# HIV/AIDS: 1920-1981-1997-2018-2025

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# Potential conflicts of interest:

- **Since May 1st, 2018, I am fulltime employee (Senior Global Medical Director) of ViiV Healthcare.**

- **ViiV healthcare does not approve of or recommend the use of medicines in any way other than that stated in the approved package inserts.**
- **For full prescribing information, refer to the package inserts approved by TFDA.**

# Hospital Clínic – Facultad de Medicina (U.B.) Barcelona (España)

| VIH (1981-2024) | Total | Mortalidad (n) | Mortalidad (%) |
|---|---|---|---|
| Mundo | 85.6m | 40.0m | 47 |
| España* | 350k | 58k | 16 |
| Cataluña* | 70k | 11.6k | 16 |
| HCU | 14k | 2.3k | 16 |
| | | | |

| COVID (2019-22) | Total | Mortalidad (n) | Mortalidad (%) |
|---|---|---|---|
| Mundo | 704m | 7.1m | 1 |
| España | 14m | 0.12m | 1 |
| | | | |

(*) estimado. m=millones. k= miles

# Magnitud de la pandemia por VIH

HCU* x 5=Catalunya x 5 = España

(*) Belgica+Dinamarca

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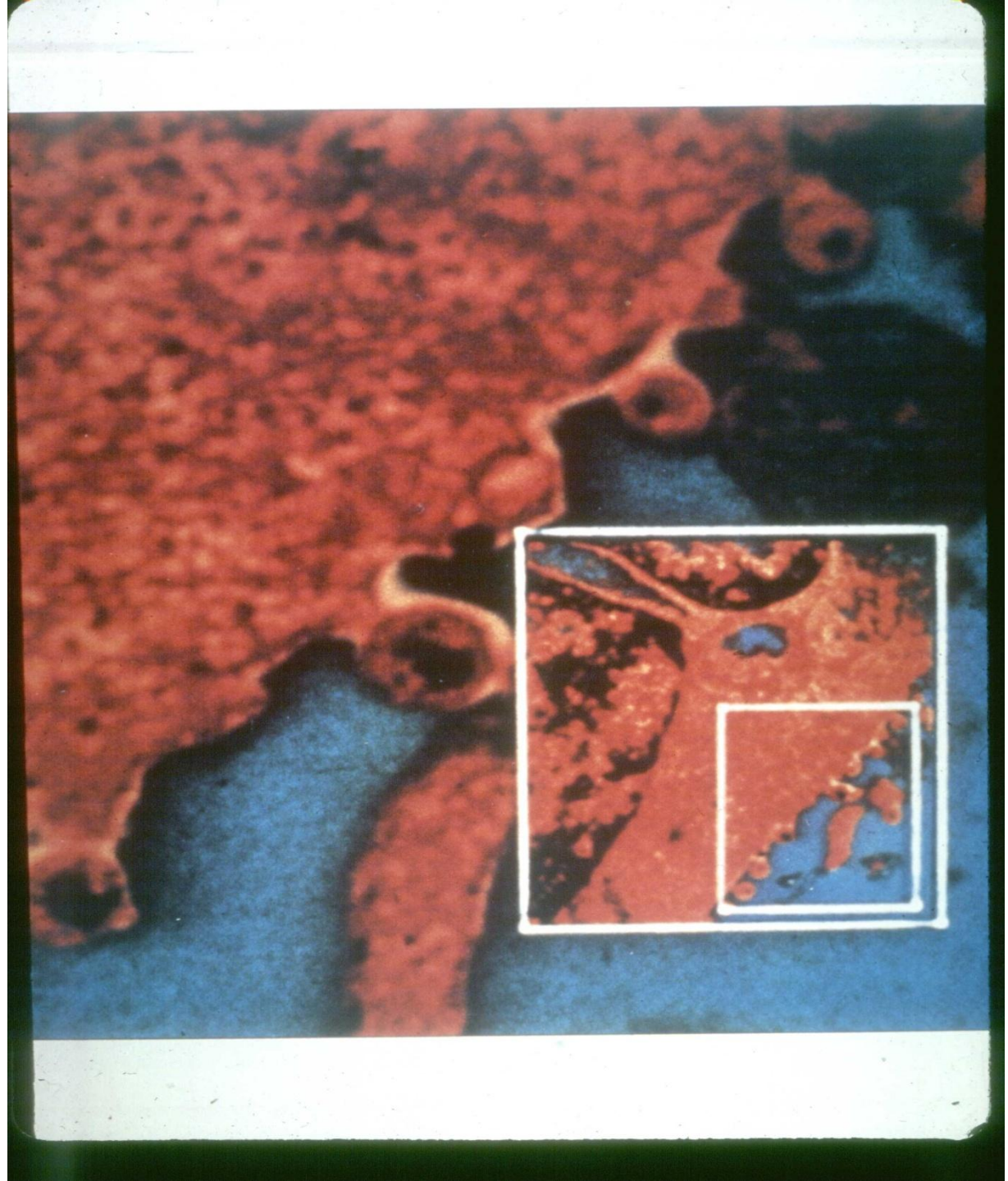
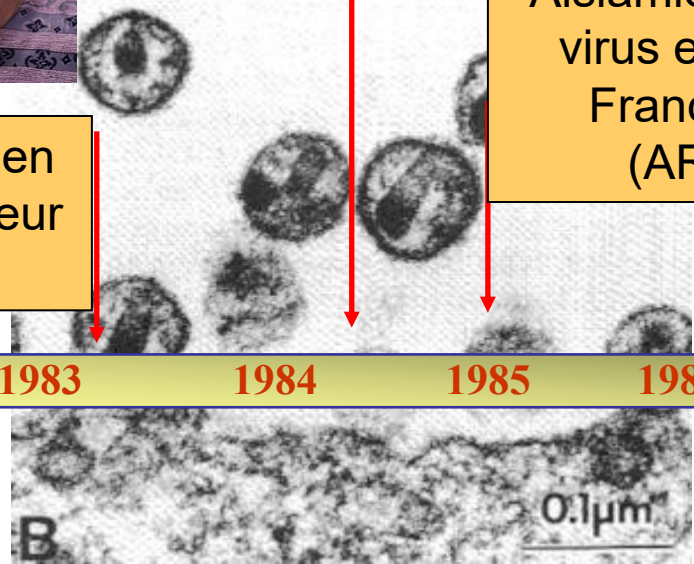


# LA ÉPOCA DE LOS DESCUBRIMIENTOS

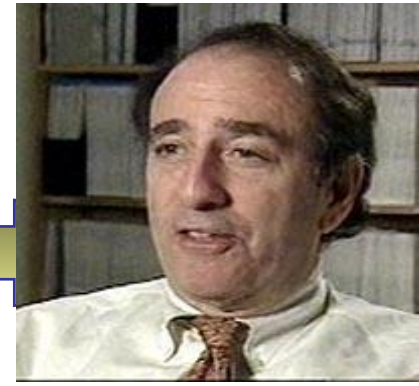
Se aisla el VIH en el Instituto Pasteur (LAV)

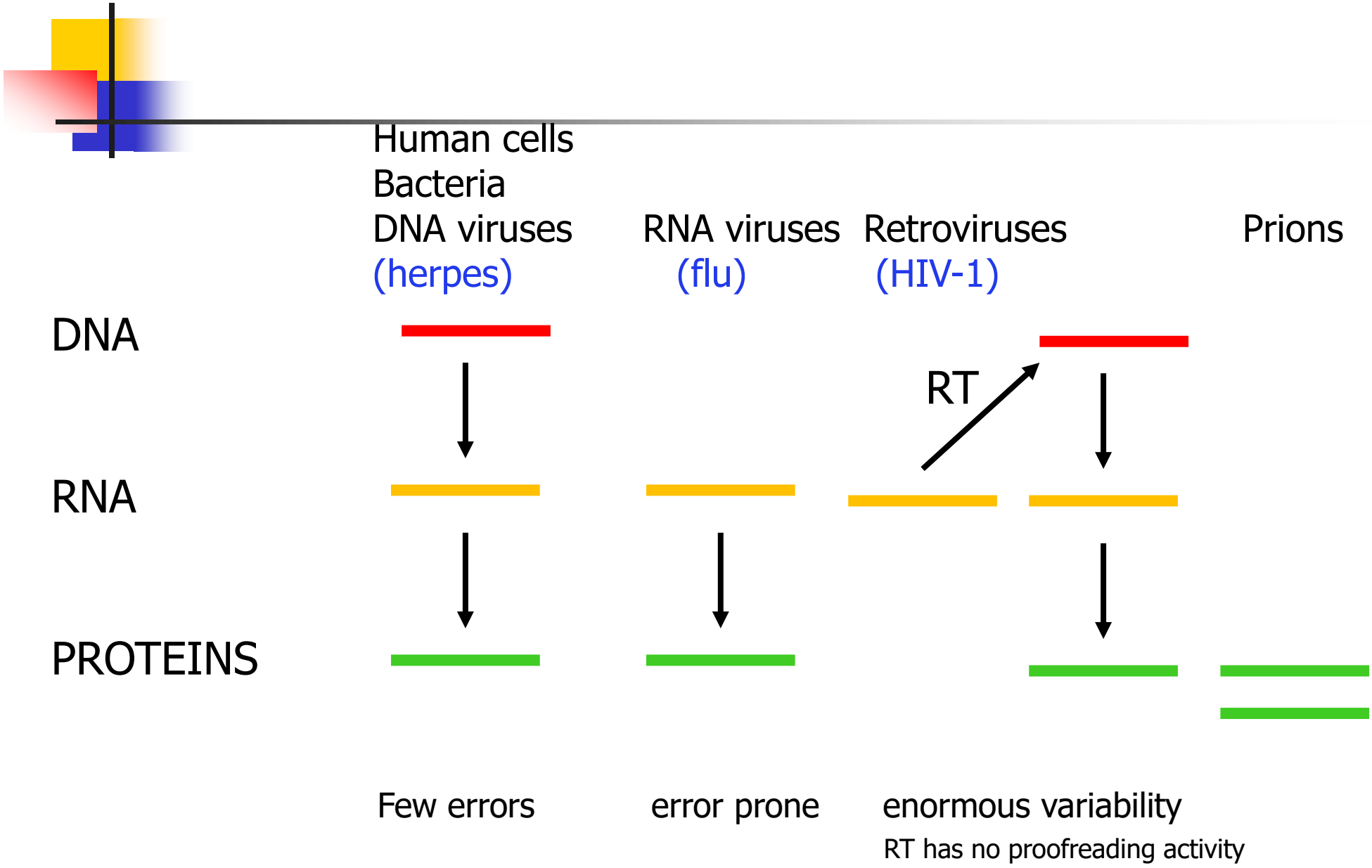
Aislamiento del virus en el NIH (HTLV-III)

Aislamiento del virus en San Francisco (ARV)

