Foro Publico en Prevención de VIH,
Lima, 2-4 Noviembre 2011

# Una nueva era:
# El tratamiento como Prevención

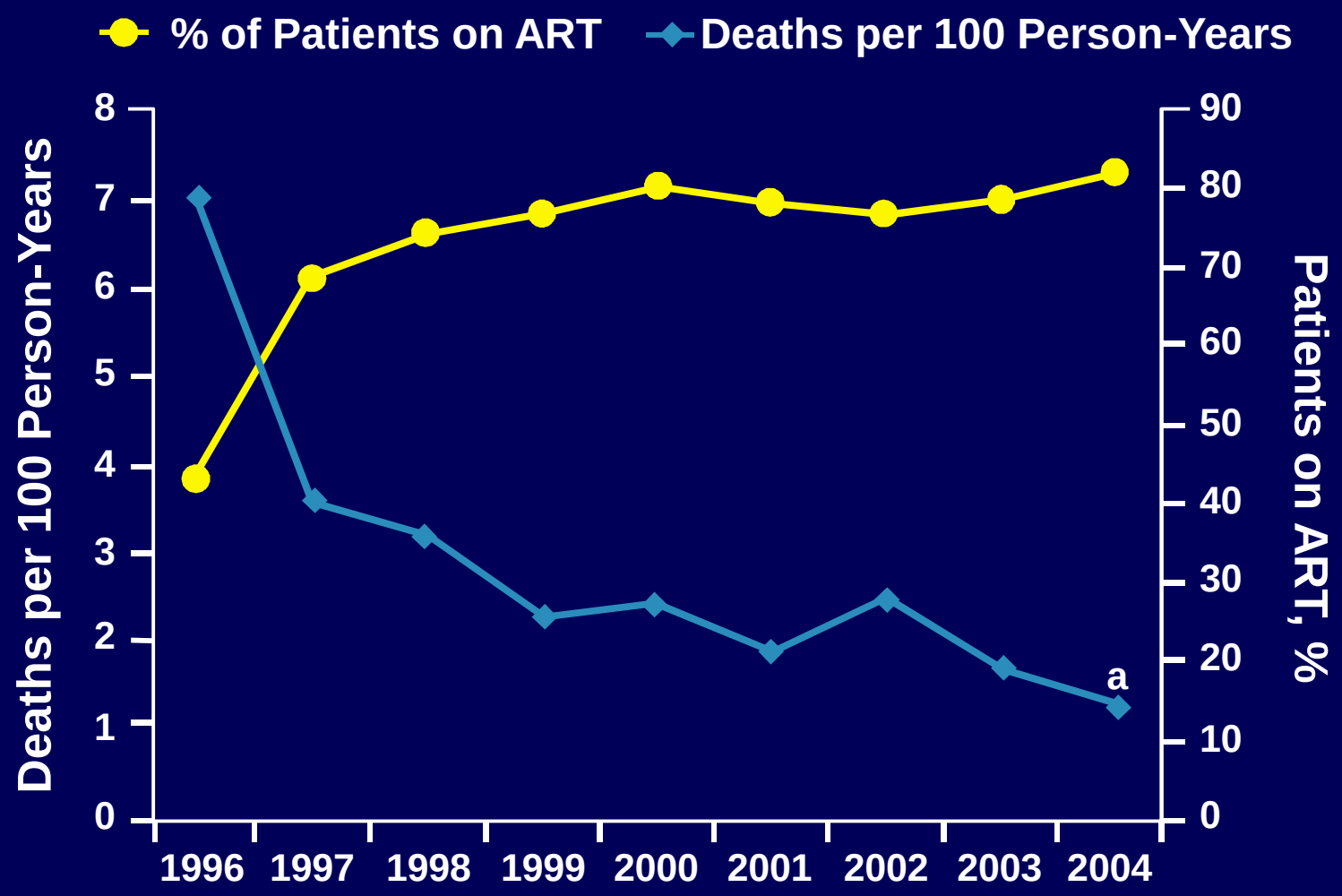
*Pedro Cahn*

HOSPITAL FERNANDEZ HF

International AIDS Society
Stronger Together

FUNDACION HUESPED
en acción contra el sida

# Effect of ART on Mortality Over Time




[a]*P* =.008 for trend.

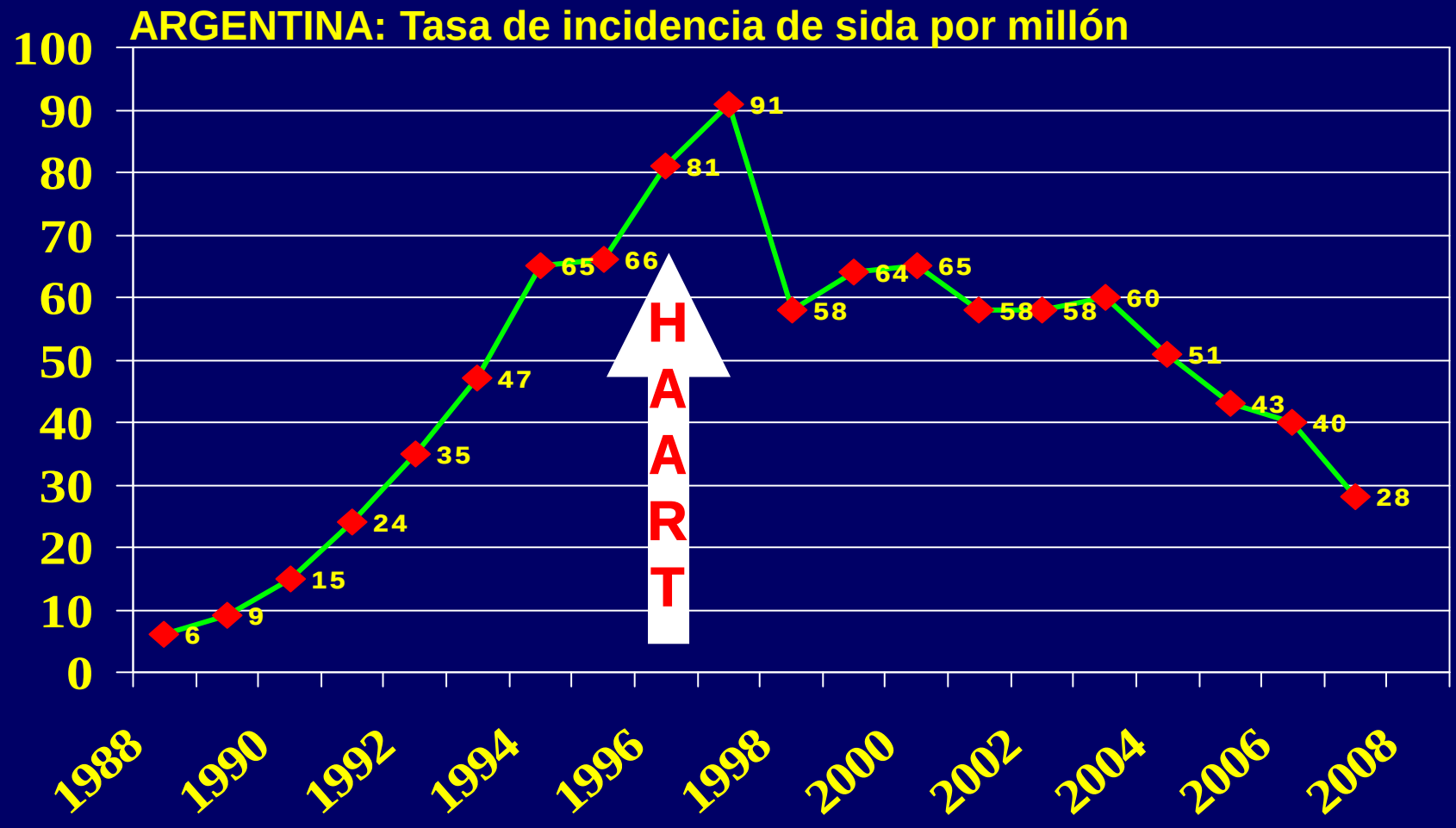
Palella FJ et al. *J Acquir Immune Defic Syndr*. 2006;43(1):27-34.

# AIDS Drugs Have Saved 3 Million Years of Life in the United States

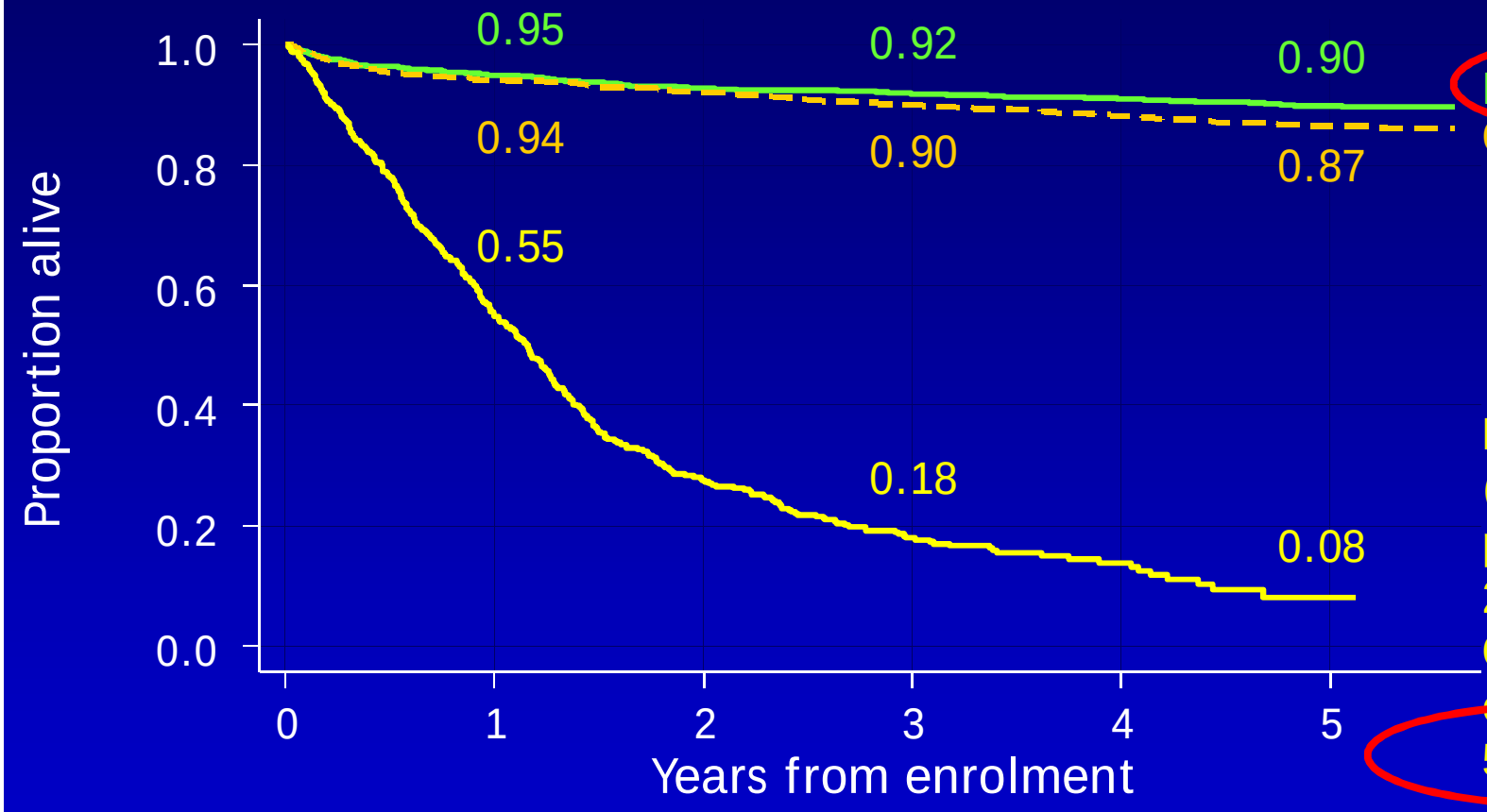
July 1, 2006
Volume 194
The Journal of Infectious Diseases

## The Survival Benefits of AIDS Treatment in the United States

RP Walensky et al.


ARGENTINA: Tasa de incidencia de sida por millón
100
90
80
70
60
50
40
30
20
10
0
1988
1990
1992
1994
1996
1998
2000
2002
2004
2006
2008
6
9
15
24
35
47
65
66
81
91
58
64
65
58
58
60
51
43
40
28
HAART

# Survival




164 events
LCM: 2.2/100 PY
CDM: 2.9/100 PY
218 events

Entebbe Cohort (Uganda): pre-ART 1996-2000, median CD4 75 at enrolment: 57.7/100 PY

**About 26 fold reduction in mortality**

*IAS 2009, Capetown*

# CIPRAHT001: Randomized Trial of When to Start ART in Haiti Clinical Endpoints and Additional Data

## Clinical Endpoints

| | Early (<200 CD4) | Standard (200-350 CD4) | Hazards Ratio (p value) |
|---|---|---|---|
| **Death** | 6 | 23 | 4.0 (.0011 ) |
| **Incident Tuberculosis** | 18 | 36 | 2.0 (.0125 ) |

- Infectious causes of death
  - Early: 1 (gastroenteritis)
  - Standard: 17 (7 gastroenteritis, 5 TB, 4 pneumonia, 1 cholangitis/sepsis)
- More toxicity from ART (especially anemia) and intensive need for lab f/u for those who deferred
- Investigators currently working with Ministry of Health to change start ART guidelines to 350 cells/mm3

*Severe P, et al. 49th ICAAC; San Francisco, CA; Sept. 12-15, 2009; Abst. H-1230c.*

# HAART Associated With Decrease in TB Prevalence in South African Township

- Cross-sectional TB and HIV prevalence surveys in community near Cape Town before (2005: n = 762) and after (2008: n = 1251) large-scale HAART rollout
  - HIV-infected population receiving HAART increased from 12% to 23% from 2005-2008
- Decrease in TB prevalence temporally associated with rollout of ART program
  - Driven by decrease in previously undiagnosed TB cases among HIV-infected individuals

| TB Status According to HIV Status, % | 2005 Study | 2008 Study | *P* Value |
|---|---|---|---|
| **HIV-infected pts** | **9.2 (n = 174)** | **3.6 (n = 306)** | **.02** |
| • Known TB infection | 4.0 | 2.3 | .24 |
| • Previously undiagnosed TB | 5.2 | 1.3 | .01 |
| **HIV-uninfected pts** | **1.2 (n = 584)** | **1.1 (n = 899)** | **.98** |
| • Known TB infection | 0.7 | 0.7 | .97 |
| • Previously undiagnosed TB | 0.5 | 0.4 | .84 |

*Middlekoop K, et al. IAS 2009. Abstract WELBB105.*

# La mortalidad en pts. HIV+ es similar a la población general con CD4 > 500 por 5-7 años

- Overall mortality in HIV-infected patients 7-fold higher than general population
- After 6th year of follow-up, mortality among patients with CD4+ cell counts ≥ 500 cells/mm$^3$ comparable to that of the general population

| Truncation for Duration of Follow-up, Yrs | Median Time Spent With CD4+ Cell Count ≥ 500 cells/mm$^3$ After Truncated Duration of Follow-up, Yrs (IQR) | Deaths, n | SMR (95% CI) |
|---|---|---|---|
| 0 (n = 1208) | 4.5 (2.1-7.0) | 37 | 2.5 (1.8-3.5) |
| 1 (n = 1156) | 4.2 (2.1-6.4) | 29 | 2.1 (1.4-3.1) |
| 2 (n = 1083) | 4.0 (2.1-5.6) | 26 | 2.2 (1.4-3.2) |
| 3 (n = 1031) | 3.5 (1.8-4.8) | 22 | 2.1 (1.3-3.2) |
| 4 (n = 967) | 3.0 (1.5-3.8) | 18 | 2.1 (1.3-3.4) |
| 5 (n = 864) | 2.4 (1.4-3.0) | 12 | 1.9 (1.0-3.2) |
| 6 (n = 763) | 1.6 (1.0-2.2) | 2 | 0.5 (0.1-1.6) |
| 7 (n = 610) | 0.9 (0.5-1.3) | 1 | 0.5 (0.0-2.6) |

Lewden C, et al. J Acquir Immune Defic Syndr. 2007;46:72-77.

