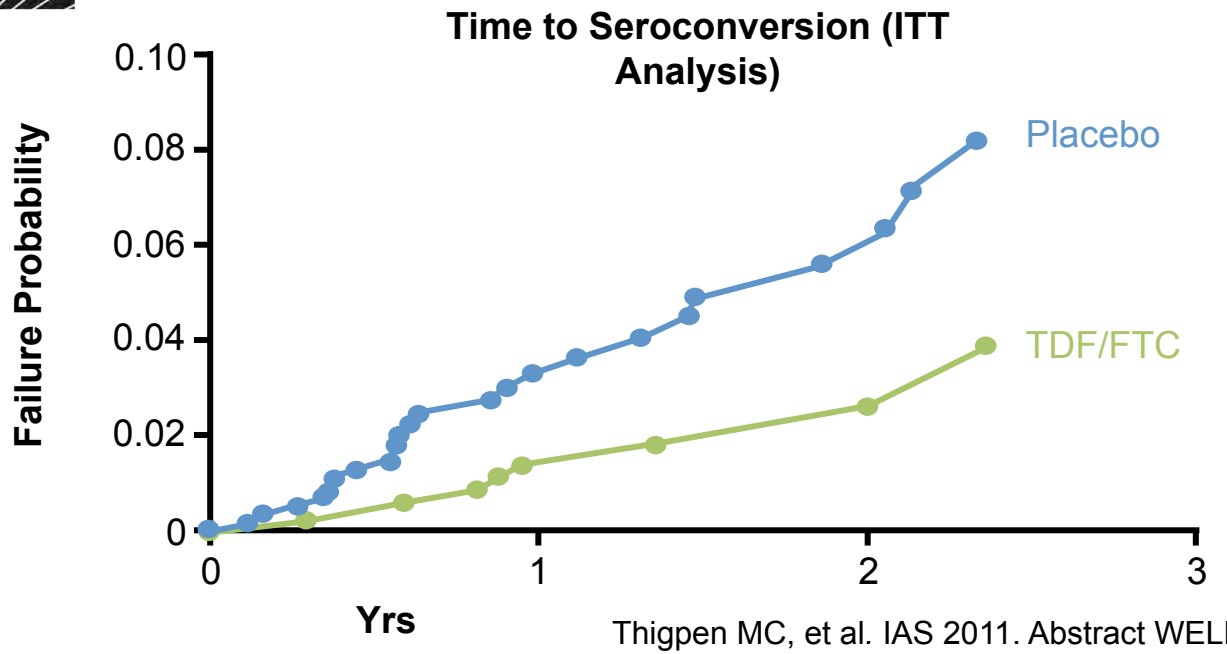
2011: PrEP Prevents Heterosexual HIV Transmission and Acquisition