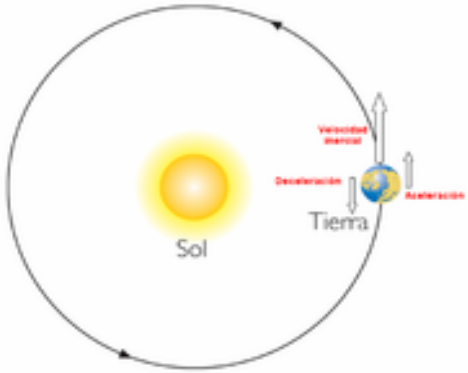



1981 1982 1983 1984 1985 1986




Human cells
Bacteria
DNA viruses
(herpes)
RNA viruses
(flu)
Retroviruses
(HIV-1)
Prions
DNA
RNA
PROTEINS
RT
Few errors
error prone
enormous variability
RT has no proofreading activity

# Challenging dogmas & introducing new paradigms: Never easy

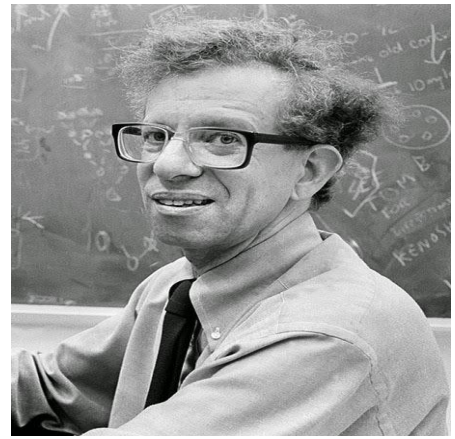


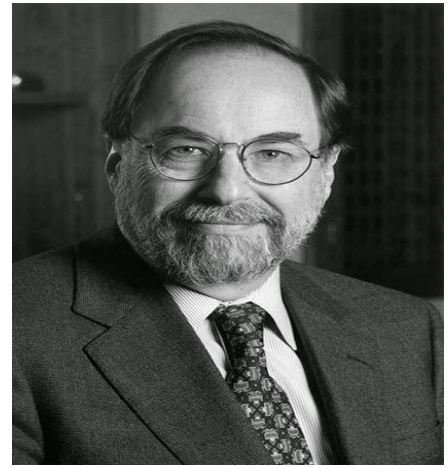

1633

Reverse transcription (1970)

RNA ⟶ DNA

**Only rehabilitated in 1939 (Pius XII) and 1992 (Jean Paul II)**





Nobel laureates, 1975

# The Origins Of HIV/AIDS


Operation INFEKTION

From Wikipedia, the free encyclopedia

**Operation INFEKTION** was a KGB disinformation campaign to spread information that the United States invented HIV/AIDS[1] as part of a biological weapons research project at Fort Detrick, Maryland. The Soviet Union used it to undermine the United States' credibility, foster anti-Americanism, isolate America abroad, and create tensions between host countries and the U.S. over the presence of American military bases (which were often portrayed as the cause of AIDS outbreaks in local populations).[2]

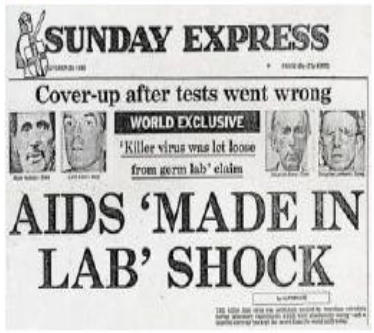
According to U.S. State Department analysts, another reason the Soviet Union "promoted the AIDS disinformation may have been its attempt to distract international attention away from its own offensive biological warfare program, which [was monitored] for decades"—in addition to anthrax, the Soviets were believed to have developed tularemia, the plague, and cholera for biological warfare purposes, as well as botulinum toxin, enterotoxins, and mycotoxins.[3] An alternative explanation is that the operation may have been in retaliation for American accusations that the Soviets used chemical weapons in Southeast Asia, later dubbed the yellow rain incident.[3]

In 1992, Russian Prime Minister Yevgeni Primakov admitted that the KGB was behind the Soviet newspaper articles claiming that AIDS was created by the US government.[1]


Sun

REVEALED:

**Hitler created AIDS virus to destroy U.S.**


SUNDAY EXPRESS

Cover-up after tests went wrong

WORLD EXCLUSIVE

'Killer virus was let loose from germ lab' claim

AIDS 'MADE IN LAB' SHOCK


THE SUN, Monday, February 7, 1989

AIDS IS THE WRATH OF GOD, SAYS VICAR

By HUGH WHITAKER

A VICAR yesterday branded the gay plague AIDS as the wrath of God.

The Rev Owen Leigh-Williams claimed homosexuals attended the Last

Ex-ballet boss is victim 53

A FORMER boss of a world famous ballet company was named



# HIV Zoonosis: How?

Bushmeat is a longstanding source of animal protein and income in the Congo Basin.

In Cameroon >18% of non-ape primate bushmeat samples were positive for SIV antibodies.


chimp

western gorilla

sooty mangabey

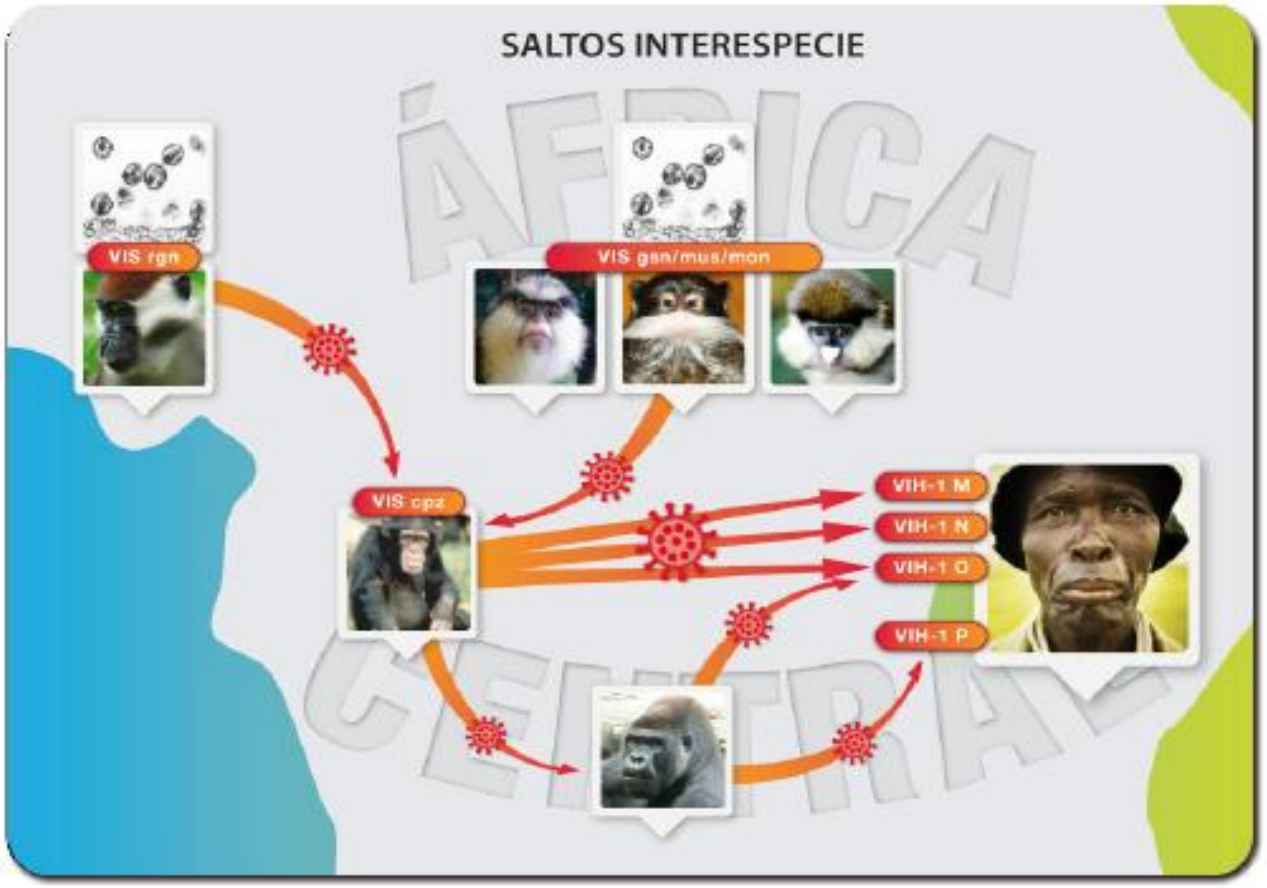
Peeters et al. (2002) Emerg. Inf. Dis.

30 AÑOS DE VIH

# TODO EMPEZÓ EN EL ORIGEN

## SALTOS INTERESPECIE 1920-50






AUTORES: José María Gatell, José Alcamí, Mayte Pérez Olmeda y José Luis de la Serna

IDEA Y PRODUCCIÓN: Wake App Health

CON EL PATROCINIO DE: GILEAD

## From animals to humans. Isolated cases & local outbreaks

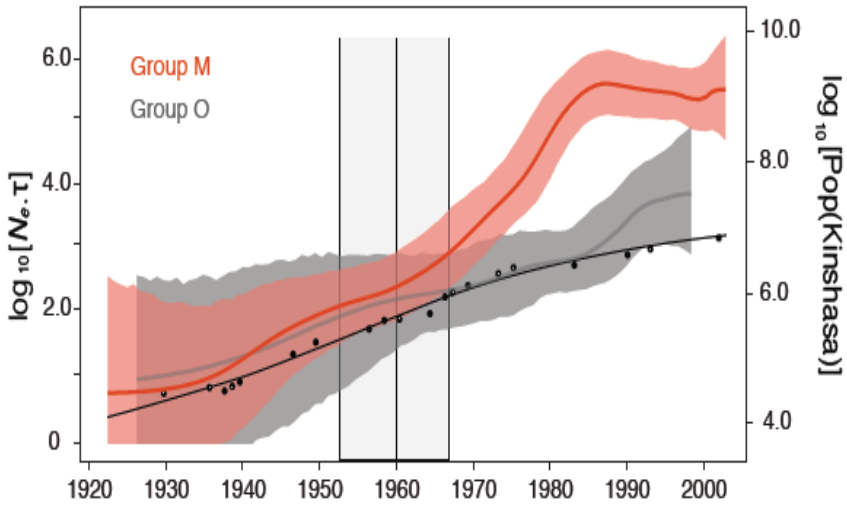
**Most emergent/new infectious diseases are zoonosis**

**Cross-species jumps are frequent but the microorganisms need to be**
**Viable in humans**
**Pathogenic for humans**
**Transmissible between humans**
**& more …….**

**Consequently: New/emergent infectious diseases will happen but is not predictable when, is not an easy phenomenon and may take time**