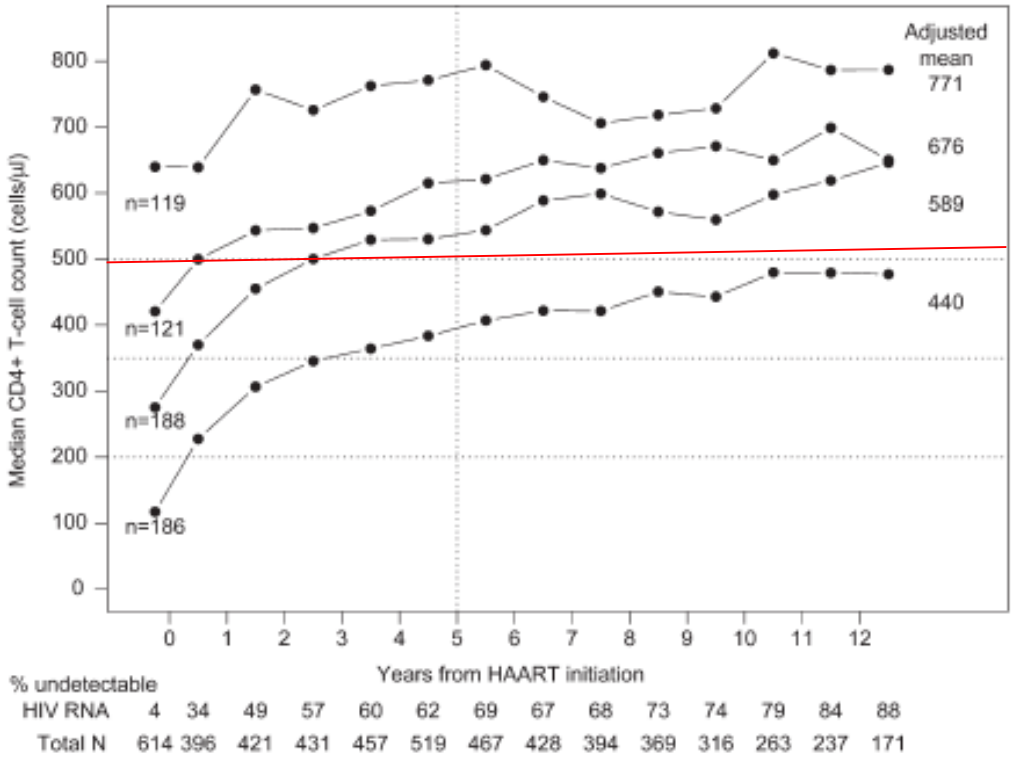



**FIGURE 2.** Trajectories of median CD4⁺ count in the 12 years after initiation of HAART, according to CD4⁺ count levels before HAART initiation among 614 HIV-positive men who contributed data after 5 years from HAART initiation. The dots are median CD4⁺ count in each time interval from HAART initiation. Horizontal dotted lines are reference lines plotted at the CD4⁺ count of 200, 350, 500 cells per microliter. The middle vertical dotted line shows the cutoff at 5 years after HAART initiation. The numbers below the labels of the *x* axis are the percentages with undetectable HIV-1 RNA and total number of men in each time interval. The numbers at the end of each line are adjusted mean CD4⁺ count at 5–12 years after HAART initiation for each pre-HAART CD4⁺ count category from the main effects multivariate model.

# Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

October 14, 2011

*Panel's Recommendations:*

- *Antiretroviral therapy (ART) should be initiated in all patients with a history of an AIDS-defining illness or with a CD4 count <350 cells/mm$^3$ (AI).*
- *ART is also recommended for patients with CD4 counts between 350 and 500 cells/mm$^3$ (A/B$^*$-II).*
- *ART should be initiated, regardless of CD4 count, in patients with the following conditions: HIV-associated nephropathy (HIVAN) (AII) and hepatitis B virus (HBV) coinfection when treatment of HBV is indicated (AIII).*
- *A combination antiretroviral (ARV) drug regimen is also recommended for pregnant women who do not meet criteria for treatment with the goal to prevent perinatal transmission (AI).*
- *For patients with CD4 counts >500 cells/mm$^3$, Panel members are evenly divided: 50% favor starting ART at this stage of HIV disease (B); 50% view initiating therapy at this stage as optional (C) (B/C-III).*
- *Patients initiating ART should be willing and able to commit to lifelong treatment and should understand the benefits and risks of therapy and the importance of adherence (AIII). Patients may choose to postpone therapy, and providers, on a case-by-case basis, may elect to defer therapy based on clinical and/or psychosocial factors.*

*Rating of Recommendations: A = Strong; B = Moderate; C = Optional*
*Rating of Evidence: I = data from randomized controlled trials; II = data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = expert opinion*

$^*$ *Panel members are divided on the strength of this recommendation: 55% voted for strong recommendation (A) and 45% voted for moderate recommendation (B).*

# IAS-USA Guidelines 2010: When to Start

| Asymptomatic Infection | Recommendation |
|---|---|
| ▪ CD4+ cell count < 500 cells/mm³ | ▪ Start HAART |
| ▪ CD4+ cell count > 500 cells/mm³ | ▪ Should be considered* |
| **Clinical Conditions Favoring Initiation of Therapy Regardless of CD4+ Cell Count** | |
| ▪ Symptomatic HIV disease<br>▪ Acute opportunistic infection<br>▪ Pregnant women<br>▪ Older than 60 yrs of age<br>▪ HIV-1 RNA > 100,000 copies/mL<br>▪ Rapid decline in CD4+ cell count (> 100 cells/mm³/yr)<br>▪ Active HBV or HCV infection<br>▪ Active or high risk for CV disease<br>▪ Symptomatic primary HIV infection<br>▪ HIVAN<br>▪ Serodiscordant couples | |

*Unless patient is elite controller or has stable CD4+ cell count and low HIV-1 RNA in absence of antiretroviral therapy.

Thompson MA, et al. JAMA. 2010;304;321-333.

# IAS-USA Guidelines 2010: When to Start



# Antiretroviral Treatment of Adult HIV Infection

## 2010 Recommendations of the International AIDS Society–USA Panel

Melanie A. Thompson, MD
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Julio S. G. Montaner, MD
Giuliano Rizzardini, MD
Amalio Telenti, MD, PhD
José M. Gatell, MD, PhD
Huldrych F. Günthard, MD
Scott M. Hammer, MD
Martin S. Hirsch, MD
Donna M. Jacobsen, BS
Peter Reiss, MD, PhD
Douglas D. Richman, MD
Paul A. Volberding, MD
Patrick Yeni, MD
Robert T. Schooley, MD

**Context** Recent data regarding the consequences of untreated human immunodeficiency virus (HIV) infection and the expansion of treatment choices for antiretroviral-naive and antiretroviral-experienced patients warrant an update of the International AIDS Society–USA guidelines for the use of antiretroviral therapy in adults with HIV infection.

**Objectives** To review new data in HIV medicine and provide updated recommendations for management of HIV-infected adults, using antiretroviral drugs and laboratory monitoring tools available in the international, developed-world setting. This report provides guidelines for when to initiate antiretroviral therapy, selection of appropriate initial regimens, patient monitoring, when to change therapy, and what regimens to use when changing.

**Data Sources and Study Selection** A panel with expertise in HIV research and clinical care reviewed relevant data published or presented at selected scientific conferences since the last panel report through April 2010. Data were identified through a PubMed search, review of scientific conference abstracts, and requests to antiretroviral drug manufacturers for updated clinical trials and adverse event data.

**Data Extraction and Synthesis** New evidence was reviewed by the panel. Recommendations were drafted by section writing committees and reviewed and edited by the entire panel. The quality and strength of the evidence were rated and recommendations were made by full panel consensus.

**Conclusions** Patient readiness for treatment should be confirmed before initiation of antiretroviral treatment. Therapy is recommended for asymptomatic patients with a CD4 cell count ≤500/μL, for all symptomatic patients, and those with specific conditions and comorbidities. Therapy should be considered for asymptomatic patients with CD4 cell count >500/μL. Components of the initial and subsequent regimens must be individualized, particularly in the context of concurrent conditions. Patients receiving antiretroviral treatment should be monitored regularly; treatment failure should be detected and managed early, with the goal of therapy, even in heavily pretreated patients, being HIV-1 RNA suppression below commercially available assay detection limits.

JAMA. 2010;304(3):321-334 www.jama.com

ALTHOUGH ERADICATION OF established human immunodeficiency virus (HIV) infection is elusive, successful antiretroviral therapy (ART) is associated with dramatic decreases in AIDS-defining conditions and their associated mortality. Expansion of treatment options and evolving knowledge require revision of guidelines for the initiation and long-term management of ART in adults with HIV infection.

Since the 2008 International AIDS Society–USA ART guidelines,[1] new data have emerged regarding timing of therapy, optimal regimen choices, and monitoring. There are also issues of special relevance to circumstances such as pregnancy, hepatitis virus coinfections, kidney disease, cardiovascular disease, and primary HIV infection. Analyses of clinical trials and epidemiologic cohorts have shed light on the role of ART in mitigating serious non-AIDS events associated with uncontrolled HIV replication. Newer drugs are better understood in terms of efficacy, toxicity, and potential uses in HIV management. New data also suggest a role for ART in the prevention of HIV transmission.

CME available online at www.jamaarchivescme.com and questions on p quiz.

## METHODS

The panel was convened in 1995 to develop evidence-based recommendations for ART for HIV-infected adults in developed-world settings.[2] Members are appointed by International AIDS Society–USA according to clinical and research expertise. Current panel members do not participate in pharmaceutical market-

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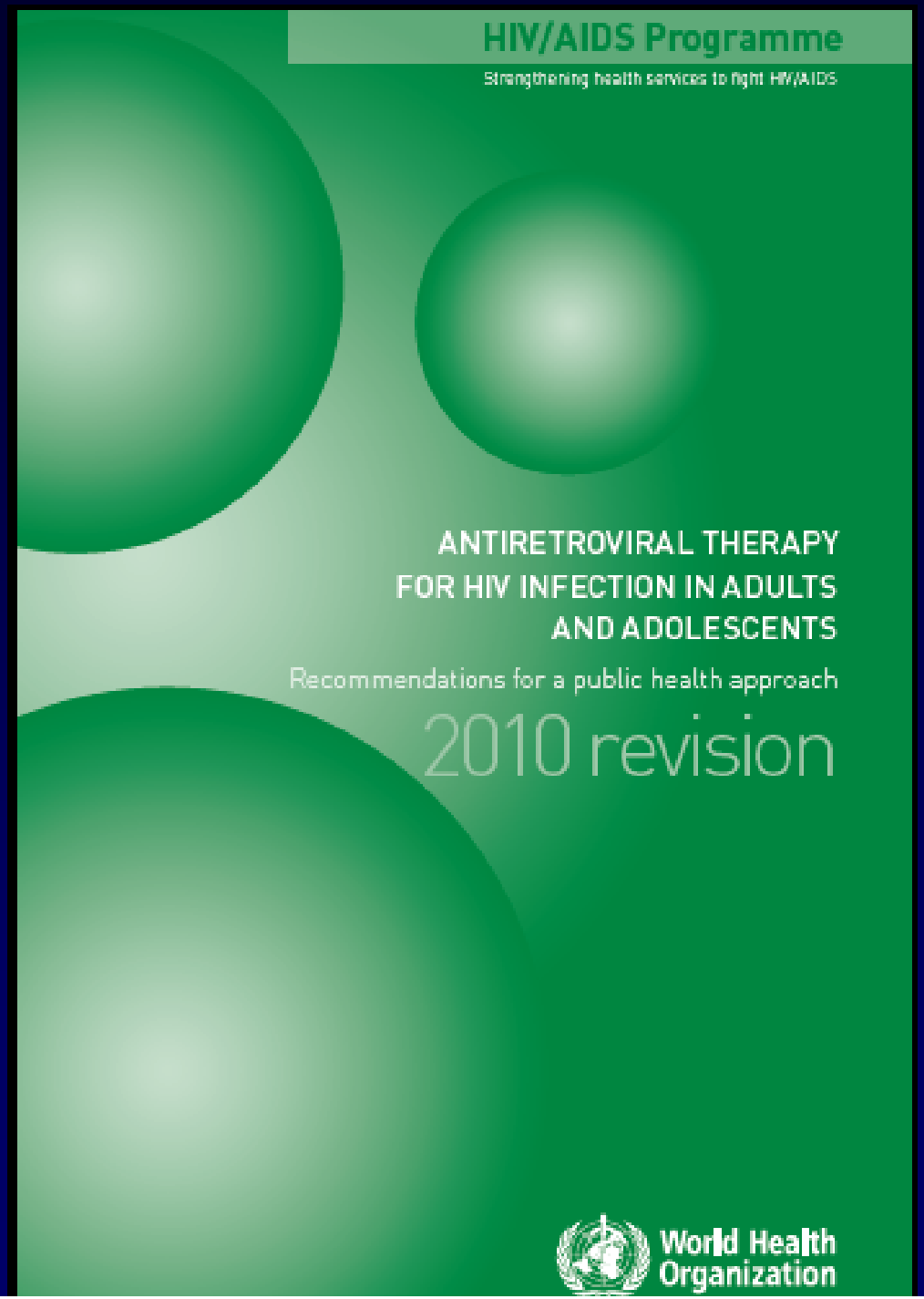

HIV/AIDS Programme
Strengthening health services to fight HIV/AIDS
ANTIRETROVIRAL THERAPY
FOR HIV INFECTION IN ADULTS
AND ADOLESCENTS
Recommendations for a public health approach
2010 revision
World Health
Organization

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<br>WHO clinical stage 3 or 4 irrespective of CD4 cell count | WHO stage 2 or 3 and CD4 ≤200 cells/mm$^3$<br>WHO stage 3 if CD4 not available<br>WHO stage 4 irrespective of CD4 cell count<br>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<br>WHO clinical stage 3 or 4 irrespective of CD4 cell count | WHO stage 1 or 2 and CD4 ≤200 cells/mm$^3$<br>WHO stage 3 and CD4 ≤350 cells/ mm$^3$<br>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$^3$<br>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 |

# When to start

- Start antiretroviral treatment in all patients with HIV who have CD4 count ≤350 cells/$mm^3$ irrespective of clinical symptoms

  **(Strong recommendation, moderate quality of evidence)**

- CD4 testing is required to identify if patients with HIV and WHO clinical stage 1 or 2 disease need to start antiretroviral treatment

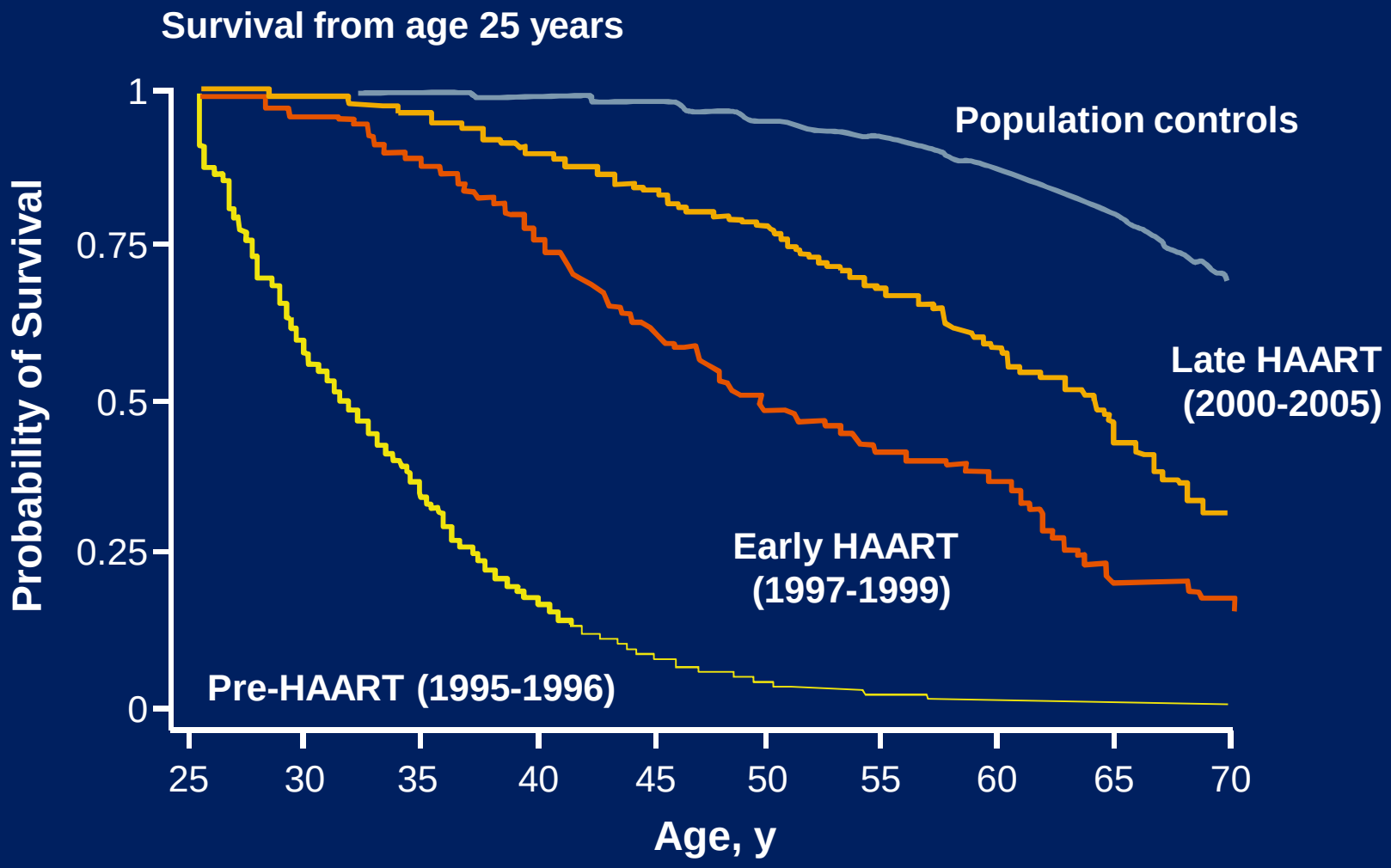
  **(Strong recommendation, low quality of evidence)**