UNIVERSITY OF WASHINGTON
INTERNATIONAL CLINICAL RESEARCH CENTER
PARTNERS PrEP STUDY

HIV MEDICATIONS HIGHLY EFFECTIVE AS PROPHYLAXIS AGAINST HIV INFECTION

CDC

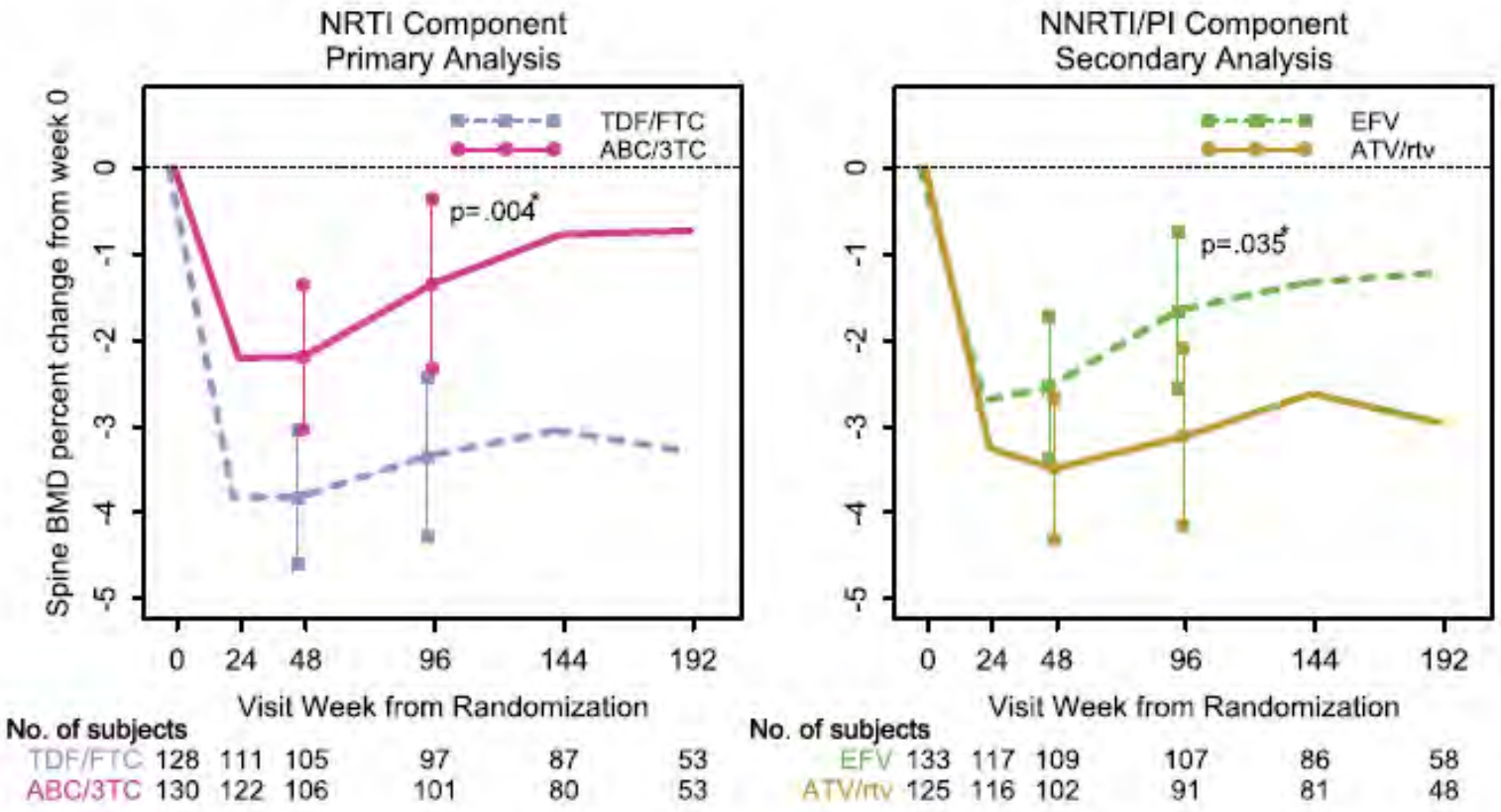
TDF-2: TDF-FTC reduces HIV infection rate by 78% on treatment