## Divergent growth trajectories of HIV-1 groups M and O

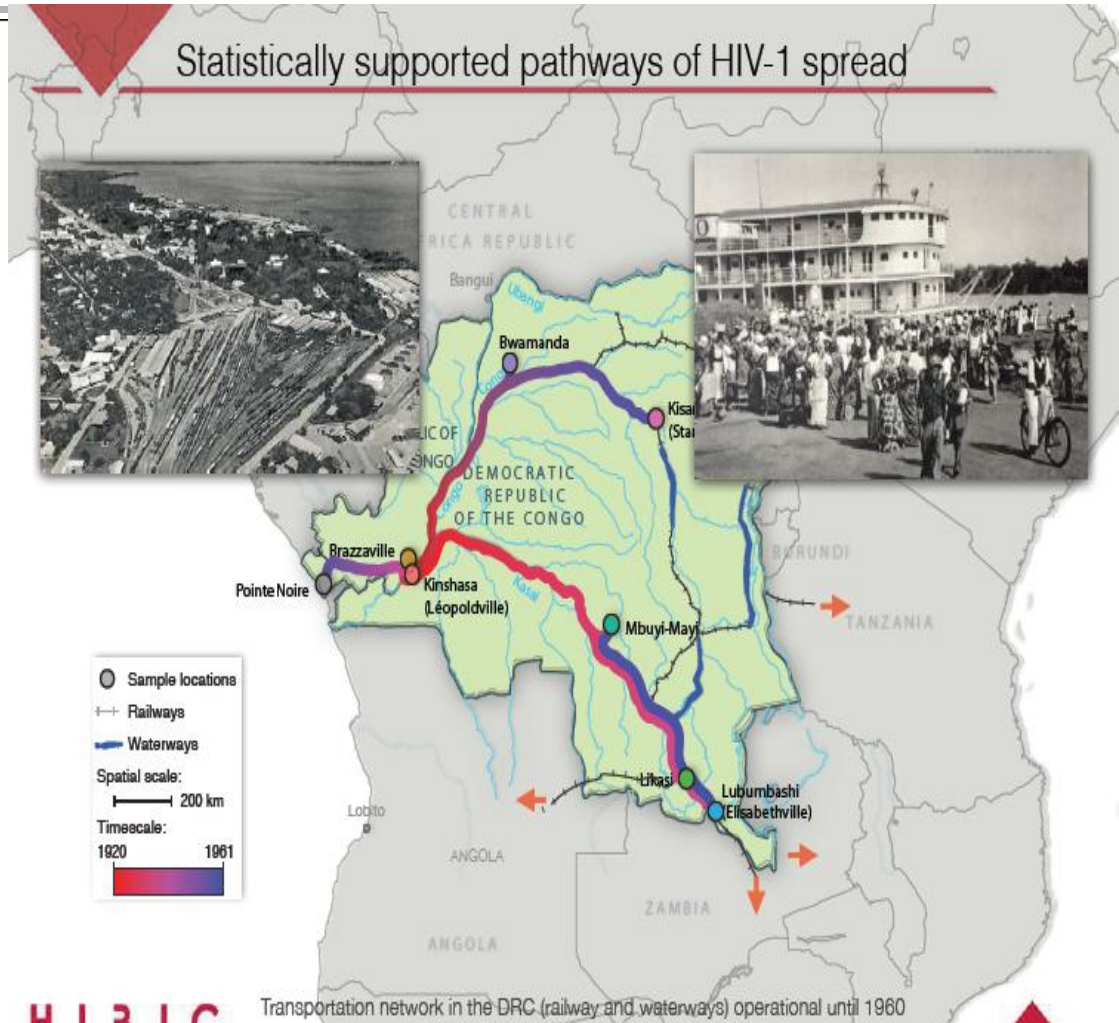
Group M transitioned from a early phase of slower exponential growth to 'super-exponential' growth sometime during 1952-68.




## Statistically supported pathways of HIV-1 spread







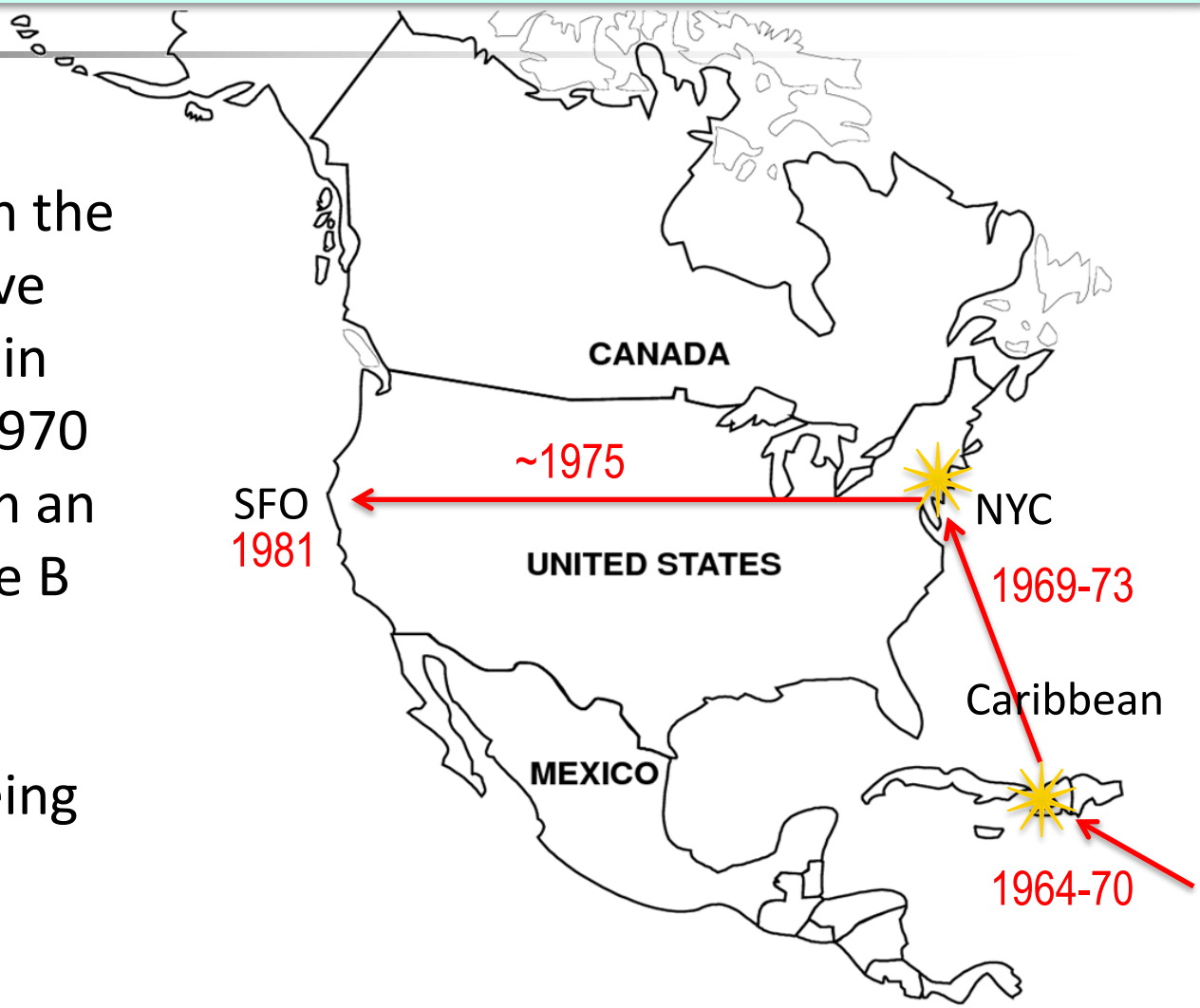

Transportation network in the DRC (railway and waterways) operational until 1960 (adapted from Huybrechts, Mouton, 1970).


HIBIC

# Early History of the North American HIV/AIDS Epidemic (#140)

By 1978-79 the HIV-1 epidemic in the U.S. already exhibited extensive genetic diversity –particularly in NYC– having emerged around 1970 from a founder virus drawn from an older and more diverse subtype B epidemic in the Caribbean

No evidence for patientt “0” being really “Zero”



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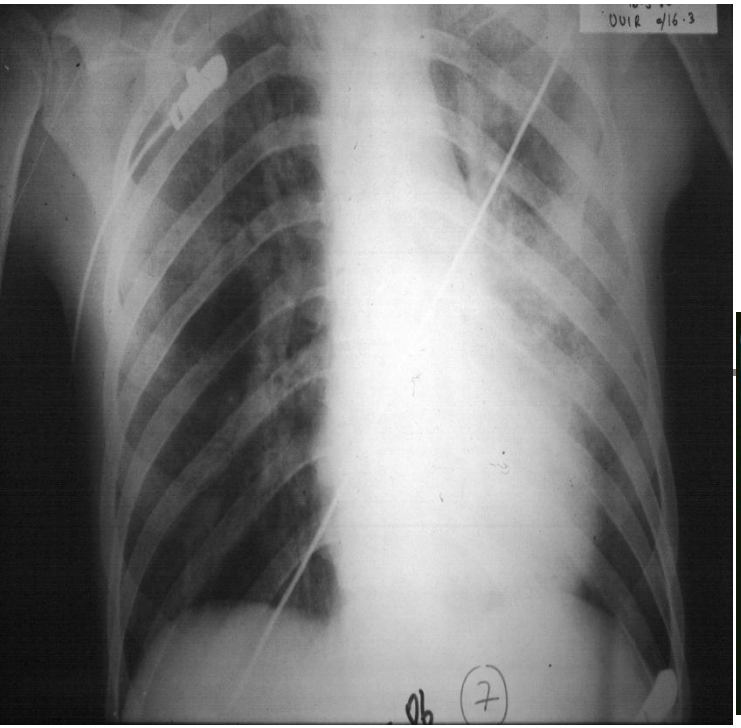
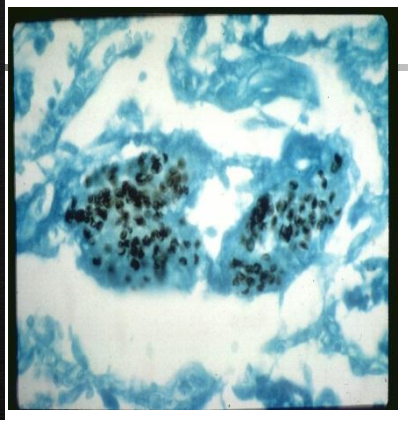


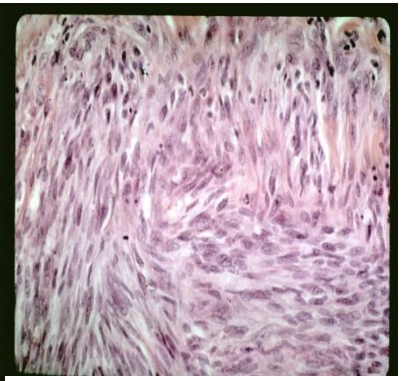
HSH



MGH 1811

1982


## PCP y SK (1981: NY y San Fran.)



ORIGINALES

Med Clin (Barc.), 1987

# Informe epidemiológico de 20 casos consecutivos de síndrome de inmunodeficiencia adquirida

Comisión* para el Estudio y Control del SIDA. Redactores de este informe: X. Latorre, J. M. Gatell y M. Baradad

*Hospital Clínic i Provincial. Barcelona*
**Comisión para el Estudio y Control del SIDA: Dr. R. Castillo (Presidente), Dra. T. Gallart (Secretaria) y Dres. J. M. Mascaró, M. Bruguera, J. M. Gatell, J. García San Miguel y M. T. Jiménez de Anta.*