- Start antiretroviral treatment in all patients with HIV and WHO clinical stage 3 or 4 irrespective of CD4 count

  **(Strong recommendation, low quality of evidence)**

*The panel placed high value on avoiding death, disease progression and likely HIV transmission over and above cost and feasibility*

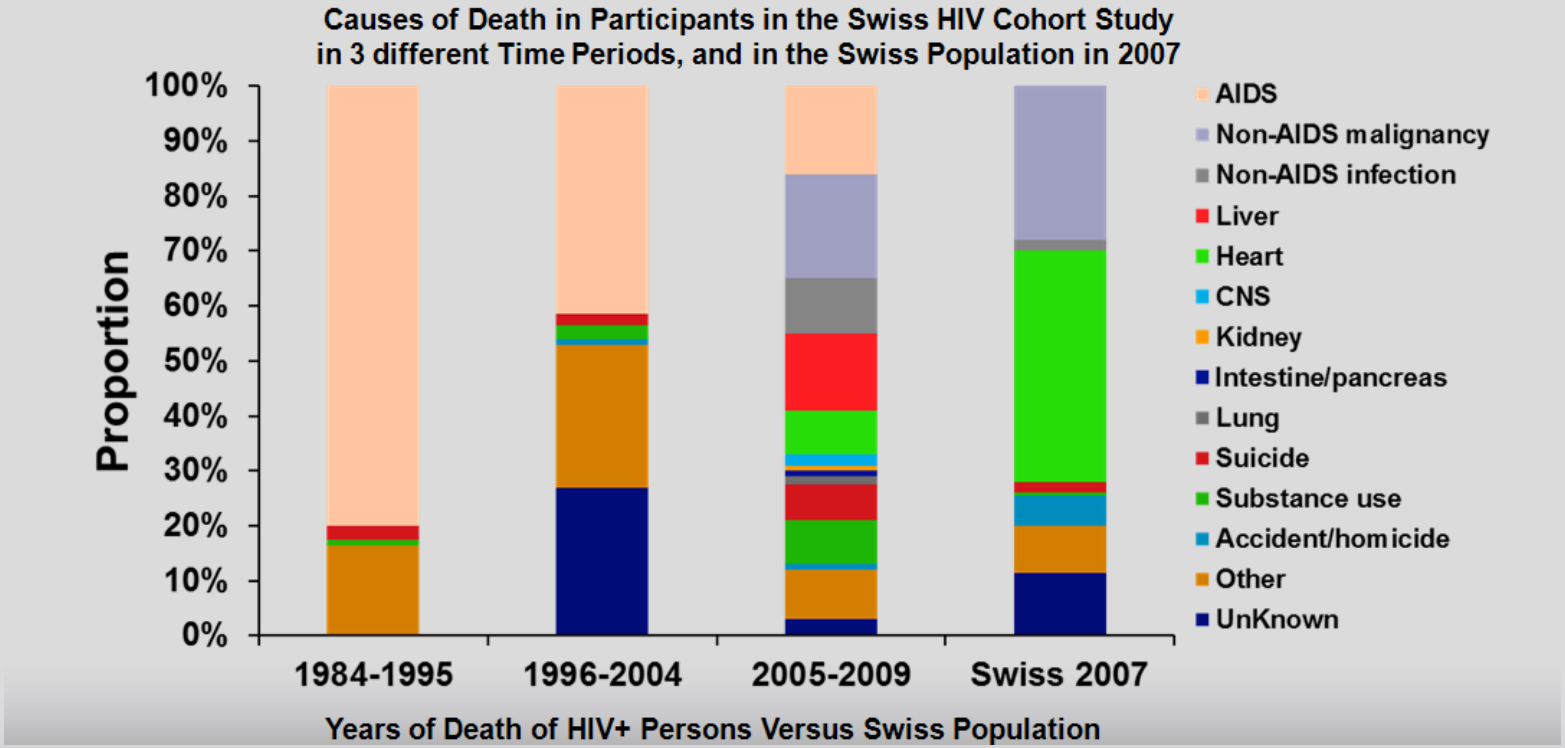
# La expectativa de sobrevida es 10 años menor en la poblacion HIV + respecto a controles HIV -




Adapted from Lohse N, et al. *Ann Intern*

# Causas de Muerte en la Cohorte Suiza (SHCS)

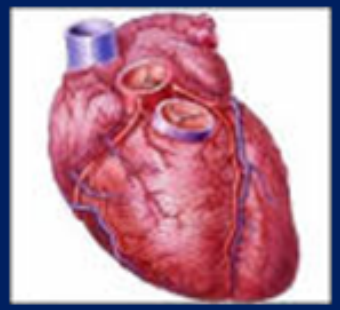
- SHCS is a prospective observational cohort
- Characteristics of participants that died from 2005-2009
- 459 deaths/9,053 participants (5.1%)

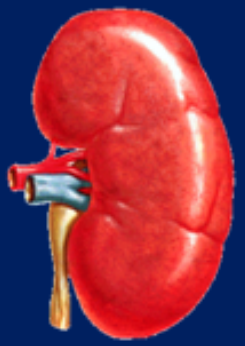


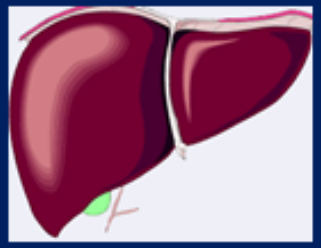

Ruppik M, et al. 18th CROI; Boston, MA; February 27-March 2, 2011. Abst. 789.

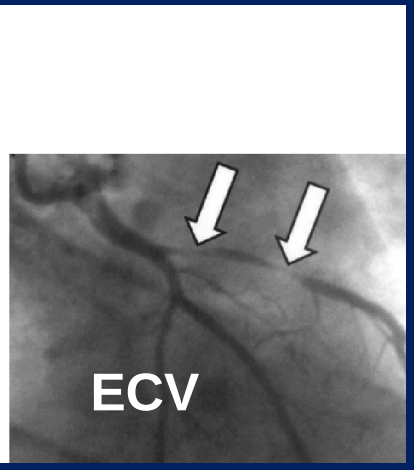
# ACTIVACION INMUNE

**INFLAMACION**

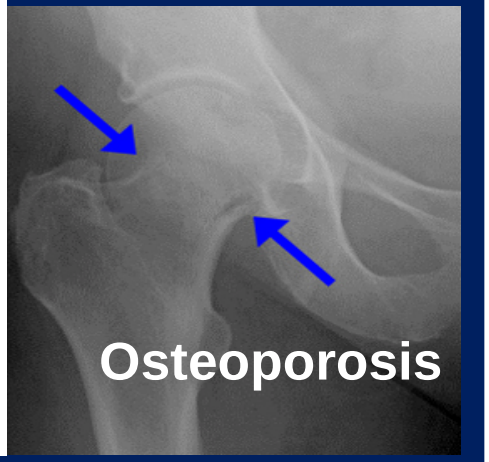


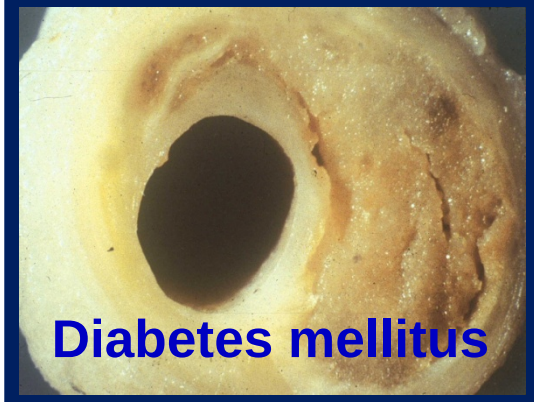





ECV

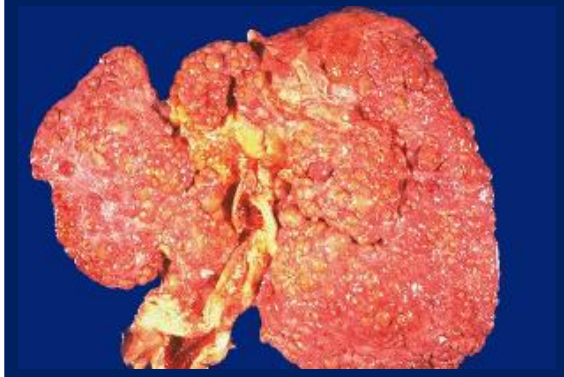

Canceres
“no marcadores”

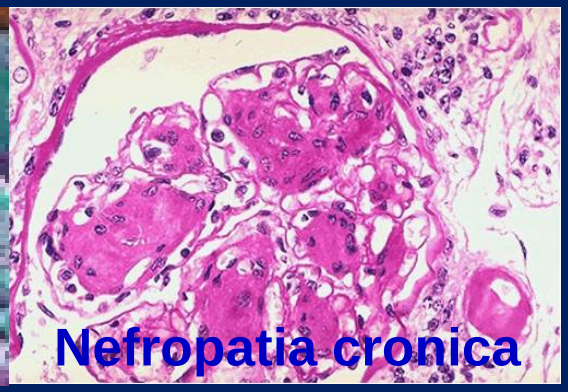

Osteoporosis


Diabetes mellitus


Fragilidad


Depresion
Trastornos Cognitivos


Hepatopatia cronica


Nefropatia cronica

# Prevencion: estrategias

- Estrategias para modificar habitos sexuales
- Condones
- Circuncision
- Microbicidas
- Vacunas

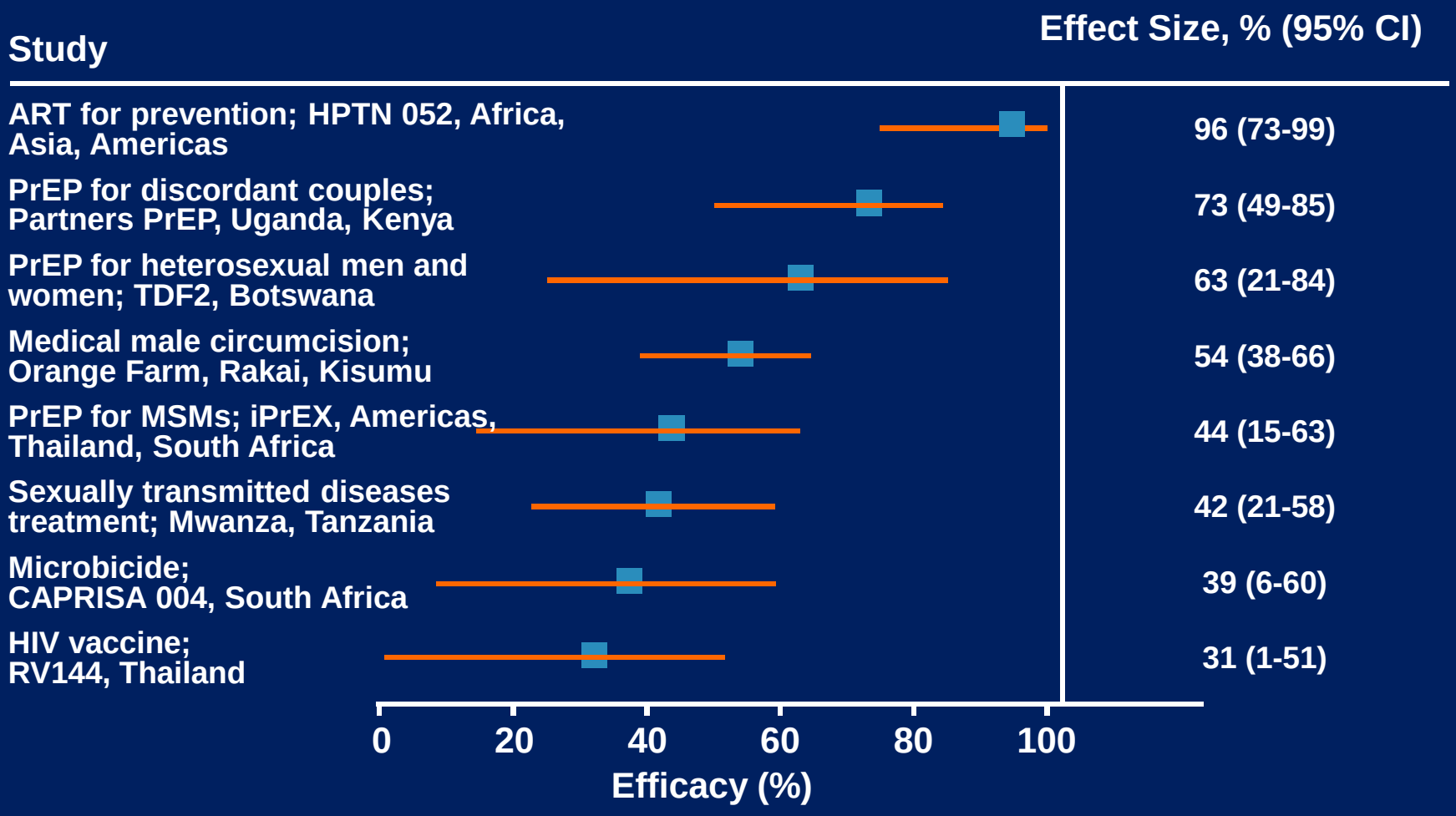
TARV

# Por que ARV para prevencion?

- Modelo animal
  - Multiples drogas han reducido la transmision, tanto como PREP o como PEP)
- Datos en humanos
  - PMTCT
  - PEP ocupacional
- Tolerabilidad de los nuevos ARV
- Disponibilidad de drogas genericas
- Fallo de otras estrategias (vacuna)