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

Second Generation HAART Era: 2006-2011

2011: Bone density change differs among ARVs



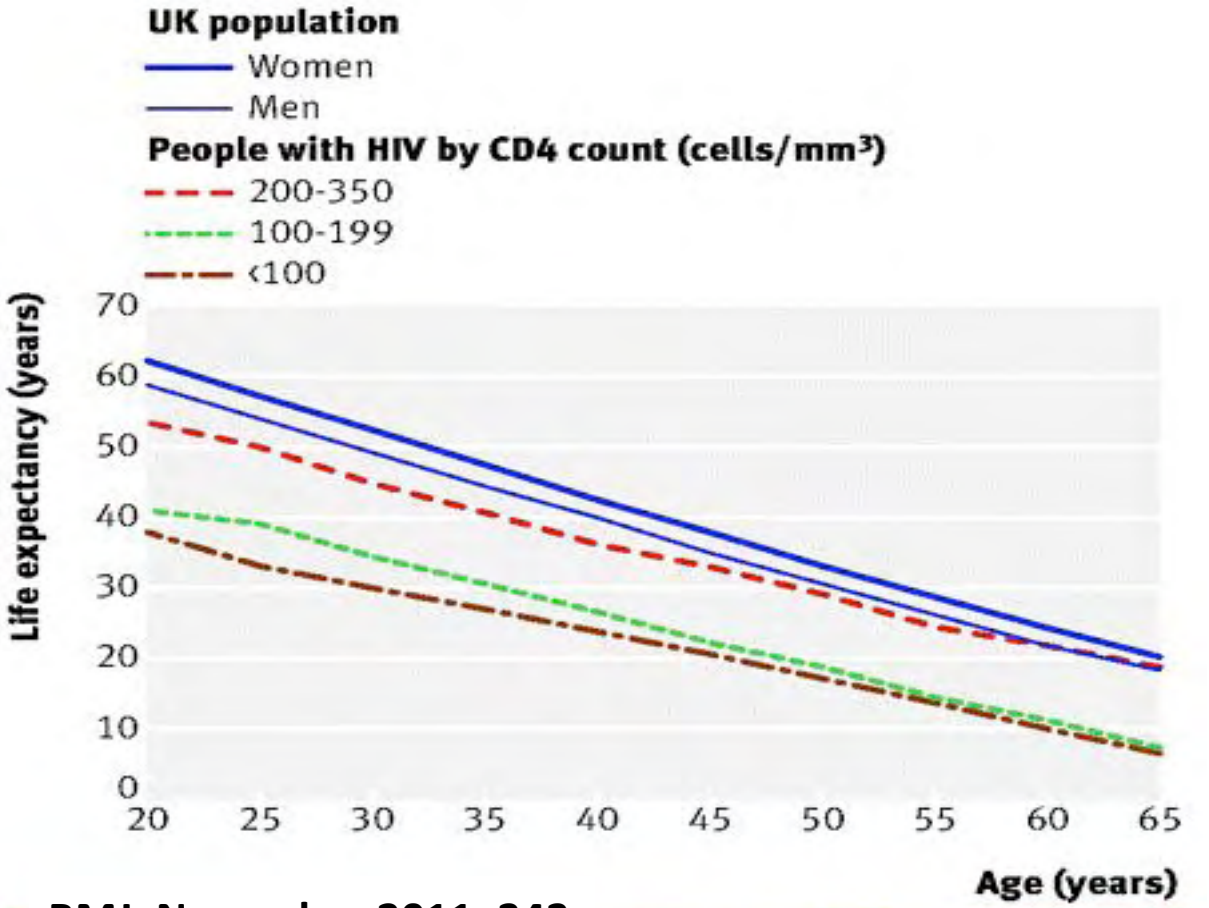
* - two-sample t-test

No significant interaction of NRTI and NNRTI/PI components (p=.63)

McComsey, J Inf Dis 2011; 203:1791.