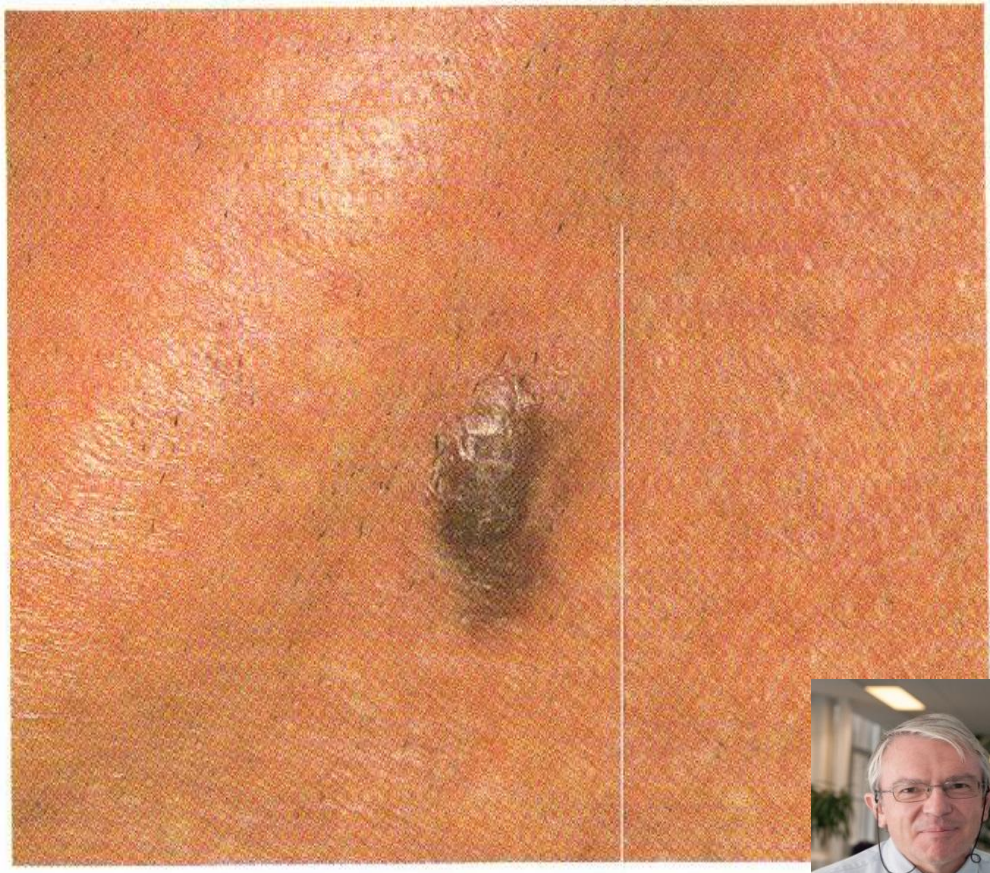


*Fig. 2. Lesiones cutáneas del sarcoma de Kaposi.*

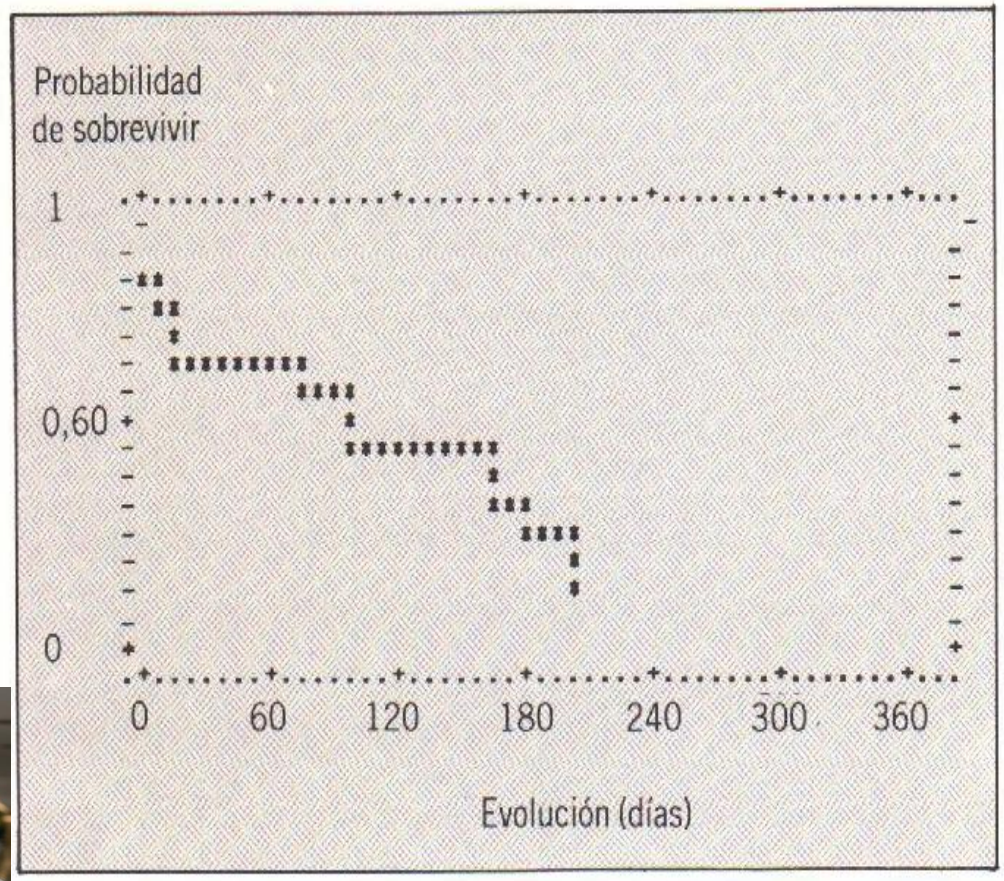



*Fig. 3. Probabilidad de supervivencia actuarial de 20 casos de pacientes con SIDA.*

# Prevalencia de anticuerpos frente al HTLV-III/LAV en subpoblaciones con riesgo de padecer un síndrome de inmunodeficiencia adquirida

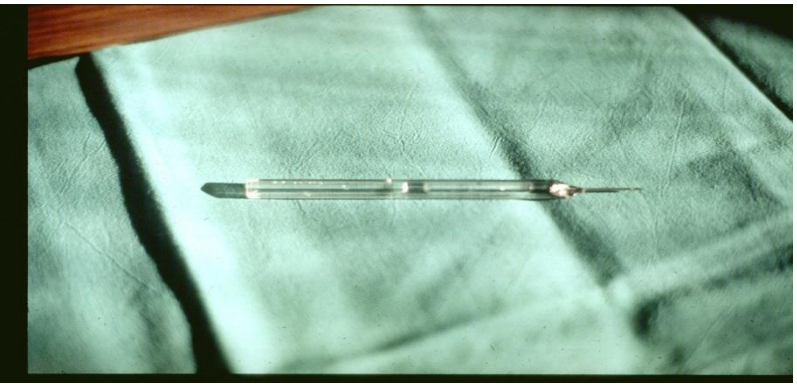
Med Clin (Barc), 1986

X. Latorre, J.M. Gatell, T. Pumarola, J.M. Miró, C. Laborí, M. Pifarré, J. Vidal, M.T. Jiménez de Anta, E. Soriano, A. Pumarola y J. García San Miguel

TABLA 2

## Prevalencia de anticuerpos anti-HTLV-III/LAV en los grupos estudiados

| | N.º de muestras estudiadas | N.º de muestras positivas (%) |
|---|---|---|
| Drogadictos | 48 | 23 (48) |
| Homosexuales | 61 | 16 (26) |
| Prostitutas | 41 | 0 (0) |
| Controles | 50 | 0 (0) |



ARTÍCULO ESPECIAL

# Estudio multicéntrico de las complicaciones infecciosas en adictos a drogas por vía parenteral en España: análisis final de 17.592 casos (1977-1991)

Grupo de Trabajo para el Estudio de Infecciones en Drogadictos

Correspondencia: Dr. J.M. Miró.
Servicio de Enfermedades Infecciosas.
Hospital Clínic i Provincial de Barcelona.
Villarroel, 170. 08036 Barcelona.

Coordinación del estudio: J.M. Miró y J.M. Gatell.
Servicio de Enfermedades Infecciosas.
Hospital Clínic i Provincial de Barcelona.

Manuscrito recibido el 2-12-1994; aceptado el 17-5-1995.

Trabajo parcialmente financiado por algunas ayudas concedidas por el Plan Nacional sobre Drogas del Ministerio de Sanidad y Consumo por la Fundación Máximo Soriano Jiménez.

*Enferm Infecc Microbiol Clin* 1995; 13: 532-539.

*ORIGINALES*

# Endocarditis infecciosa en drogadictos. Presentación de 25 casos procedentes del área de Barcelona

J.M. Gatell*, J.M. Miró*, J. Mensa*, M.A. Moreno*, J. Mañá*, F. Segura**, J. Paré***, P. Nadal****, M. Ingelmo+, A. Urbano Márquez++, M.T. Jiménez de Anta+++ y J. García San Miguel*

*Servicios de Enfermedades Infecciosas, Cardiología, Area de Vigilancia Intensiva, Patología General, Medicina Interna C y Microbiología. Hospital Clínico y Provincial de Barcelona. Clínica de la Mare de Déu de la Salut. Sabadell*

Publicado en la Revista MEDICINA CLINICA
Vol. 80 - Núm. 7 - 5 de Marzo 1983 - Págs. 293 al 299