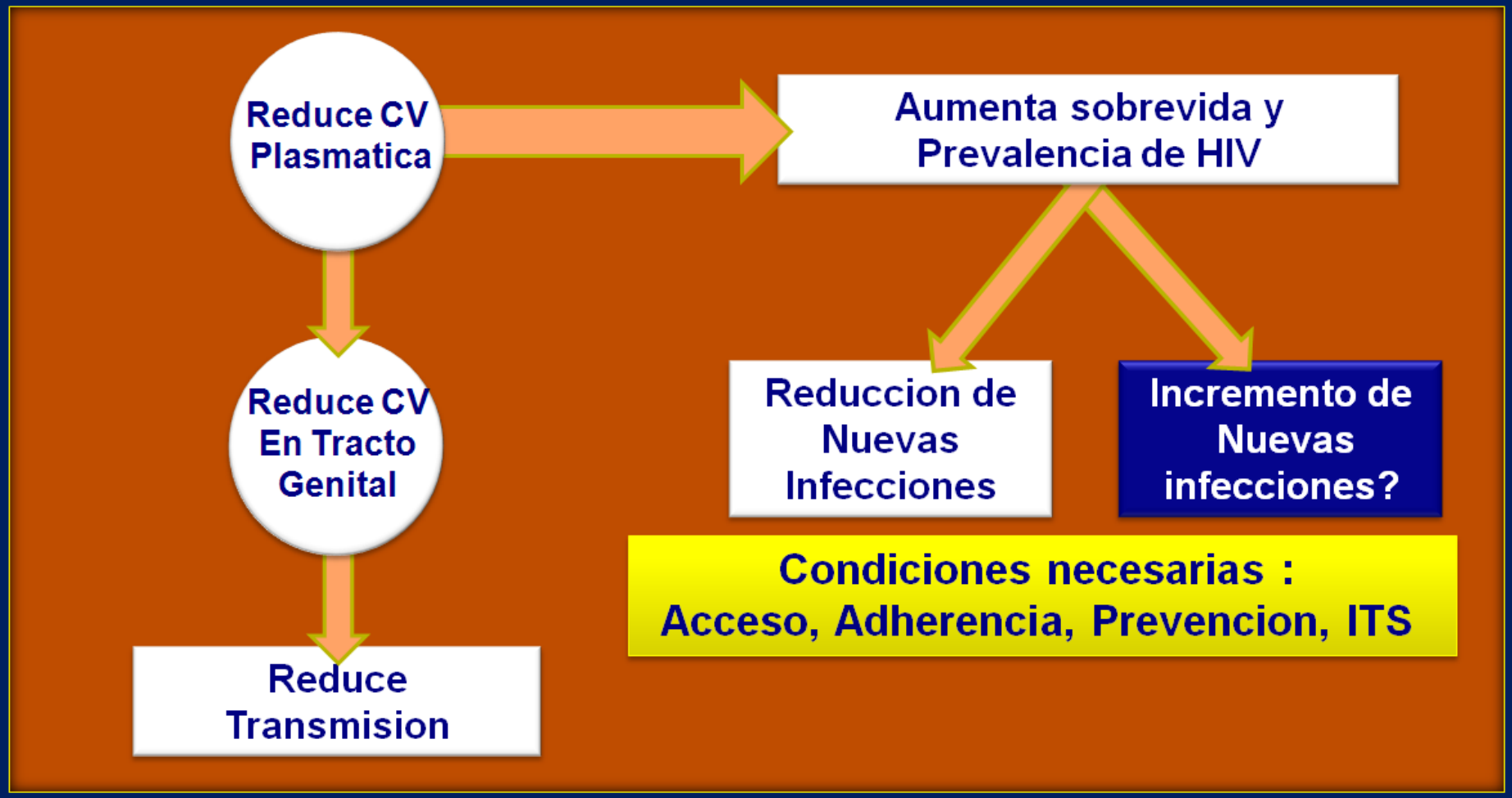
**Connor EM, et al. *N Engl J Med.* 1994;331:1173-1180.**
**Cardo DM, et al. *N Engl J Med.* 1997;337:1485-1490.**
**Grant RM, et al. *Clin Infect Dis.* 2010;50(suppl 3):S96-S101.**
**Venkatesh KK, et al. *Future Virol.* 2010;5:405-415.**

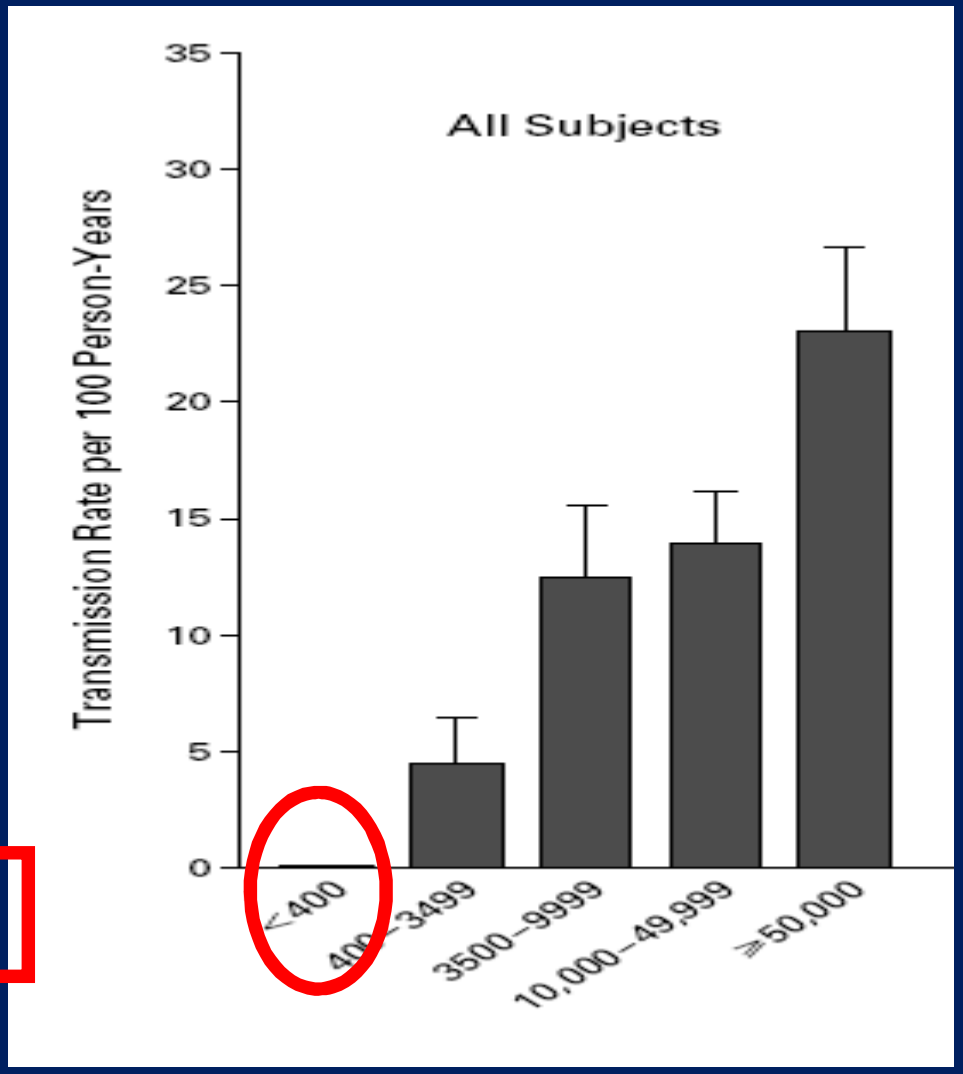
# Eficacia de estrategias de prevencion de ensayos clinicos randomizados




*Abdool Karim SS, et al. Lancet. 2011;*

# ARV: Impacto en la Transmision






**No transmission if VL « undetectable »**

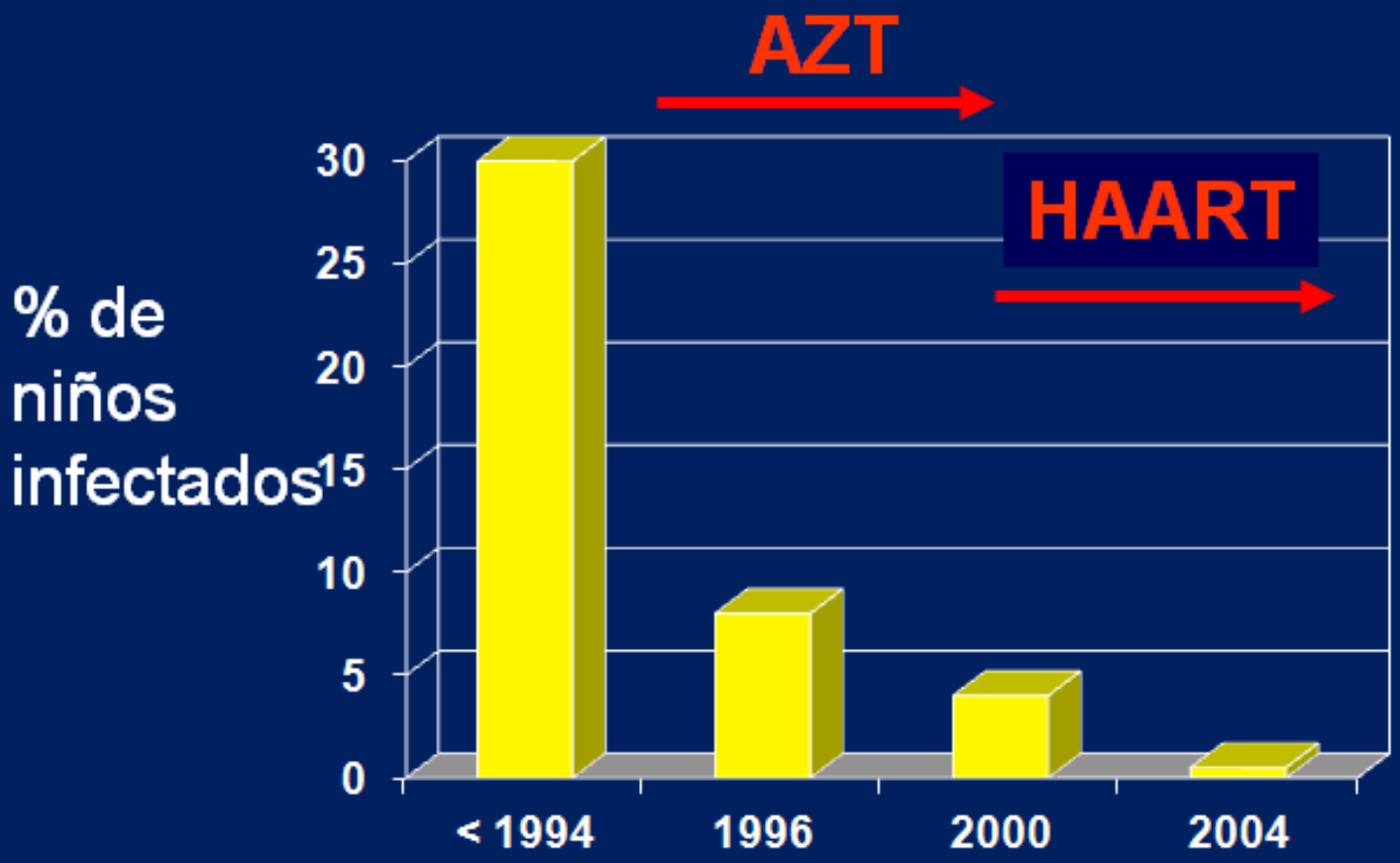
« Rakai » Study: Transmission risk as a function of plasma viral load

*Quinn et al. N Engl J Med 2000*

# Transmision Materno-Fetal

| Maternal HIV-1 RNA Level, % | Infants Infected |
|---|---|
| < 1000 copies/mL (n = 57) | 0 |
| 1000-10,000 copies/mL (n = 193) | 16.6 |
| > 10,000-50,000 copies/mL (n = 183) | 21.3 |
| > 50,000-100,000 copies/mL (n = 54) | 30.9 |
| > 100,000 copies/mL (n = 64) | 40.6 |

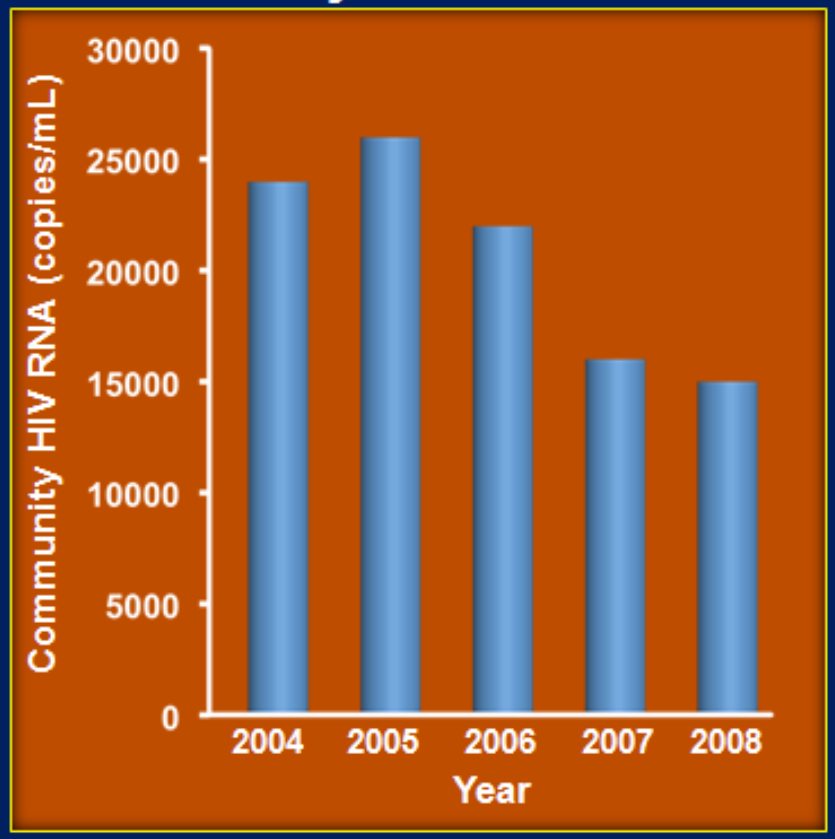
# Transmision Materno-Fetal



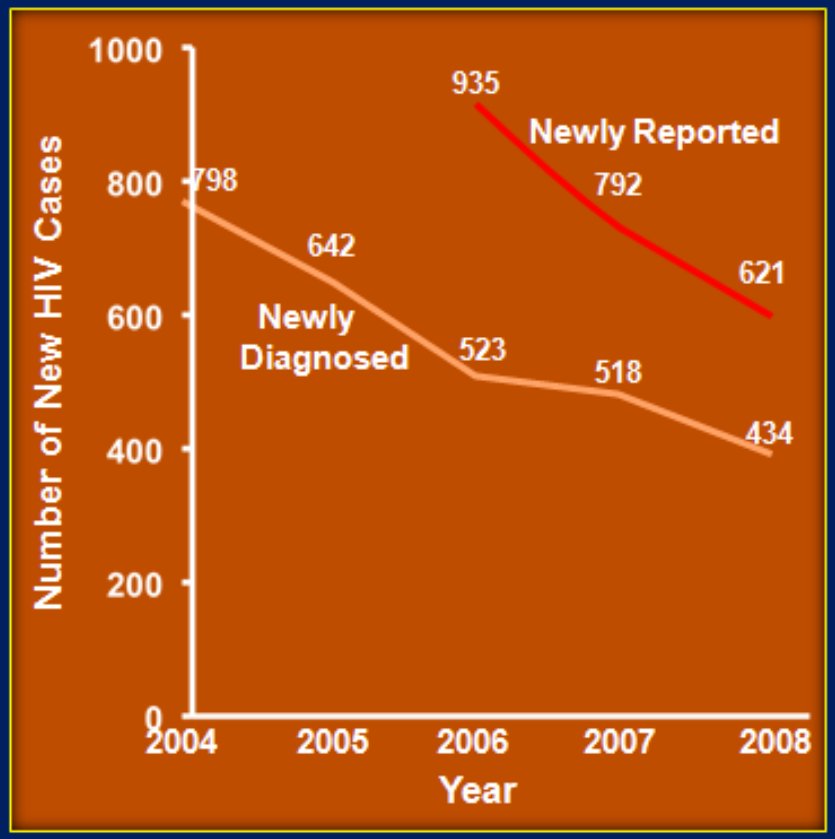

*Coovadia J: NEJM 2004*

# Reductions in HIV RNA, Newly Diagnosed and Reported Cases in SF (2004-2008)

## Community HIV RNA Levels



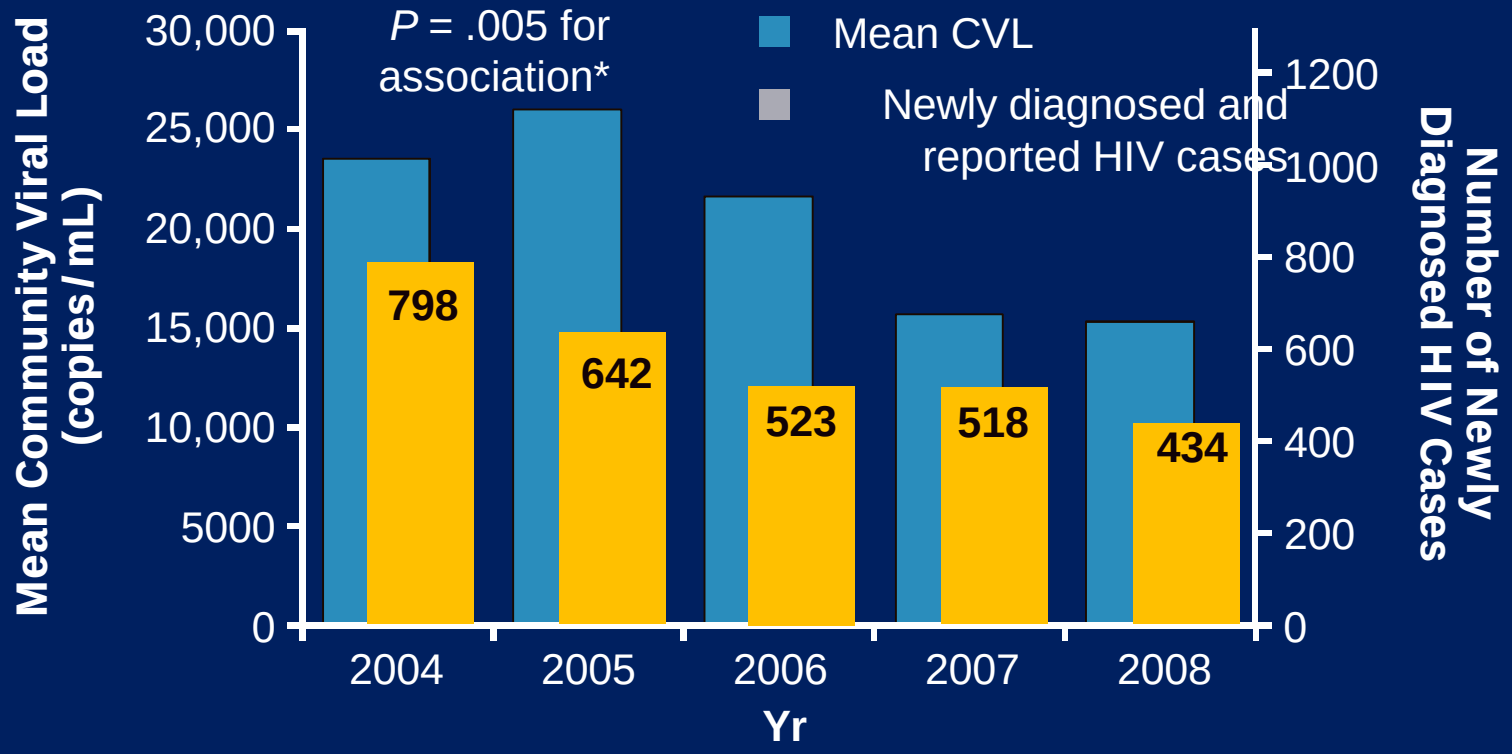

## New HIV Cases




n=12,512 unduplicated HIV-positive individuals.
Das M, et al. *PLoS ONE*. 2010;5:e11068.