Second Generation HAART Era: 2006-2011

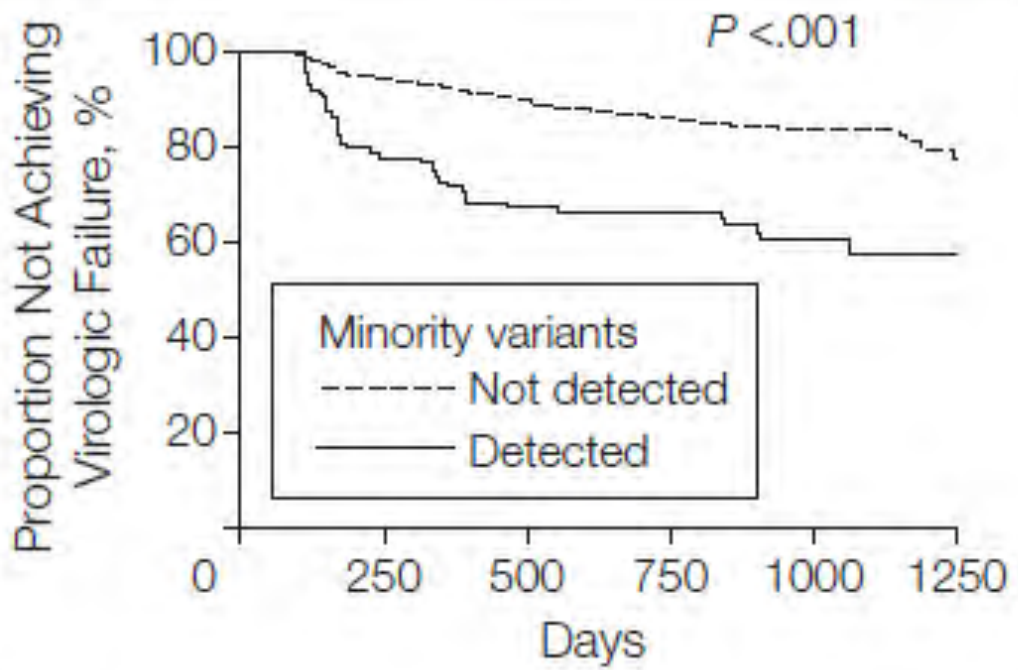
2011: Older aged patients do better when HAART initiated at higher CD4



BMJ, November 2011, 343

Second Generation HAART Era: 2006-2011

2011: Minority Resistance Variants (MV) Increase risk of initial failure



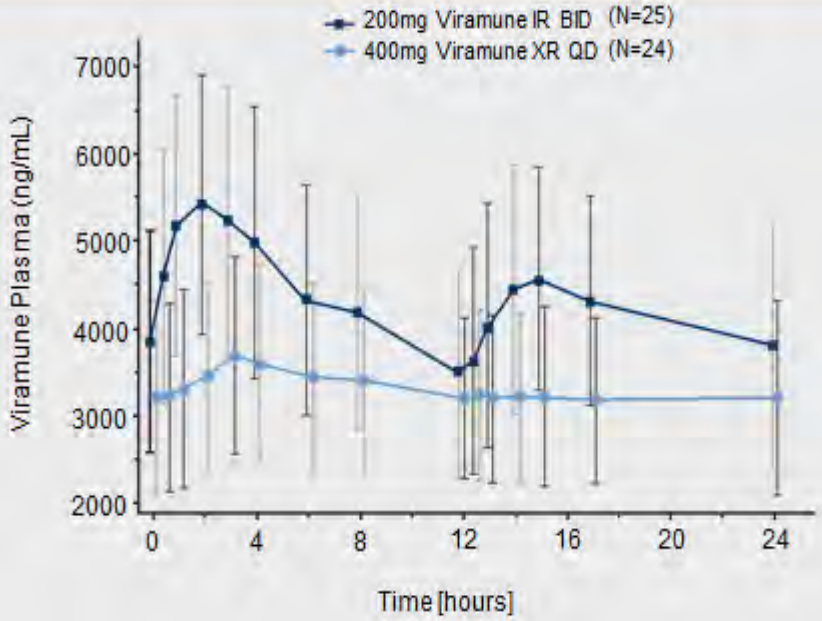
No. at risk						
Minority variants						
Not detected	691	620	455	398	344	46
Detected	117	86	60	53	37	7

Li, JAMA 2011; 305:1327.