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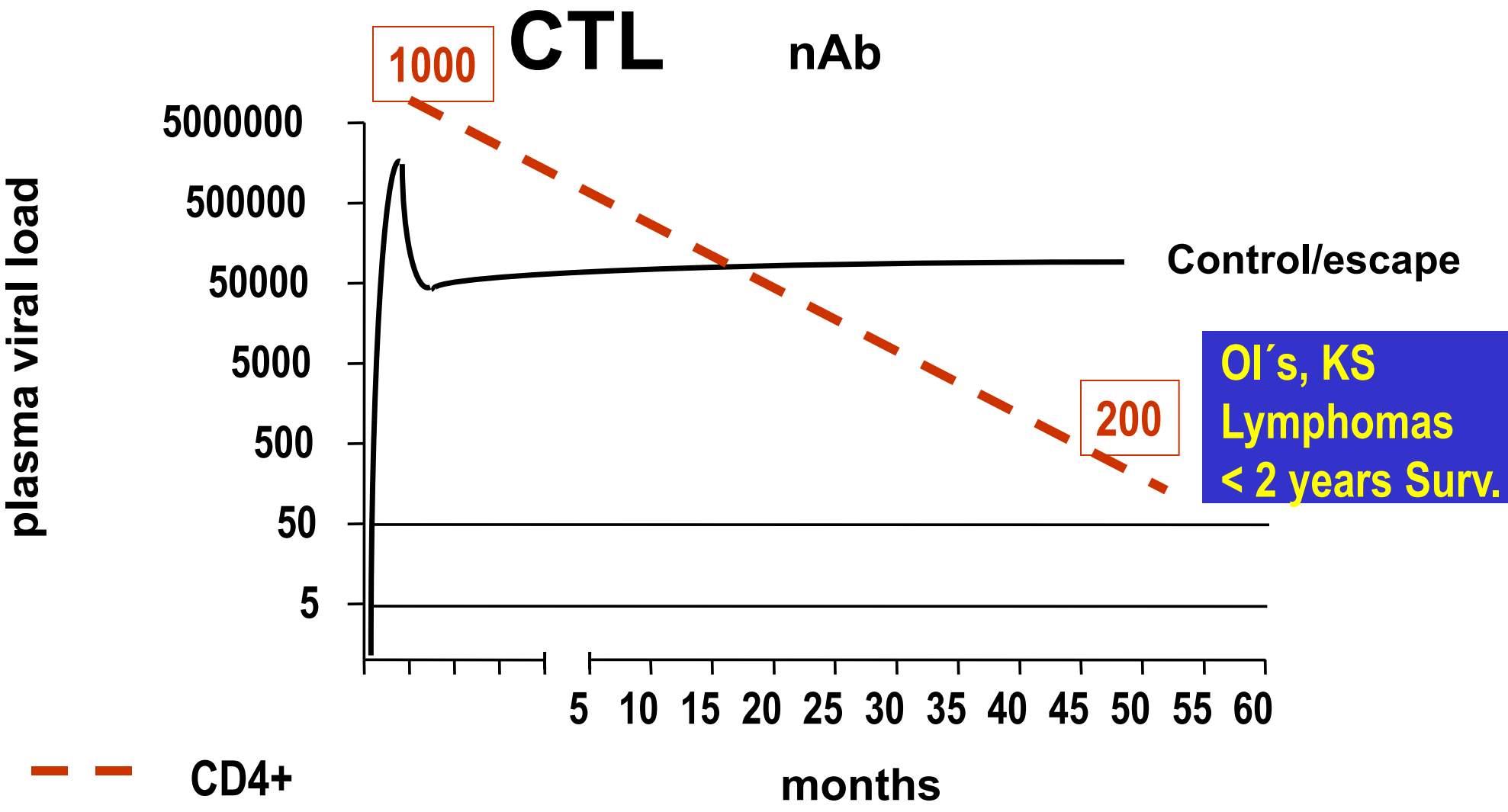
Loto.Nero


CTL
nAb
1000
200
plasma viral load
5000000
500000
50000
5000
500
50
5
Control/escape
Ol´s, KS
Lymphomas
< 2 years Surv.
5 10 15 20 25 30 35 40 45 50 55 60
months
CD4+

# Characteristics of tuberculosis in HIV-infected patients: a case-control study

AIDS, 1988

Eladio Soriano, Josep Mallolas, Josep M. Gatell, Xavier Latorre, Josep M. Miró, Mirta Pecchiar, Josep Mensa, Antoni Trilla and Asunción Moreno

**Table 2.** Localization of the tuberculosis in the cases and in the controls.

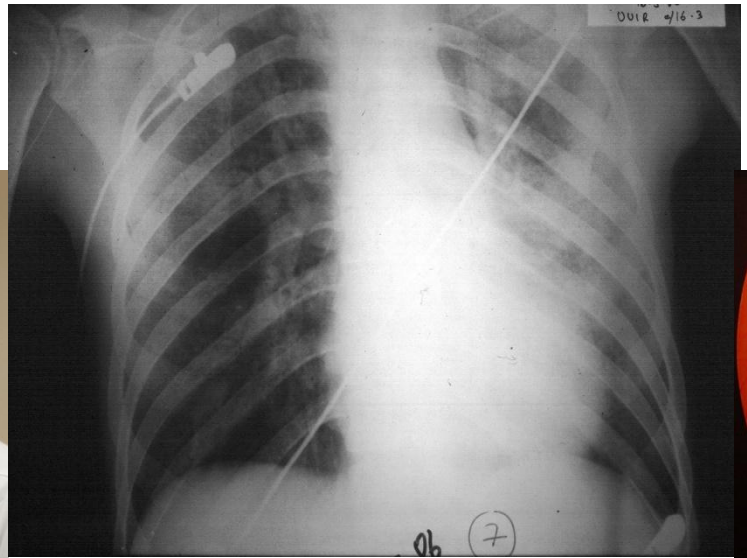
| | Cases | | Controls | |
|---|---|---|---|---|
| | n | % | n | % |
| Only lung | 25 | 39 | 59 | 91 |
| Lung and other | 39 | 60 | 60 | 92 |
| Only lymph nodes | 20 | 31 | 0 | |
| Lymph nodes + other | 25 | 39 | 0 | |
| Bone or joint involvement | 8 | 12 | 1 | 2 |
| Central nervous system involvement | 5 | 8 | 1 | 2 |
| Disseminated forms | 7 | 11 | 0 | |

NS, not significant

# Central nervous system toxoplasmosis in AIDS patients: efficacy of an intermittent maintenance therapy

Enric Pedrol, José M. González-Clemente, Josep M. Gatell, Josep Mallolas, Josep M. Miró, Francesc Graus*, Ramiro Alvarez*, Josep M. Mercader†, Joan Berenguer†, M. Teresa Jiménez de Anta‡, M. Eugenia Valls‡ and Eladio Soriano

AIDS, 1990



Eur J Clin Microbiol Infect Dis (1999) 18:473–477



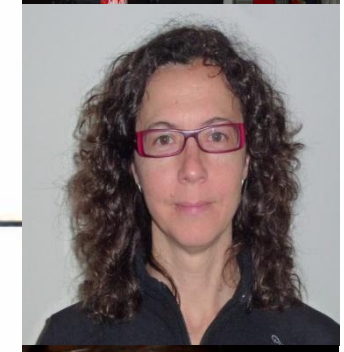
*Article*

# *Pseudomonas aeruginosa* Bacteremia in Patients In with Human Immunodeficiency Virus Type 1

F. Vidal, J. Mensa, J.A. Martínez, M. Almela, F. Marco, J.M. Gatell, C. Rich
E. Soriano, M.T. Jiménez de Anta

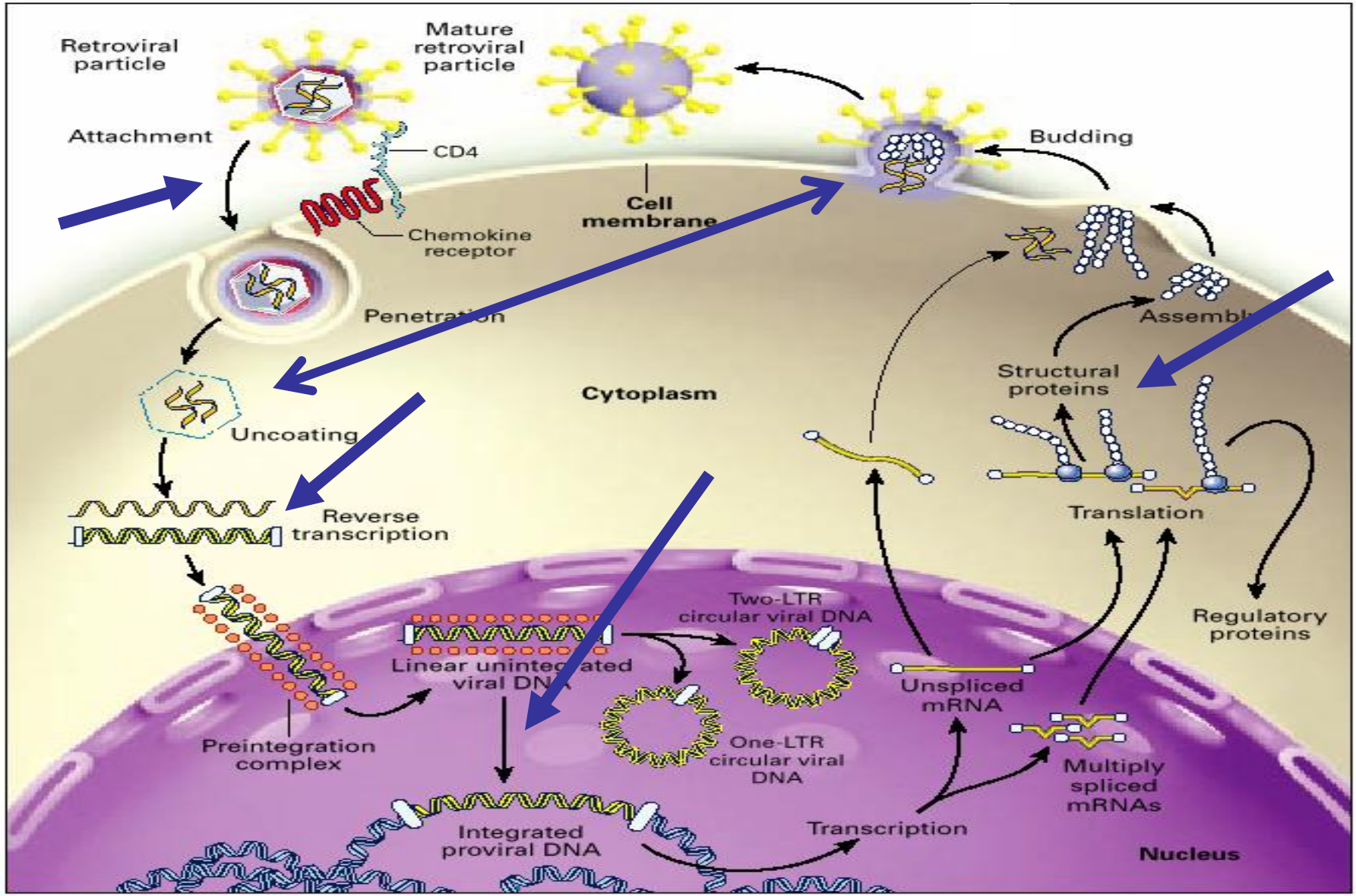
**Table 1** Incidence and mortality of *Pseudomonas a* bacteremia among patients with different high-risk clini tions

| Clinical condition | No. of patients admitted | No. of episodes of *P. aeruginosa* bacteremia | No. of episodes of *P. aeruginosa* bacteremia/ 1000 admittances |
|---|---|---|---|
| All | 219.692 | 283 | 1.3 |
| Cancer | 19.973 | 39 | 2 |
| SOT | 1.096 | 26 | 24* |
| BMT | 403 | 19 | 47* |
| Leukemia | 1.101 | 26 | 24* |
| Lymphoma | 1.056 | 27 | 26* |
| ICU | 6.048 | 58 | 9.6* |
| HIV-1 | 4.283 | 43 | 10* |



*$P < 0.05$

SOT, solid organ transplantation; BMT, bone marrow t tation; ICU, hospitalization in the intensive care unit


Retroviral particle
Mature retroviral particle
Attachment
CD4
Chemokine receptor
Cell membrane
Budding
Penetration
Assembly
Structural proteins
Cytoplasm
Uncoating
Reverse transcription
Translation
Two-LTR circular viral DNA
Linear unintegrated viral DNA
Regulatory proteins
Unspliced mRNA
Preintegration complex
One-LTR circular viral DNA
Multiply spliced mRNAs
Integrated proviral DNA
Transcription
Nucleus