# Community Viral Load Mirrors Reduced Rate of New HIV Cases in San Francisco

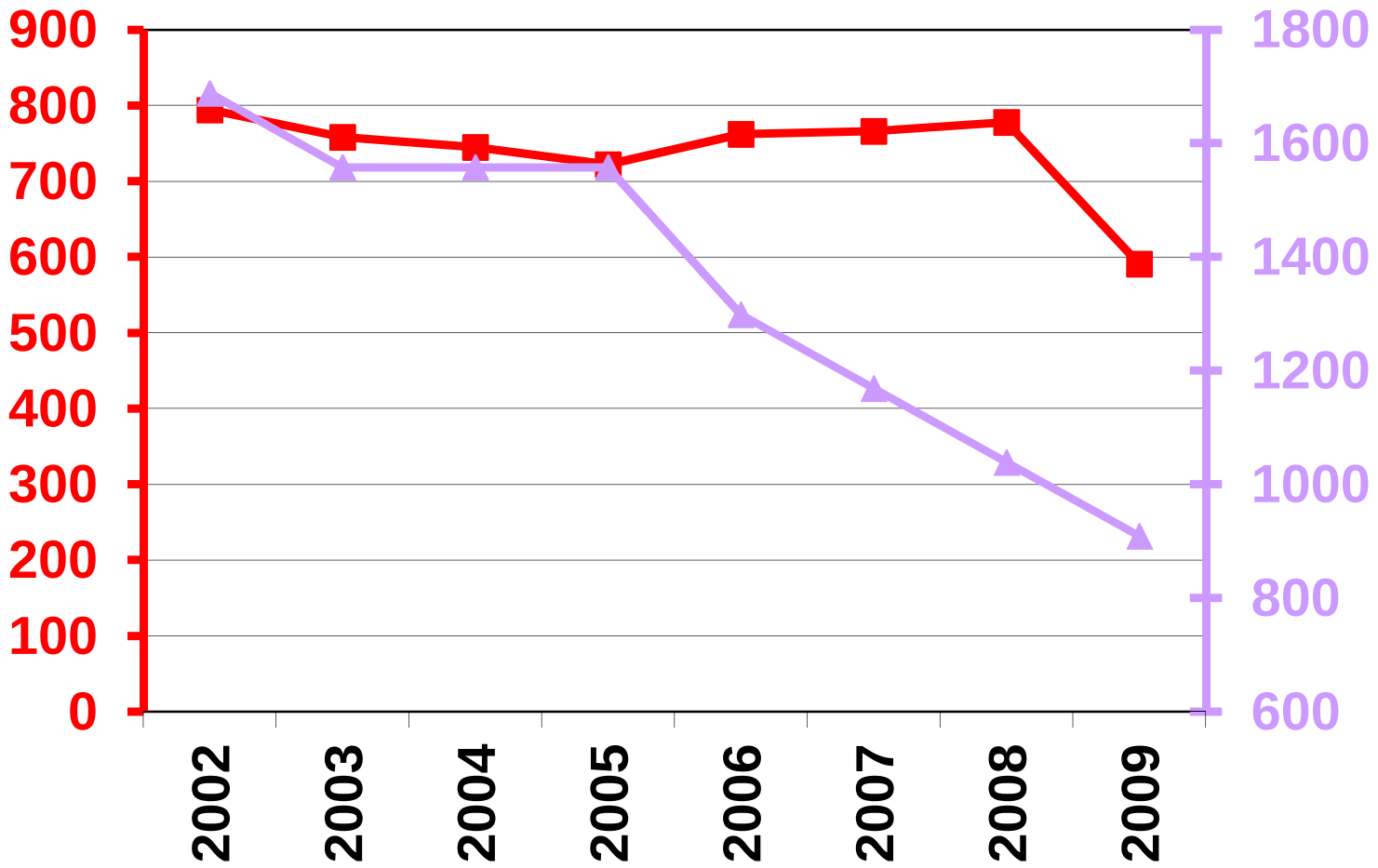
- Retrospective analysis of relationship between community viral load (mean of summed individual HIV-1 RNA results per yr) and new HIV diagnoses




*Data insufficient to prove significant association with reduced HIV incidence.

Das-Douglas M, et al. CROI 2010. Abstract 33. Reproduced with permission.

# Switzerland: Newly Diagnosed HIV Infections, and N of pts with viremia > 500 in the SHCS*




* SHCS = Swiss HIV Cohort Study

*Lancet* 2006; 368: 531–36

# The case for expanding access to highly active antiretroviral therapy to curb the growth of the HIV epidemic

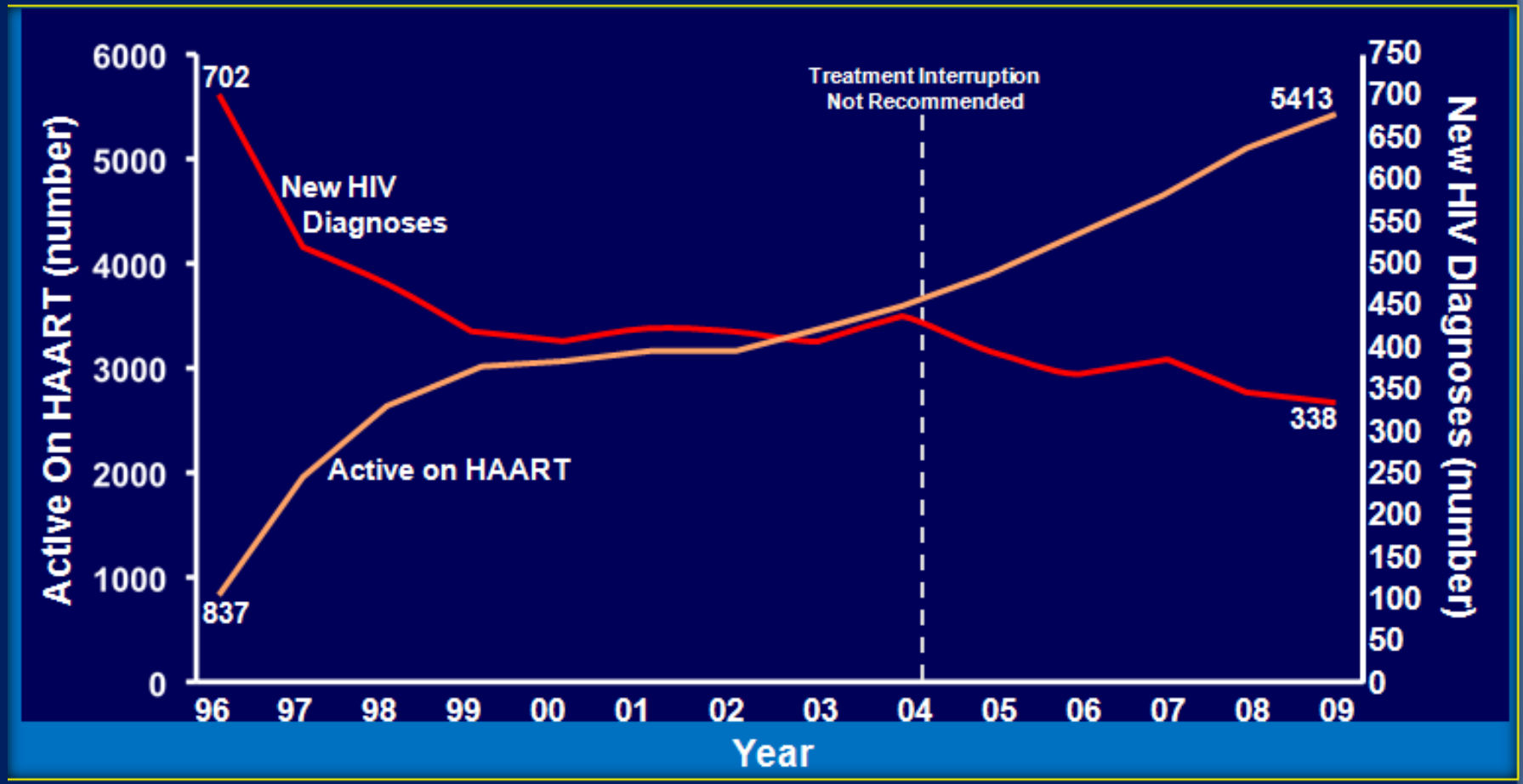
*Julio S G Montaner, Robert Hogg, Evan Wood, Thomas Kerr, Mark Tyndall, Adrian R Levy, P Richard Harrigan*

"The upshot of this widespread failure to recognize that AIDS is an exceptional crisis and threat is that the response to the pandemic is not made commensurate to the challenges—and so the epidemic escalates even while it erodes our capacities to check it."

*Dr Peter Piot, UNAIDS Executive Director*[1]

## Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study

Julio S G Montaner, Viviane D Lima, Rolando Barrios, Benita Yip, Evan Wood, Thomas Kerr, Kate Shannon, P Richard Harrigan, Robert S Hogg, Patricia Daly, Perry Kendall




*Montaner JS, et al. Lancet. 2010;376:532-539.*

# Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study

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Lancet 2010; 376: 532–39

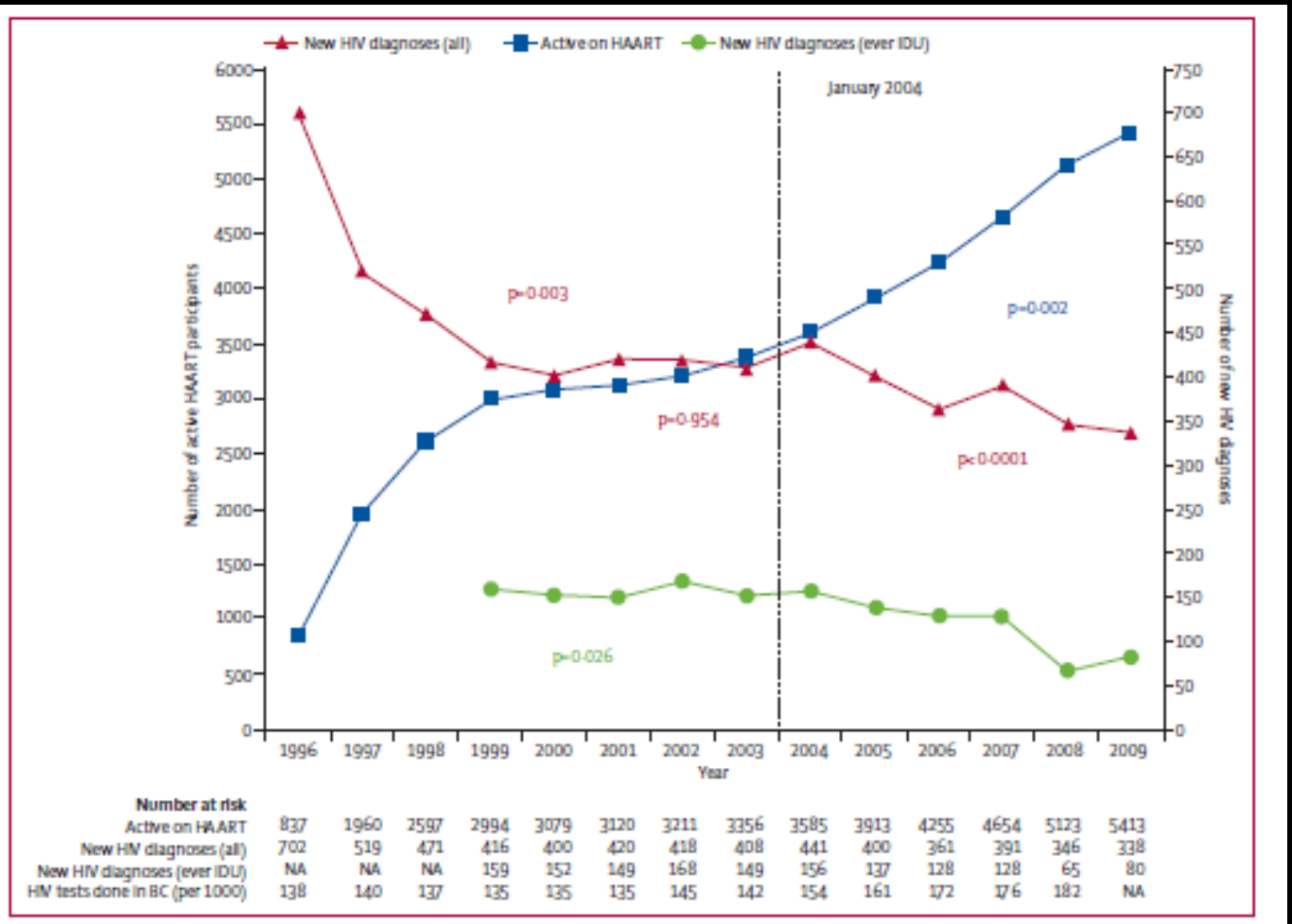
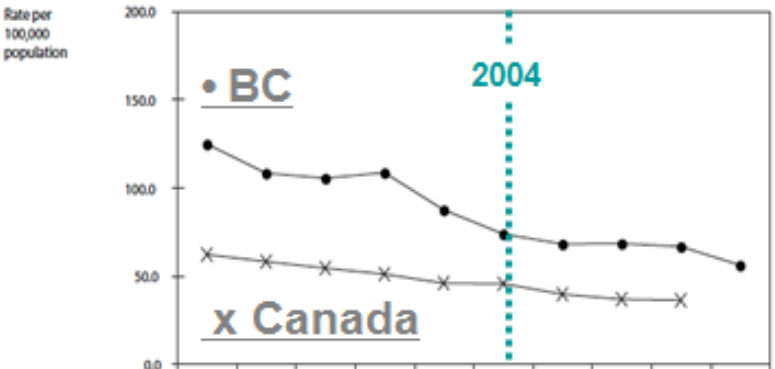


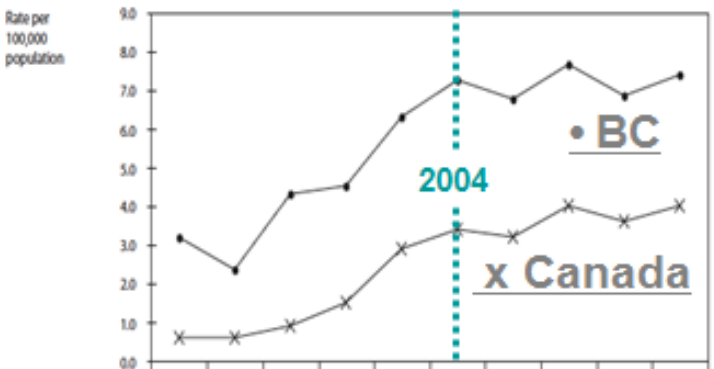

*Figure 1:* **Number of active HAART participants and number of new HIV diagnoses per year in British Columbia, Canada, 1996–2009**
p values are for trend and were obtained from the generalised additive model. Injecting drug user (IDU) refers to individuals who have ever injected illicit drugs. HAART=highly active antiretroviral therapy. BC=British Columbia. NA=not available.