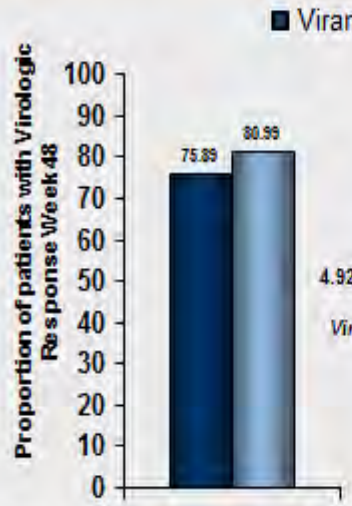
Second Generation HAART Era: 2006-2011

2011: NNRTI NVP-extended release

VERXVE: PK Sub-study at Day 28: Results



VERXVE: Sustained Virologic Response at Week 48 (VL <50 copies/mL, FAS)



Viramune IR: 75.89% (384/506)
Viramune XR: 80.99% (409/505)

Adjusted difference
4.92% in favour of Viramune XR, with 95% CI of (−0.11, 9.96)

Viramune XR shows non-inferiority to Viramune IR within pre-specified margin of −10%

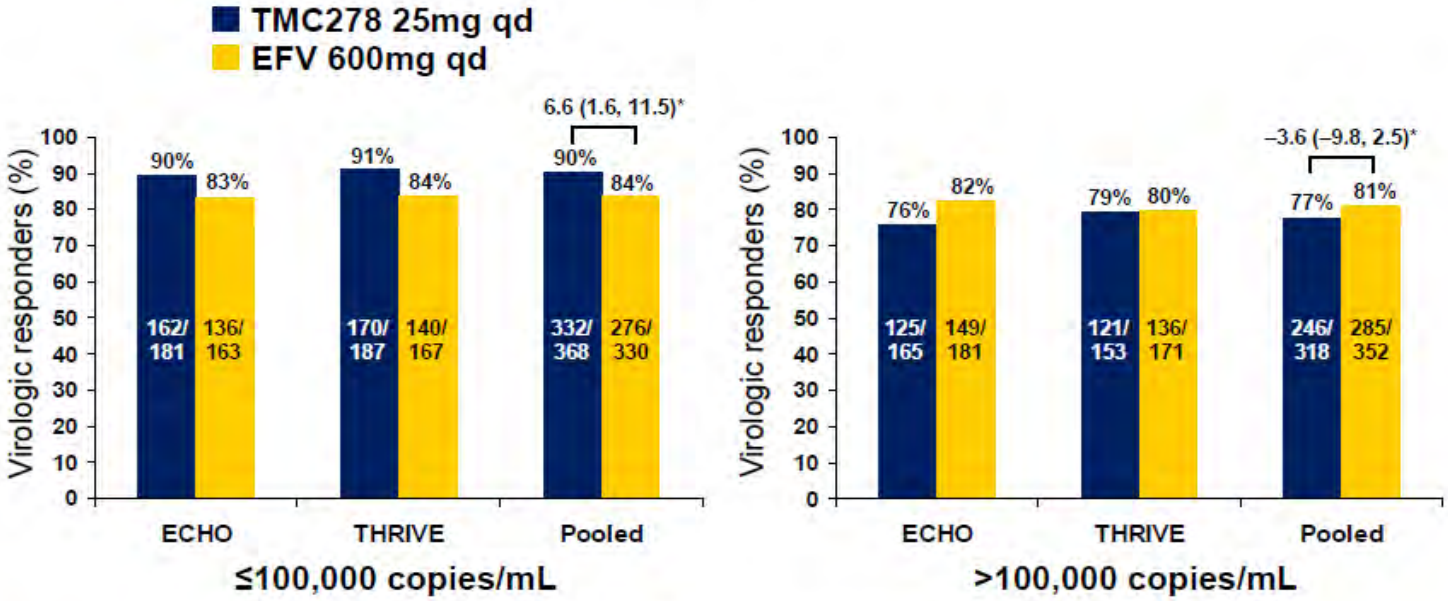
Virologic response was independent of age, gender, race or geographic region

FAS = Full analysis set

Second Generation HAART Era: 2006-2011

2011: 5th NNRTI: Rilpivirine receives selective approval

ECHO and THRIVE: VL <50 copies/mL by baseline VL (ITT-TLOVR)



- NRTI background had no effect on virologic response
- No differences between treatment groups in virologic response by gender, region or race

*Difference in response rates (95% CI)