# Comparison of ribavirin and placebo in CDC group III human immunodeficiency virus infection

SPANISH RIBAVIRIN TRIAL GROUP

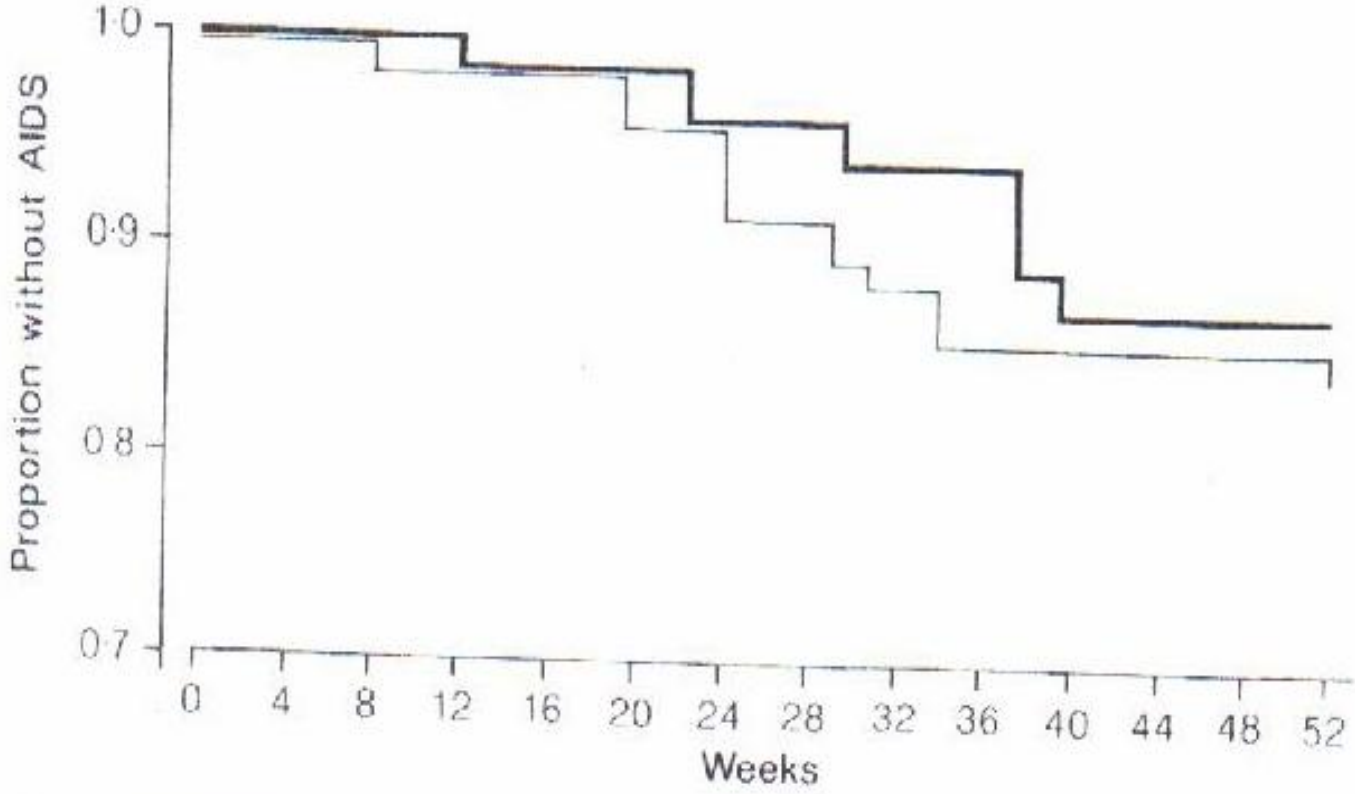



**Fig 1—Estimated cumulative probability of progression to AIDS: life-table analysis.**

——— ribavirin; ——— placebo.

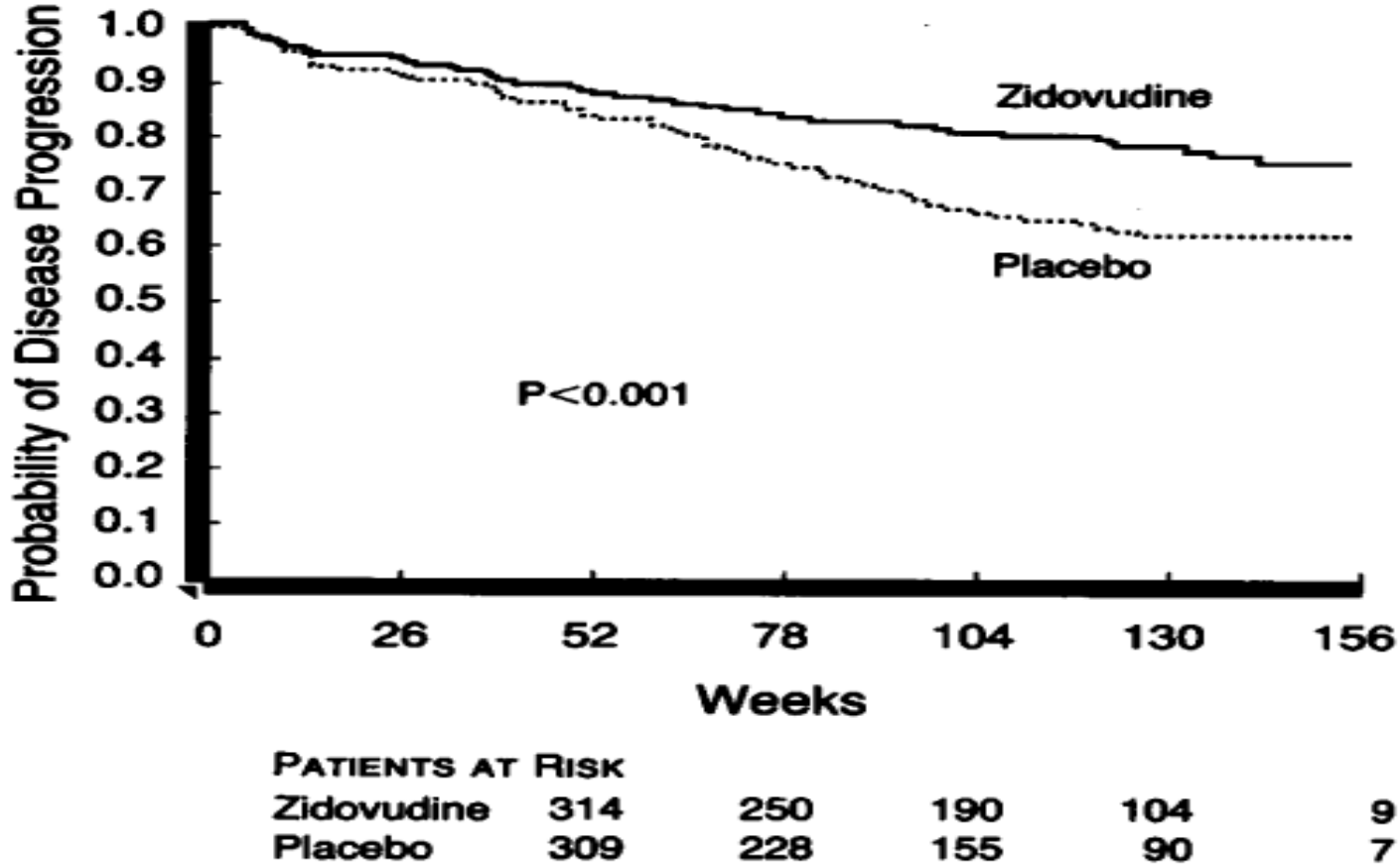
The New England
Journal of Medicine



Volume 329 JULY 29, 1993 Number 5

# ZIDOVUDINE IN PERSONS WITH ASYMPTOMATIC HIV INFECTION AND CD4+ CELL COUNTS GREATER THAN 400 PER CUBIC MILLIMETER

DAVID A. COOPER, M.D., JOSÉ M. GATELL, M.D., PH.D., SUSANNE KROON, M.D., NATHAN CLUMECK, M.D., JUDITH MILLARD, PH.D., FRANK-D GOEBEL, M.D., JOHAN N. BRUUN, M.D., GEORG STINGL, M.D., REX L. MELVILLE, M.B., JUAN GONZÁLEZ-LAHOZ, M.D., PH.D., JOHN W. STEVENS, B.SC., A. PAUL FIDDIAN, M.B., AND THE EUROPEAN–AUSTRALIAN COLLABORATIVE GROUP*



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# Hospital Clinic. Barcelona, June 2013. N=4500