## Hepatitis C, 1999-2008




| | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|---|---|---|---|---|---|
| BC Hepatitis C Reports | 4984 | 4359 | 4282 | 4446 | 3617 | 3086 | 2879 | 2935 | 2898 | 2479 |
| BC Hepatitis C Rate | 124.3 | 107.9 | 105.0 | 108.0 | 87.0 | 73.4 | 67.6 | 67.9 | 66.2 | 55.8 |
| Canadian Hepatitis C Rate | 61.7 | 57.8 | 54.1 | 50.7 | 45.5 | 45.1 | 39.3 | 36.5 | 35.8 | |

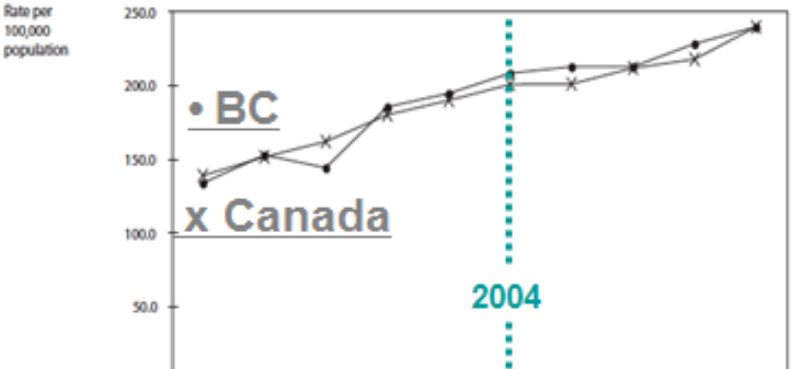
## Infectious Syphilis, 1999-2008




| | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008* |
|---|---|---|---|---|---|---|---|---|---|---|
| BC Syphilis Reports | 128 | 95 | 176 | 186 | 262 | 305 | 288 | 331 | 300 | 328 |
| BC Syphilis Rate | 3.2 | 2.4 | 4.3 | 4.5 | 6.3 | 7.3 | 6.8 | 7.7 | 6.8 | 7.4 |
| Canadian Syphilis Rate | 0.6 | 0.6 | 0.9 | 1.5 | 2.9 | 3.4 | 3.2 | 4.0 | 3.6 | 4.0 |

*2008 Canadian rate is projected and is subject to change (Public Health Agency of Canada, 2009).

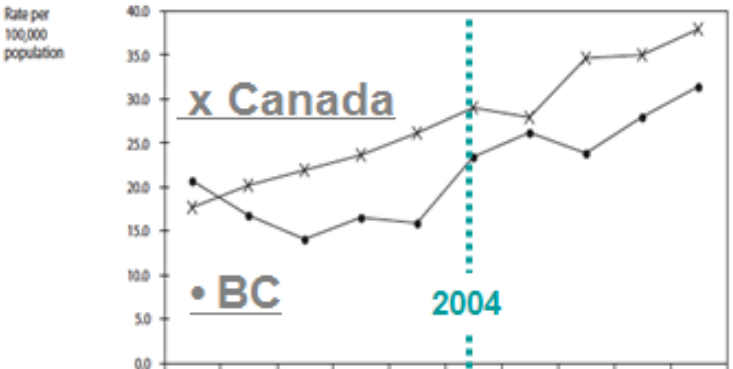
## Genital Chlamydia, 1999-2008




| | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008* |
|---|---|---|---|---|---|---|---|---|---|---|
| BC Chlamydia Reports | 5,343 | 6,150 | 5,855 | 7,603 | 8,071 | 8,733 | 9,045 | 9,172 | 9,971 | 10,629 |
| BC Chlamydia Rate | 133.2 | 152.3 | 143.6 | 184.7 | 194.2 | 207.7 | 212.3 | 212.3 | 227.6 | 239.3 |
| Canadian Chlamydia Rate | 138.2 | 150.9 | 161.4 | 179.4 | 189.4 | 200.1 | 200.4 | 211.4 | 217.3 | 239.3 |

2008 Canadian rate is projected and is subject to change (Public Health Agency of Canada, 2009).

## Gonorrhea, 1999-2008

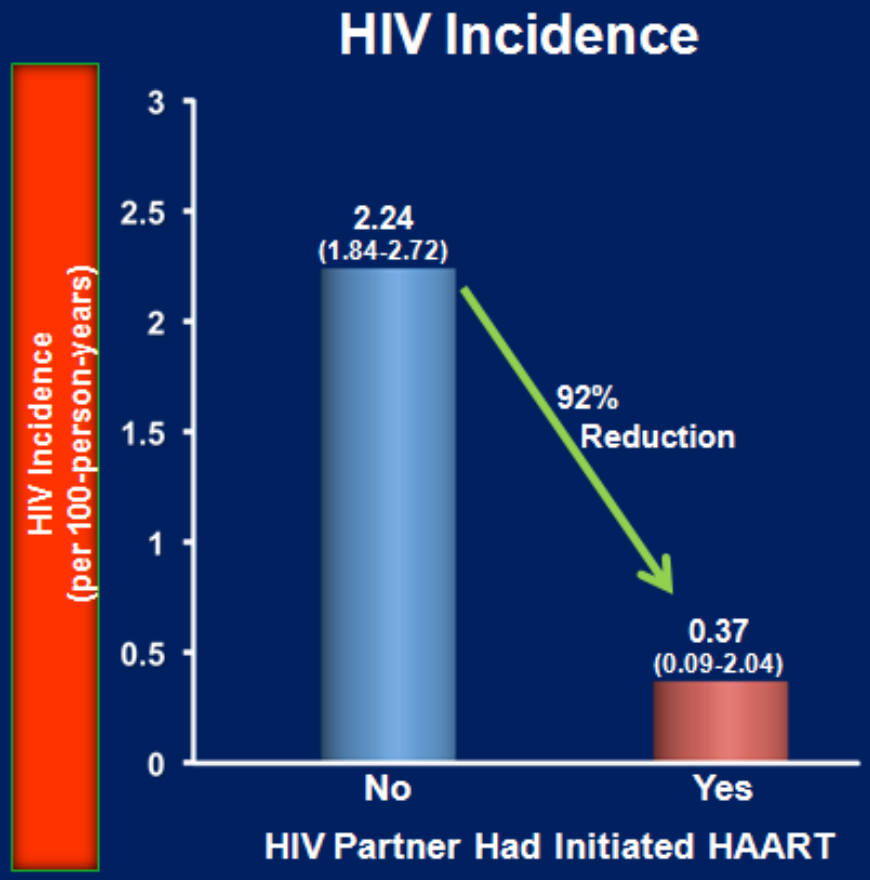



| | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008* |
|---|---|---|---|---|---|---|---|---|---|---|
| BC Gonorrhea Reports | 827 | 675 | 571 | 675 | 656 | 979 | 1,111 | 1,026 | 1,220 | 1,391 |
| BC Gonorrhea Rate | 20.6 | 16.7 | 14.0 | 16.4 | 15.8 | 23.3 | 26.1 | 23.7 | 27.9 | 31.3 |
| Canadian Gonorrhea Rate | 17.6 | 20.1 | 21.8 | 23.5 | 26.0 | 28.9 | 27.8 | 34.5 | 34.9 | 37.8 |

*2008 Canadian rate is projected and is subject to change (Public Health Agency of Canada, 2009).

# Partners for the Prevention of HSV/HIV Transmission Study: Discordant Couples

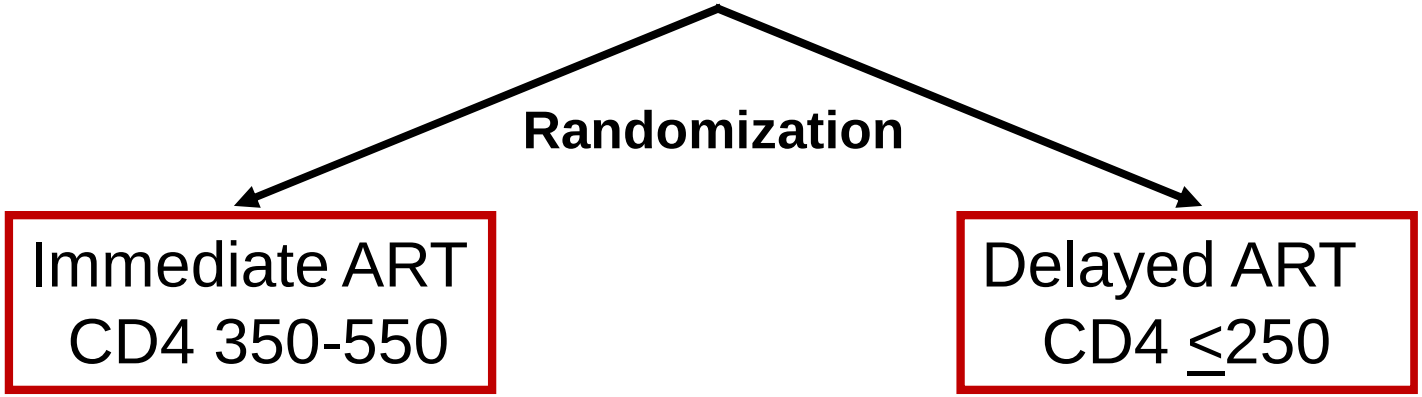
- Prospective *cohort* analysis (n=3381 discordant couples)
  - HIV-infected persons initiating HAART (n=349)
    - 14 sites in 7 Sub-Saharan countries
- Linked HIV transmission (n=103)
  - Only 1 from HIV-infected person who initiated HAART
  - Adjusted incidence rate ratio
    - 0.08% (0.00-0.57; *P*=0.004)
- Sexual risk behaviors
  - Before versus after HAART
    - 6.2% versus 3.7% (*P*=0.03)
  - No change in sexual frequency




Donnell D, et al. *Lancet.* 2010;375:2092-2098.

# HPTN 052 Study Design

Stable, healthy, serodiscordant couples, sexually active
CD4 count: 350 to 550 cells/$mm^3$




**Primary Transmission Endpoint**
Virologically-linked transmission events

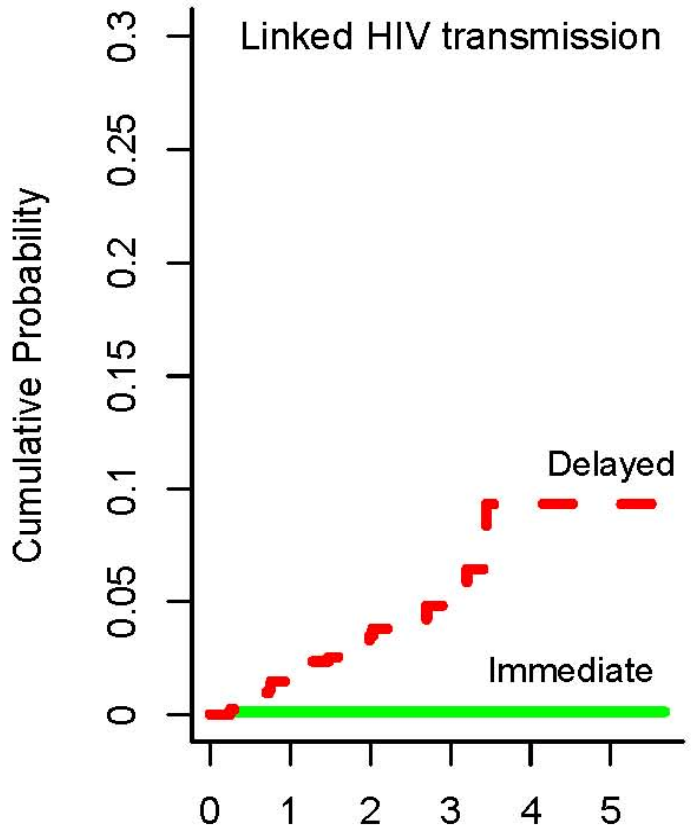
**Primary Clinical Endpoint**
WHO stage 4 clinical events, pulmonary tuberculosis, severe bacterial infection and/or death

# DSMB Recommendation
## April 28, 2011

**“The Board recommends that the results of the trial be announced as soon as possible”**

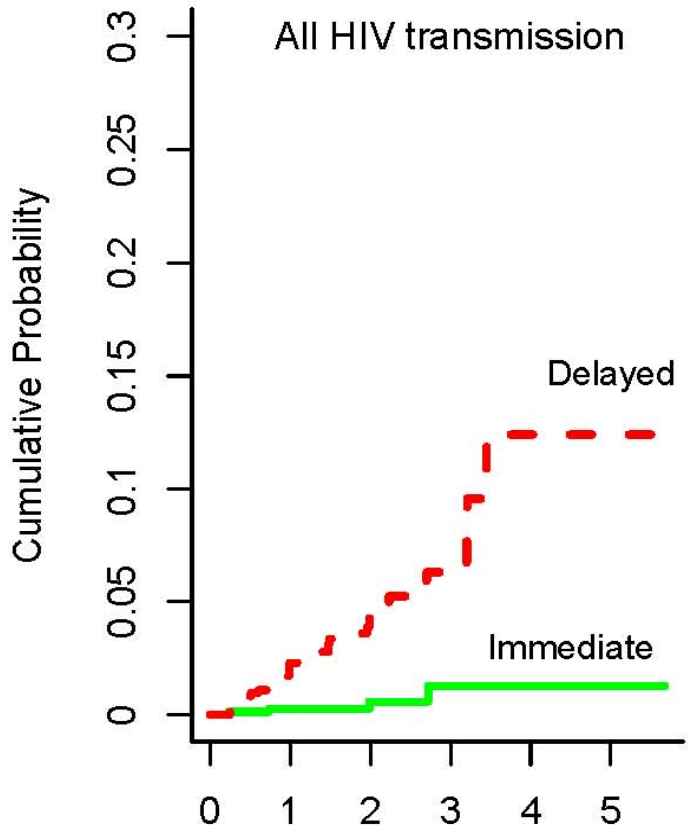
**HPTN 052 continues to follow couples, but all HIV-infected participants are being offered ART**

# HPTN052: HIV-1 Transmissions




**No. at Risk**

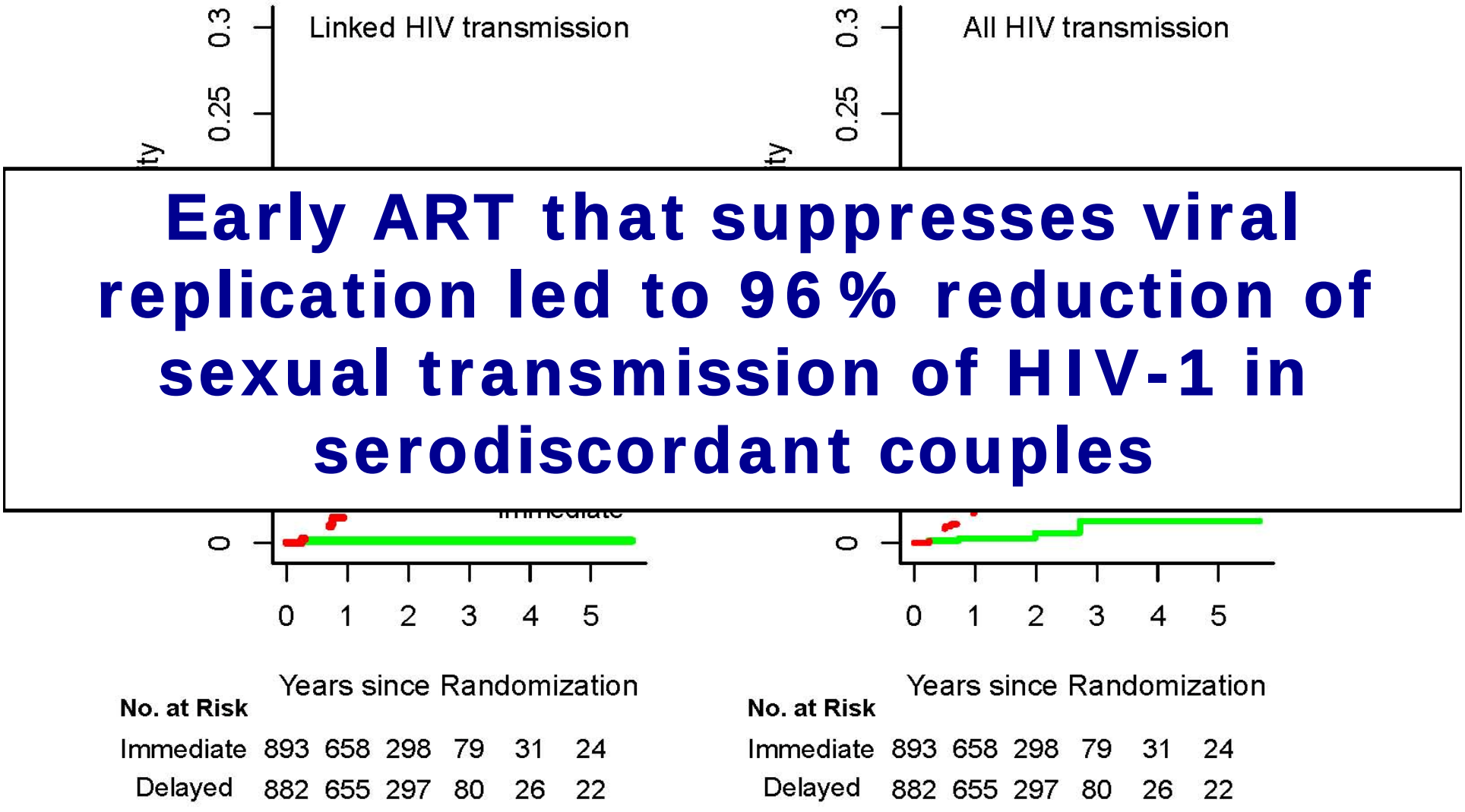
| | | | | | | |
|---|---|---|---|---|---|---|
| Immediate | 893 | 658 | 298 | 79 | 31 | 24 |
| Delayed | 882 | 655 | 297 | 80 | 26 | 22 |