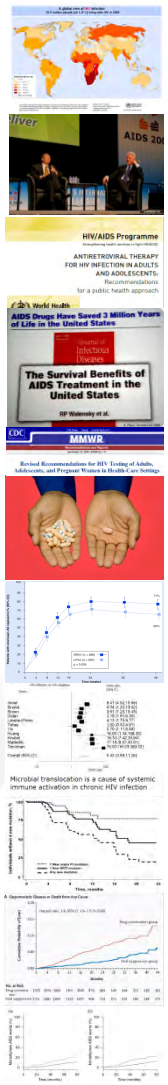
Cohen C, et al. XVIIIth IAC 2010; Abstract THLBB206

Second Generation HAART Era: 2006-2011

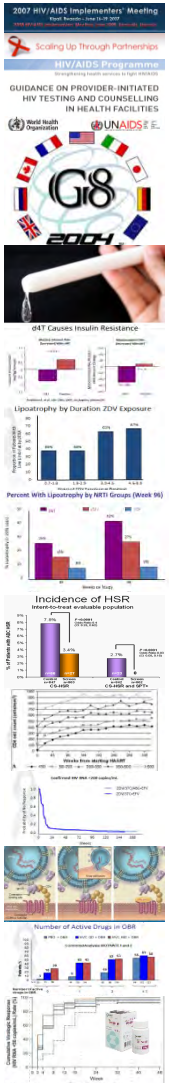
2011: 2nd 2-class Single Tablet Regimen: Complera

Second Generation HAART Era: 2006-2011

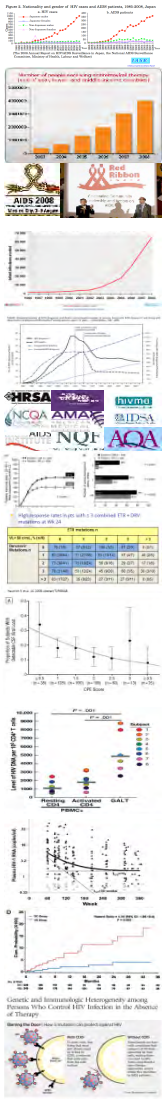
2006



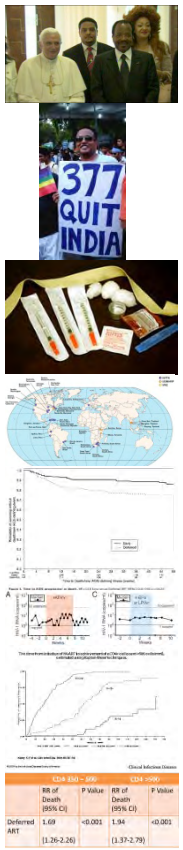
2007



2008



2009



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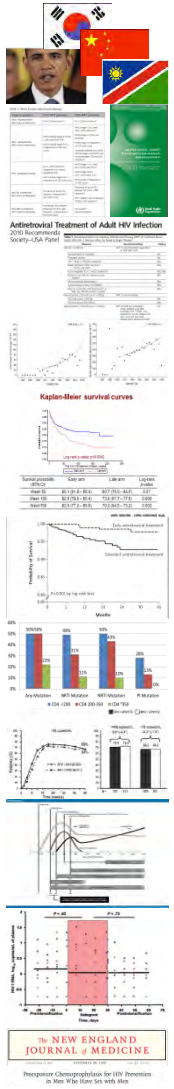

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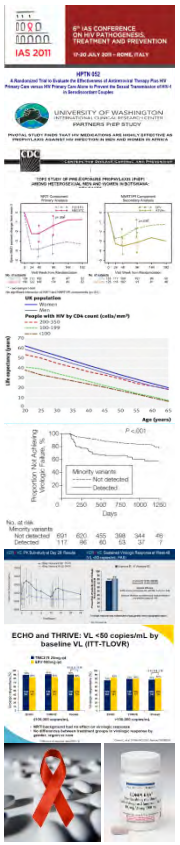

Evolution of HIV treatment paradigms