Fig

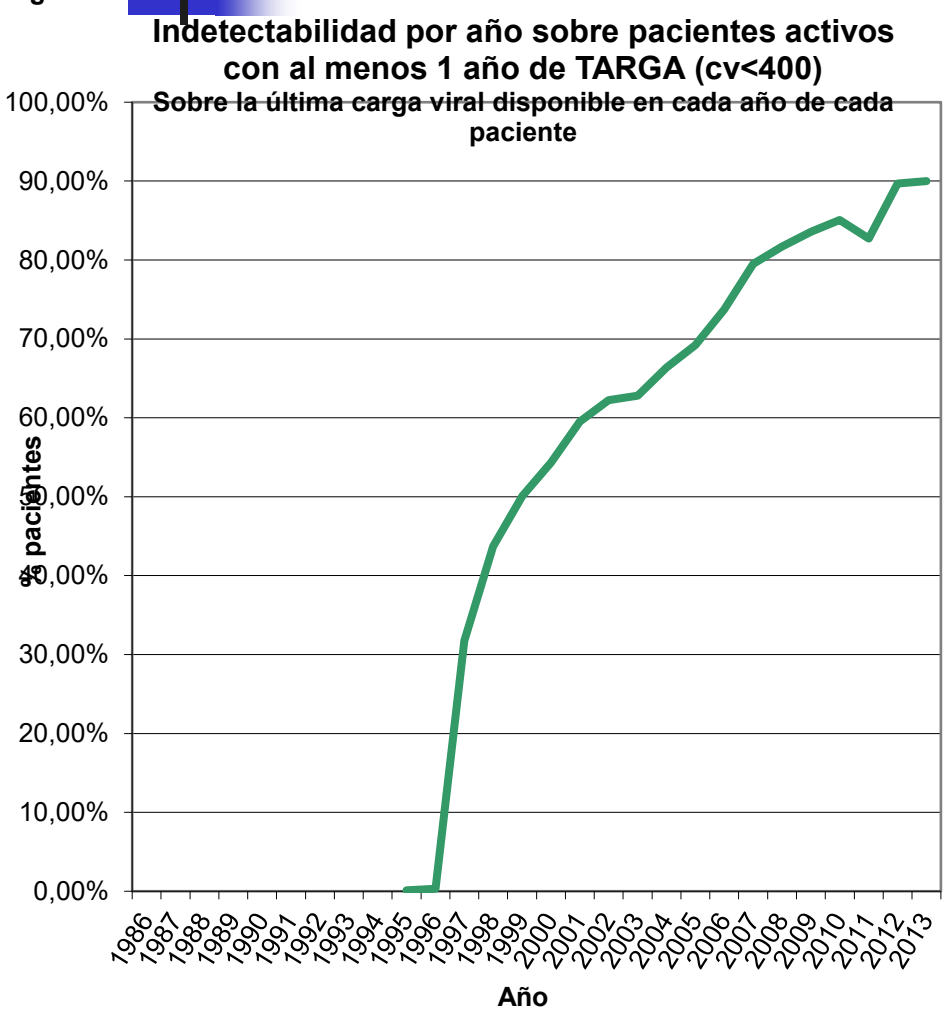
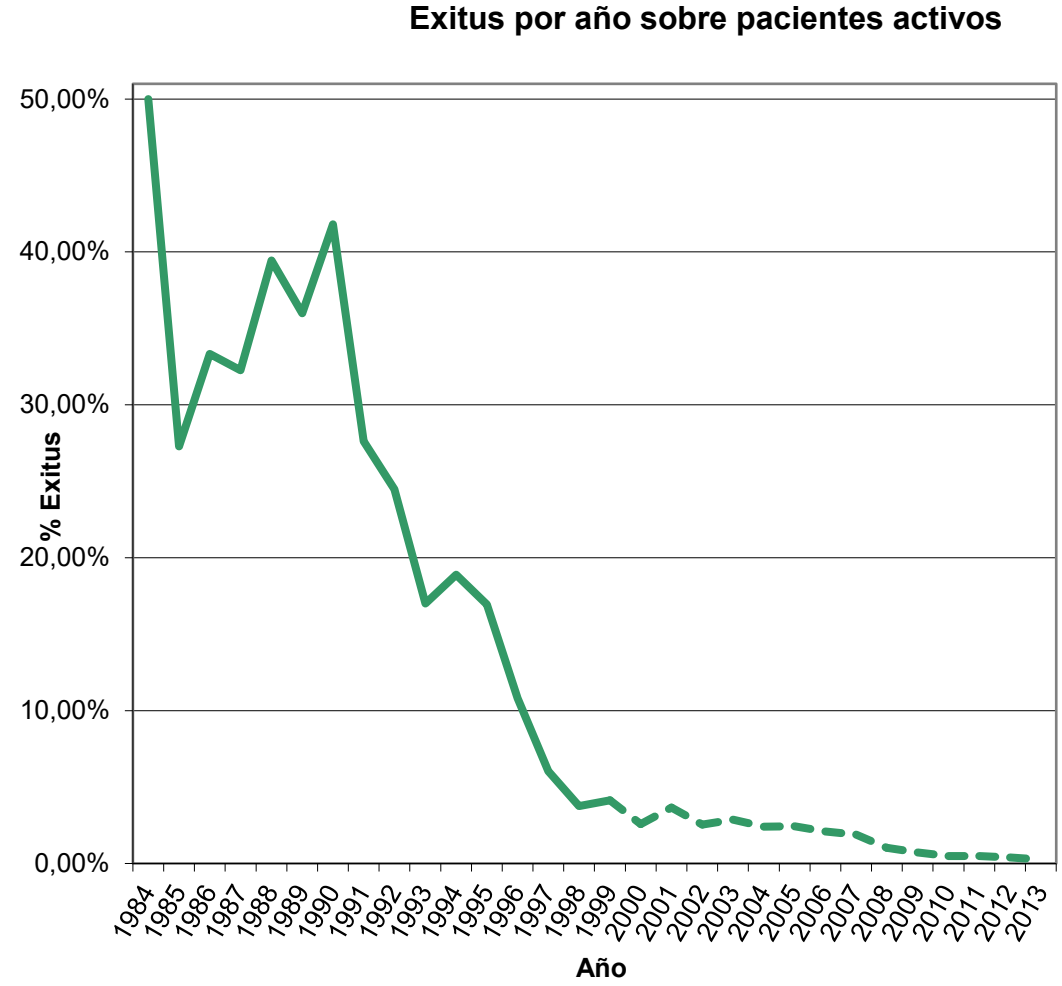



Fig.

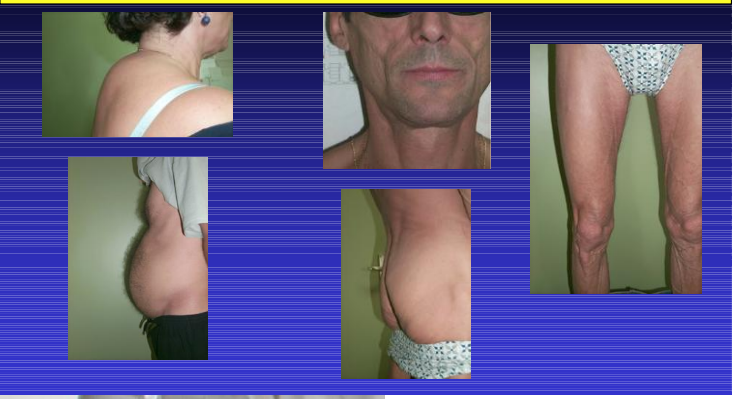


# Risk of lipodystrophy in HIV-1-infected patients treated with protease inhibitors: a prospective cohort study

Lancet, 2001

*Esteban Martinez, Amanda Mocroft, Miguel A García-Viejo, José B Pérez-Cuevas, José L Blanco, José Mallolas, Luis Bianchi, Ignacio Conget, Jordi Blanch, Andrew Phillips, José M Gatell*

**Lipodystrophy is easy to diagnose**



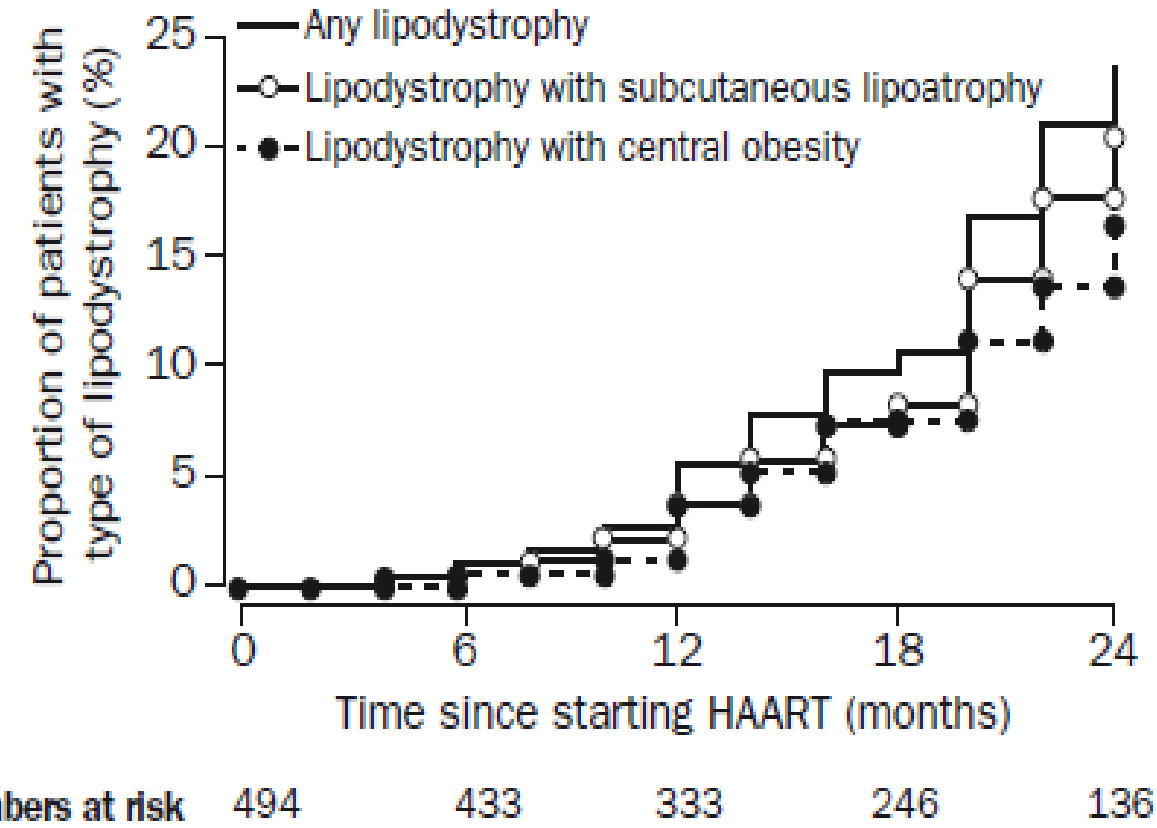



Figure 3: **A Kaplan-Meier curve showing progression to any lipodystrophy**

CID, 2004

# Mitochondrial Effects of HIV Infection on the Peripheral Blood Mononuclear Cells of HIV-Infected Patients Who Were Never Treated with Antiretrovirals

Òscar Miró,[1] Sònia López,[1] Esteban Martínez,[2] Enric Pedrol,[3] Ana Milinkovic,[2] Elisabeth Deig,[3] Glòria Garrabou,[1] Jordi Casademont,[1] Josep M. Gatell,[2] and Francesc Cardellach[1]

[1]Mitochondrial Research Laboratory, Muscle Research Unit, Department of Internal Medicine, and [2]Infectious Disease Unit, Hospital Clínic, August Pi i Sunyer Biomedical Research Institute, School of Medicine, University of Barcelona, Barcelona, and [3]HIV-Unit, Department of Internal Medicine, Fundació Hospital–Asil de Granollers, Granollers, Catalonia, Spain

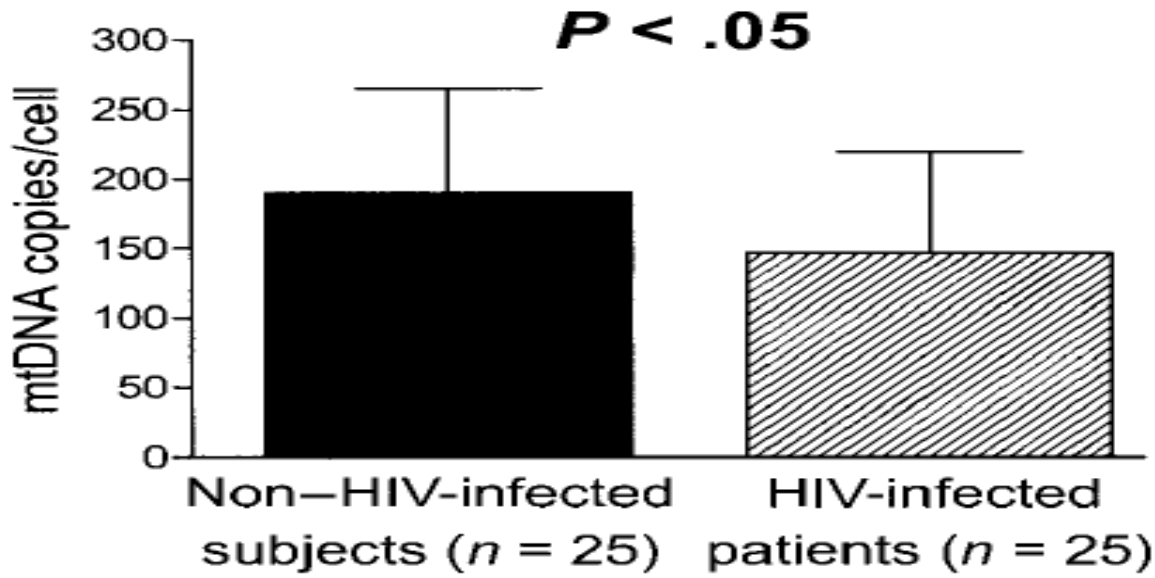



**Figure 1.** Quantification of mtDNA. Bars denote the results (expressed as mean values ± SD) for each group. Antiretroviral-naive HIV-infected individuals had a significant decrease in the number of mtDNA copies per PBMC, compared with healthy (non–HIV-infected) individuals. Comparison between groups was performed using Student's *t* test. $P < .05$ denoted statistical significance.