**No. at Risk**

| | | | | | | |
|---|---|---|---|---|---|---|
| Immediate | 893 | 658 | 298 | 79 | 31 | 24 |
| Delayed | 882 | 655 | 297 | 80 | 26 | 22 |

# HPTN052: HIV-1 Transmissions




**Early ART that suppresses viral replication led to 96% reduction of sexual transmission of HIV-1 in serodiscordant couples**

# Sexual Behaviors: Baseline and Follow-up

| | | Immediate (N=886) | | Delayed (N=876) | |
|---|---|---|---|---|---|
| | | Enrollment | Follow-up | Enrollment | Follow-up |
| **Index pregnancy** | | 63 | 47 | 59 | 79 |
| **STDs*** | **Index** | 1% - 5% | 0% - 3% | 1% - 5% | 0% - 3% |
| | **Partner** | 1% - 3% | 0% - 2% | 1% - 2% | 0% - 4% |
| **Sexual activity**** | **Index** | 72% | 62% - 74% | 74% | 53% - 70% |
| | **Partner** | 72% | 67% - 81% | 73% | 62% - 76% |
| **Condom use**** | **Index** | 94% | 92% - 97% | 92% | 92% - 100% |
| | **Partner** | 92% | 90% - 100% | 92% | 92% - 100% |

***STDs include hepatitis B, syphilis, gonorrhea, and *C. trachomatis***
****Self-reported data**

# Multivariate Analysis – Linked Transmission

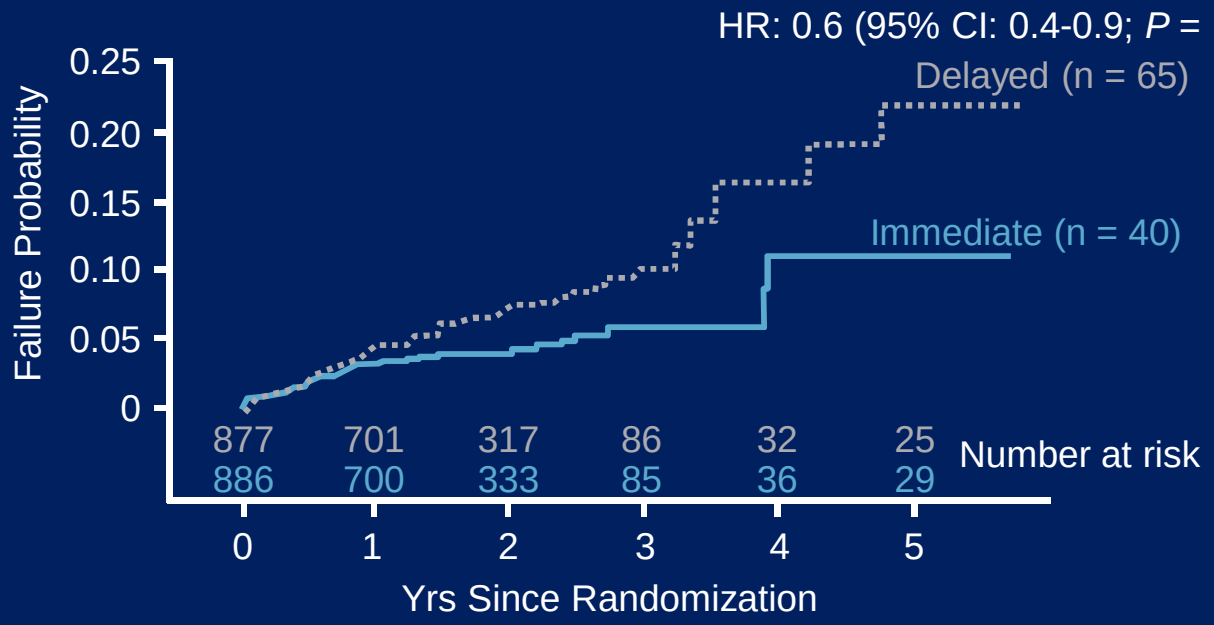
| Variable | Hazard Ratio | 95% Confidence Interval |
|---|---|---|
| **Treatment** (immediate vs. delayed) | 0.04 | [0.01 - 0.28] |
| **Baseline CD4** (per 100 CD4 Increment) | 1.24 | [1.00 - 1.54] |
| **Baseline VL** (per unit log increment) | 2.84 | [1.51 - 5.41] |
| **Baseline condom use** (100% vs. <100%) | 0.33 | [0.12 - 0.91] |
| **Gender (HIV +)** (male vs. female) | 0.73 | [0.33 - 1.65] |

# OK, pero el beneficio para el paciente?

(Muerte, WHO Estadio 4,  TB  pulmonar o infeccion bacteriana severa)

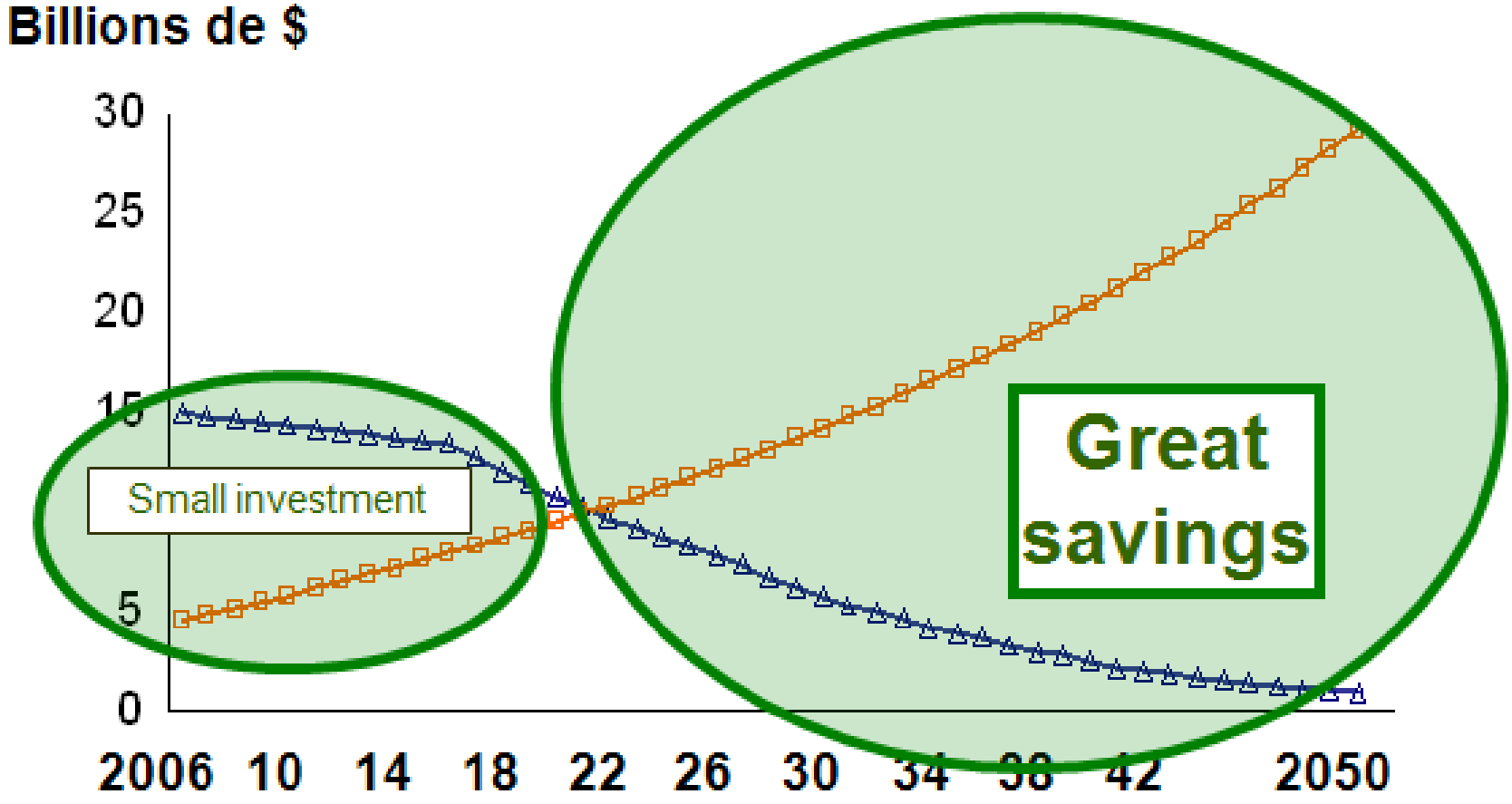
**HPTN 052: Primary Clinical Events During Follow-up**

- 41% reduction in HIV-related clinical events in HIV-infected patients randomized to immediate vs delayed therapy
  - Excess events in delayed arm driven mainly by TB (33 vs 17 cases), particularly extrapulmonary TB (17 vs 3 cases)c




Grinsztejn B, et al. IAS 2011. Abstract MOAX0105.
Cohen MS, et al. N Engl J Med. 2011;[Epub ahead of print].

# Costs of HAART




*Lima VD et al. JID 2008*
*Hogg et al. Unpublished, 2006*

# Que hemos aprendido?

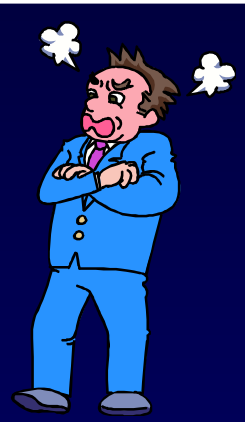
- ✓ La infeccion es controlable, pero no erradicable
- ✓ HAART es suficientemente potente para reducir CV en 6 logs
- ✓ Esto permite la recuperacion inmune
- ✓ En consecuencia se reducen la morbilidad, las hospitalizaciones y la mortalidad
- ✓ HAART impacta en la incidencia de enf. cardiovascular, hepatica, renal y “canceres no asociados a sida”, si es iniciado a tiempo
- ✓ HAART salva vidas y **reduce la transmision**, lo que impacta a nivel individual y **poblacional**
- ✓ No hay vacuna efectiva en el horizonte cercano
- ✓ Por cada 2 nuevos casos en tratamiento, 5 nuevas infecciones
- ✓ Controlar la epidemia requiere un nuevo enfoque: **Prevencion+Tratamiento**
- ✓ El estigma, la discriminacion y la falta de voluntad politica agravan la epidemia

# Estrategias exitosas

| Riesgo | Intervencion | Tratamiento | Eficacia |
|---|---|---|---|
| Transfusion | Testeo universal | No aplica | 99-100% |
| Vertical | Testeo iniciado por el proveedor | Ofrecido 100% | 98-99 |
| Sexual | Estudios de cohorte, evidencias ecologicas, estudio prospectivo | Temprano | 96% |

## Pregunta para los próximos años….

**Existe algun paciente absolutamente NO ELEGIBLE para iniciar ARV?**

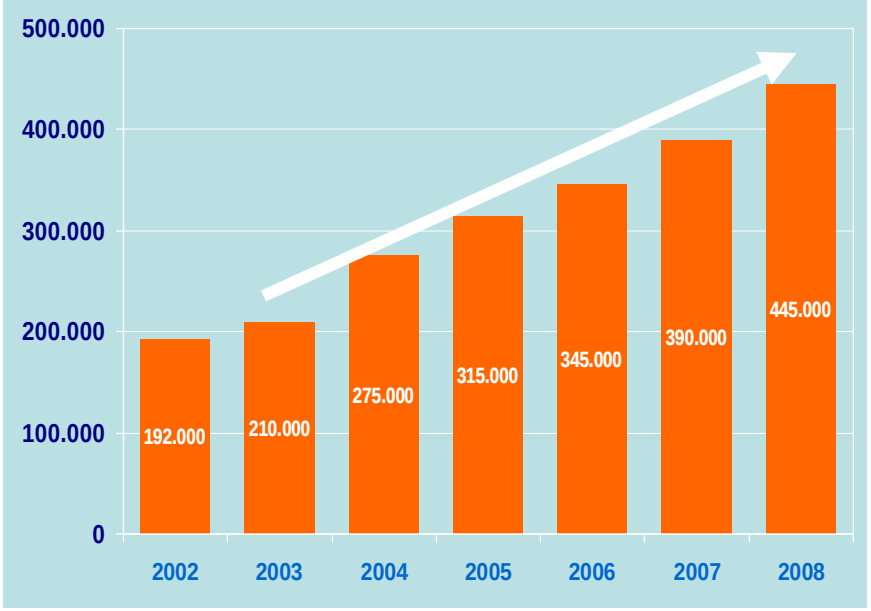


Solo el que no esté preparado...

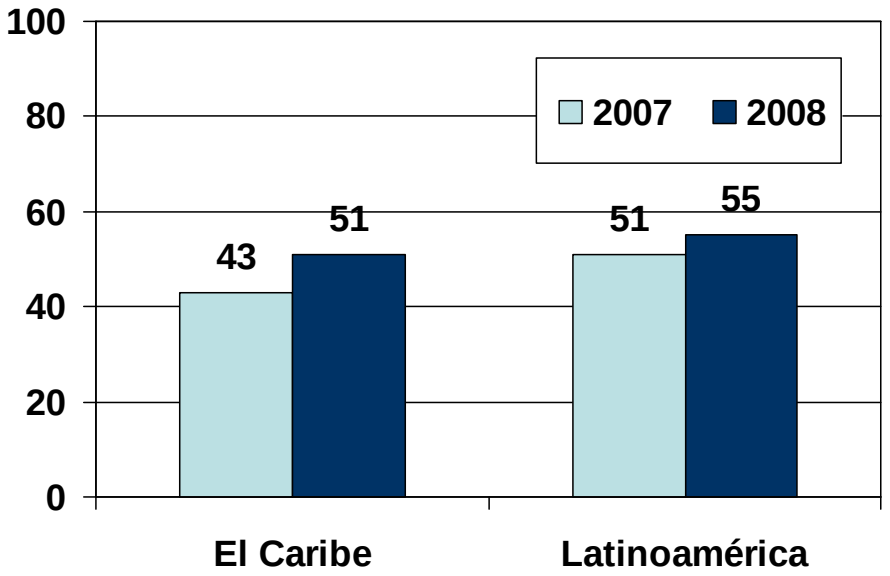
**Que implicancias tiene esto para Latinoamerica?**

# Acceso a TARV en Latinoamerica

## Número de personas en TARV



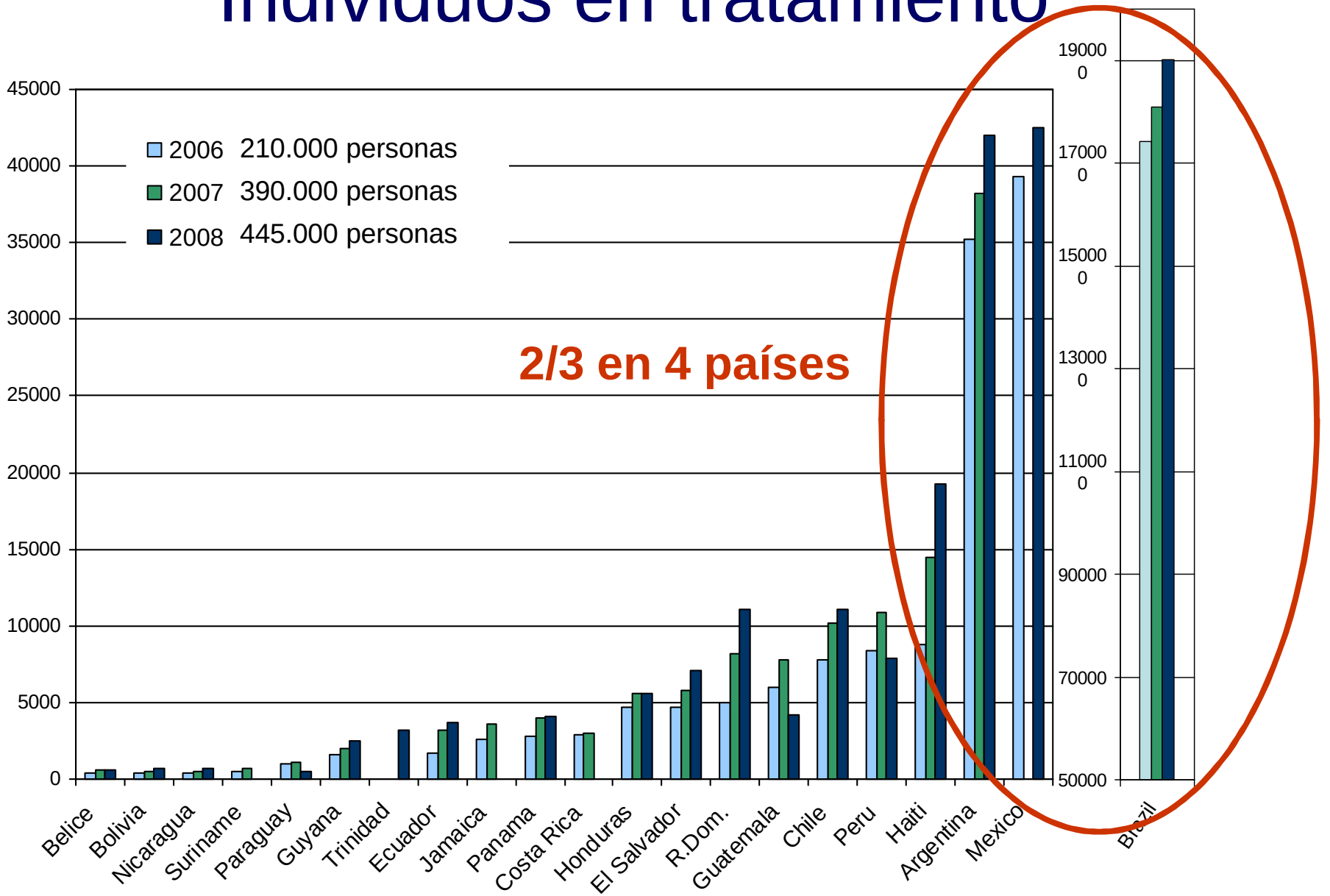

## Porcentaje de cobertura ARVs




- En la región se observa un aumento sostenido del numero de personas que ingresan a tratamiento.
- Discreta mejora en el porcentaje de cobertura

**Avances y fortalezas**

# Individuos en tratamiento




Avances y fortalezas

Organización Panamericana de la Salud
Organización Mundial de la Salud

OPS respuesta al VIH

# Current gaps in access to care and treatment in Latin America (LA)

•Abstract THPE0881

•Omar Sued[1], Luise. Martin[2], Bertha Gomez[1], María Dolores Pérez-Rosales[1], Marcelo Vila[1], Rafael Mazín[1], Mónica Alonso[1] and Hirnschall Gottfried[1]

[1]Pan American Health Organization, FCH-HI, Washington, US,
[2] Carlo Schmid Program Fellow, PAHO, Washington, US

•**Background:** Antiretroviral treatment (ART) coverage in LA ranked first among developing regions with 54% (51-59%) in 2008. However, scaling-up this year was less than in other regions. The identification of country-specific factors hindering universal access targets is indispensable for improve national HIV responses.

•**Methods:** 2008 country data collected by PAHO for the UA 2009 Report, peer-reviewed literature, national HIV reports and country-specific information provided by national HIV PAHO representatives were summarized to identify barriers to increase ART coverage.

•**Results:**

- Lack of access to HIV testing remains as a major obstacle to expand ART coverage across the whole region:
  - Testing not integrated in primary health care services
  - Low number of health facilities offering HIV testing
  - Frequent stigma and discrimination (S&D) and impaired access of MARPs and vulnerable populations.
- Specific barriers to HIV testing:
- limitations for using rapid tests for general population in Colombia, Argentina, Panama, Guatemala, Costa Rica, Ecuador, Paraguay
- procurement difficulties reported in Bolivia, Guatemala, Honduras, El Salvador, Paraguay, Perú and Nicaragua;
- lack of trained human resources in Perú, Paraguay, Honduras, Ecuador and Bolivia
- Missed testing opportunities (e.g. HIV testing in TB patiens and pregnant women) in several countries
- Late diagnosis resulting in higher risk of early mortality (Argentina, Chile, México, Paraguay)
- Inadequate referral systems
- Lack of laboratory capabilities
- High inequity in access (particularly among MARPs, young and indigenous populations)

•Number of people (≥15 years) who received and HIV test during 2008, and number of test per 1,000 population (≥15 years)

| Country | Tested | HIV test/1000 |
|---|---|---|
| Ecuador | 314,868 | 45 |
| Guatemala | 27,112 | 4 |
| Honduras | 88,189 | 24 |
| Mexico | 1,228,298 | 21 |
| Nicaragua | 118,592 | 40 |
| Paraguay | 72,276 | 22 |

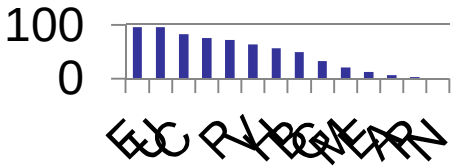
•Number of Health Facilities with T&C and ratio of population ≥15 years per testing facility, 2008

| Country | Number of facilities | Population per facility |
|---|---|---|
| Bolivia | 225 | 21,000 |
| El Salvador | 515 | 6,000 |
| Guatemala | 183 | 35,000 |
| Honduras | 655 | 6,000 |
| Paraguay | 102 | 31,000 |

Preventing mother-to-child transmission of HIV in Latin America, 2008

| Country | N of pregnant women HIV+ who received ART for PTMI | Period | Pregnant women tested for HIV | | Low estimate | High estimate | Infants born to women HIV+ receiving ART for PTMI | | Infants born to women HIV+ receiving a virological test by 2 m of age | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Reported number | Estimated coverage | | | Reported number | Estimated coverage | Reported number | Estimated coverage |
| Argentina | 2 463 | Jan 08–Dec 08 | 598 123 | 87% | >95% | >95% | 2 280 | >95% | ... | |
| Bolivia | 35 | Jan 08–Dec 08 | 42 726 | 16% | 6% | 21% | 28 | 8% | 23 | 7% |
| Brazil | 6 844 | Jan 08–Dec 08 | 2 381 280 | 77% | | | 7 511 | | 2 306 | |
| Chile | 203 | Jan 08–Dec 08 | 126 097 | 50% | 32% | >95% | ... | | 141 | 36% |
| Costa Rica | 21 | Jan 06–Dec 06 | 61 000 | 81% | 13% | 50% | 40 | 43% | 40 | 43% |
| Cuba | 41 | Jan 07–Dec 07 | 112 434 | >95% | 34% | >95% | 41 | 55% | 41 | 55% |
| Ecuador | 277 | Jan 08–Dec 08 | 222 564 | 79% | 24% | 81% | 274 | 39% | ... | |
| El Salvador | 189 | Jan 08–Dec 08 | 87 186 | 70% | 23% | 69% | 155 | 29% | ... | |
| Guatemala | 321 | Jan 08–Dec 08 | 102 957 | 23% | 9% | 29% | 159 | 7% | ... | |
| Honduras | 300 | Jan 08–Dec 08 | 108 509 | 54% | 27% | 94% | 125 | 18% | 229 | 34% |
| Mexico | 458 | Jan 08–Dec 08 | 757 863 | 37% | 5% | 16% | 58 | 1% | ... | |
| Nicaragua | 53 | Jan 08–Dec 08 | 55 340 | 40% | 65% | >95% | 53 | >95% | ... | |
| Panama | 71 | Jan 07–Dec 07 | ... | | 13% | >95% | 154 | 70% | ... | |
| Paraguay | 156 | Jan 08–Dec 08 | 55 266 | 36% | 29% | >95% | 121 | 38% | 2 | 1% |
| Peru | 477 | Jan 08–Dec 08 | 425 480 | 70% | 29% | >95% | 402 | 44% | ... | |
| Uruguay | 53 | Jan 06–Dec 06 | 5 852 | 12% | | | 68 | | 70 | |
| Venezuela | 310 | Jan 06–Dec 06 | ... | | 8% | 27% | ... | | ... | |

•Percentage of TB patients that know his/her HIV status, 2008




•**Conclusions:** Common barriers to ART persist across the region. HIV testing needs to be expanded, ideally integrated into primary care with low-cost and rapid methodologies. Adequate referral systems for timely treatment need to be established. MARPs access to testing and care need to be ensured.

•Training of human resources and capacity building are needed to reduce S&D, allow access to key populations and increase coverage.

•**References:**

• Universal Access Report 2009, Global WHO TB database, PAHO HIV Focal Point survey 2009, PAHO evaluations (El Salvador, Paraguay and Guatemala), NAP websites, Bastos et al Int J Epid 2008, Tuboi et al JAIDs 2009, Cesar et al Plos 2010, Aldridge et al, BMC 2009, Protto et al Rev Pan Sal Pub 2008, Zala et al JIAS 2008, Rodrigues Junior et al Rev Pan Salud Pub, 2009, Cortes et al, Rev Med Chil 2009.

- **Barreras de acceso:**
  - Testeo no integrado en atencion primaria
  - Estigma y discriminacion a poblaciones vulnerables
- Escaso uso de test rapidos en Colombia, Argentina, Panama, Guatemala, Costa Rica, Ecuador, Paraguay
- Logisticas de aprovisionamiento, insuficiencia de recursos humanos entrenados
- Oportunidades perdidas (TB, ITS, embarazo)
- Falta de infraestructura de laboratorios
- Elevada inequidad en el acceso, en especial para poblaciones en riesgo, pueblos originarios, pobres y excluidos.

# Cross-Sectional Analysis of Late HAART Initiation in Latin America and the Caribbean: Late Testers and Late Presenters

Brenda Crabtree-Ramírez[1], Yanink Caro-Vega[1], Bryan E. Shepherd[2], Firas Wehbe[3], Carina Cesar[4], Claudia Cortés[5], Denis Padgett[6], Serena Koenig[7,8], Eduardo Gotuzzo[9], Pedro Cahn[4], Catherine McGowan[10], Daniel Masys[3], Juan Sierra-Madero[1]*, on behalf of the CCASAnet Team

## Rates of LT and LP

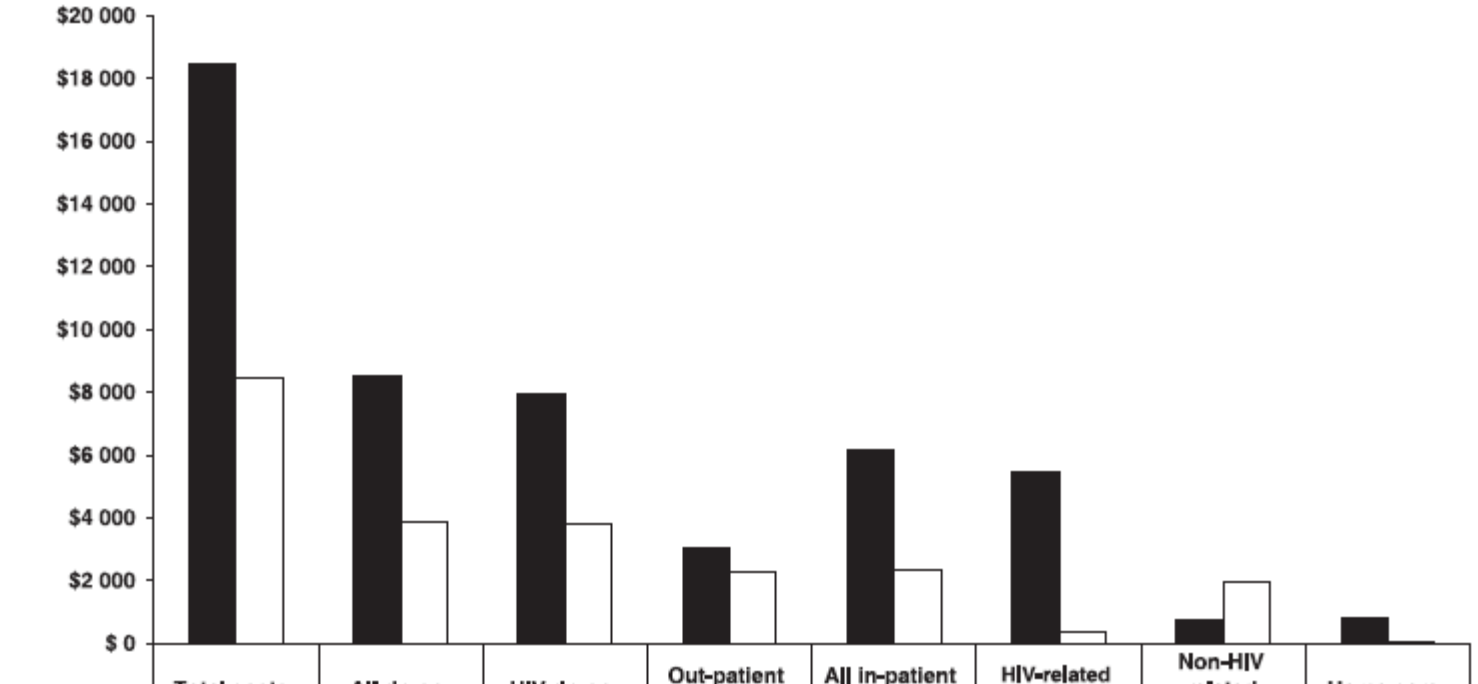
Of 6047 LHI with a recorded date of HIV diagnosis, 3331 (55%) were late testers and 2716 (45%) were late presenters, corresponding to 42% and 34% of the 7901 patients in the overall cohort with complete data.

**76% are late starters**

# The high cost of medical care for patients who present late (CD4 < 200 cells/μL) with HIV infection

HB Krentz,[1,2] MC Auld[3] and MJ Gill[1,2]

*HIV Medicine* (2004), 5, 93–98




| | Total costs | All drugs | HIV drugs | Out-patient care | All in-patient care | HIV-related hospitalizations | Non-HIV related hospitalization | Home care |
|---|---|---|---|---|---|---|---|---|
| ■<200/μL | $18 448 | $8 539 | $7 918 | $3 015 | $6 162 | $5 431 | $736 | $817 |
| □>200/μL | $8 455 | $3 839 | $3 780 | $2 284 | $2 308 | $365 | $1 943 | $35 |

Mean cost per patient per month by category for the 12 months following HIV diagnosis (in Canadian dollars).

# LETTER TO PARTNERS | 2010

Michel Sidibé
*Executive Director*
UNAIDS

The role of antiretroviral treatment in stopping new infections and how it can be effectively used as part of combination HIV prevention approaches must be further explored, as shown by Dr Julio Montaner, President of the International AIDS Society.

# Prevencion + Tratamiento


Modified from T. Coates

# La estrategia faltante…

## En conclusion….

- ✓ HIV produce una enfermedad cronica (inflamatoria)
- ✓ HIV daña mas alla del sida “clásico”
- ✓ Los ARV actuales son mas seguros y amigables
- ✓ El TARV es una herramienta de salud publica
- ✓ El desafío: diagnosticar a tiempo!
- ✓ Mientras discutimos si 200, 350, 500 o mas CD4, tratemos a todos los que califican!