# Factors Associated with Severe Impact of Lipodystrophy on the Quality of Life of Patients Infected with HIV-1

CID, 2004

**Jordi Blanch,[1] Araceli Rousaud,[2] Esteban Martínez,[3] Elisa De Lazzari,[4] Ana Milinkovic,[3] Josep-Maria Peri,[1] José-Luís Blanco,[3] Jesús Jaen,[1] Victor Navarro,[1] Guillem Massana,[1] and Josep-Maria Gatell[3]**

[1]Clinical Institute of Psychiatry and Psychology, [2]Fundació Clínic per a la Recerca Biomèdica—Institut d'Investigacions Biomèdiques Agustí Pi i Sunyer, [3]Clinical Institute of Infectious Diseases and Immunology, and [4]Epidemiology and Biostatistics Unit, Hospital Clínic Universitari de Barcelona, Spain

**Table 4. Result of univariate and multivariate analysis of significant factors associated with the degree of quality of life impairment, as measured by the Dermatology Life Quality Index (DLQI).**

| | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| Variable | β | 95% CI | P | β | 95% CI | P |
| Time since diagnosis of HIV-1 infection[a] | 0.011 | 0.002–0.020 | .014 | … | … | … |
| Injection drug use[b] | 0.951 | 0.009–1.893 | .048 | … | … | … |
| Severity of side effects[a] | 0.952 | 0.454–1.450 | <.001 | 0.662 | 0.174–1.151 | .008 |
| LD changes, by location | | | | | | |
| Breast | 1.563 | 0.537–2.589 | .003 | 1.322 | 0.370–1.371 | .001 |
| Face | 0.827 | 0.034–1.620 | .041 | … | … | … |
| Legs | 0.986 | 0.048–1.925 | .039 | … | … | … |

**NOTE.** The degree of quality of life impairment was evaluated by means of the proportional odds model, with the total score of the DLQI serving as the dependent variable and divided into 4 categories: mild impairment (score range, 0–2.5), moderate impairment (score range, 2.5–5), considerable impairment (score range, 5–9), and major impairment (score, >9). Variables with a significant *P* value in the univariate model were entered in the multivariate model. HIV-1, HIV type 1.

[a] Continuous variable.
[b] Compared with other routes of transmission.

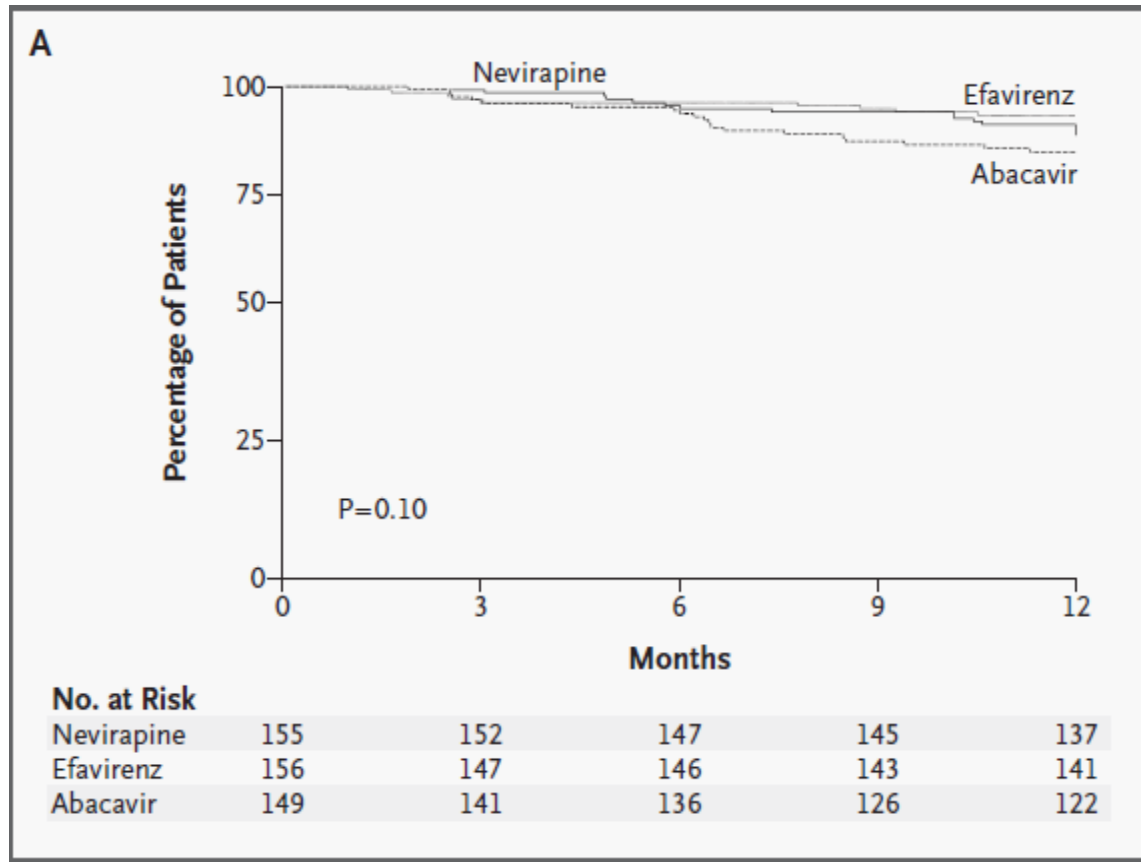
The NEW ENGLAND JOURNAL of MEDICINE

2003

ORIGINAL ARTICLE

# Substitution of Nevirapine, Efavirenz, or Abacavir for Protease Inhibitors in Patients with Human Immunodeficiency Virus Infection

Esteban Martínez, M.D., Juan A. Arnaiz, M.D., Daniel Podzamczer, M.D., David Dalmau, M.D., Esteban Ribera, M.D., Pere Domingo, M.D., Hernando Knobel, M.D., Melcior Riera, M.D., Enric Pedrol, M.D., Lluis Force, M.D., Josep M. Llibre, M.D., Ferran Segura, M.D., Cristóbal Richart, M.D., Cristina Cortés, M.D., Manuel Javaloyas, M.D., Miquel Aranda, M.D., Ana Cruceta, M.D., Elisa de Lazzari, B.Sc., and José M. Gatell, M.D., for the Nevirapine, Efavirenz, and Abacavir (NEFA) Study Team*




| No. at Risk | | | | | |
|---|---|---|---|---|---|
| Nevirapine | 155 | 152 | 147 | 145 | 137 |
| Efavirenz | 156 | 147 | 146 | 143 | 141 |
| Abacavir | 149 | 141 | 136 | 126 | 122 |

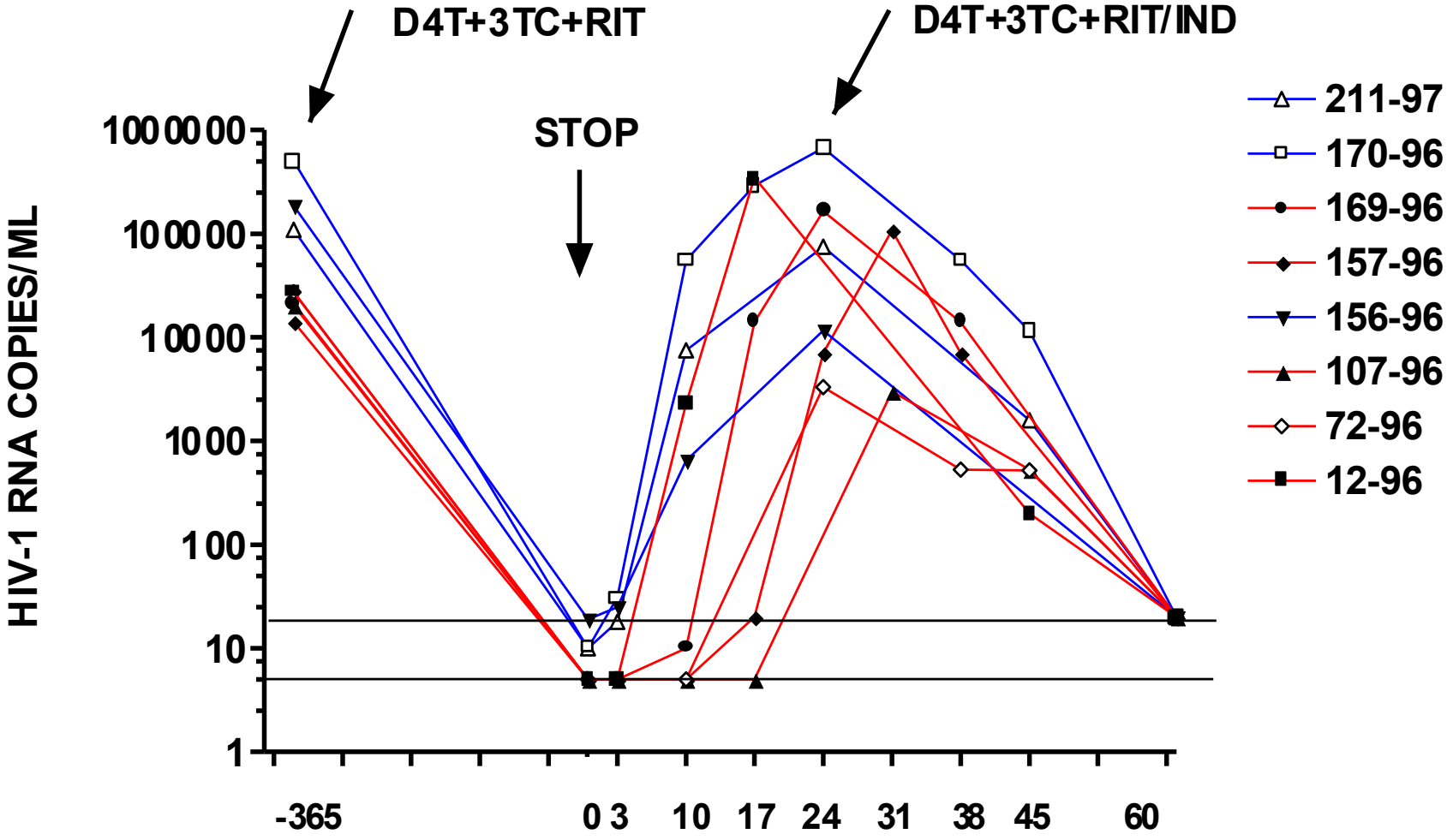
FAST TRACK

# Dynamics of viral load rebound and immunological changes after stopping effective antiretroviral therapy

Felipe García[a], Montserrat Plana[b], Carmen Vidal[c], Anna Cruceta[a], William A. O´Brien[d], Giuseppe Pantaleo[e], Tomás Pumarola[c], Teresa Gallart[b], José M. Miró[a] and José M. Gatell[a]

AIDS, 1999

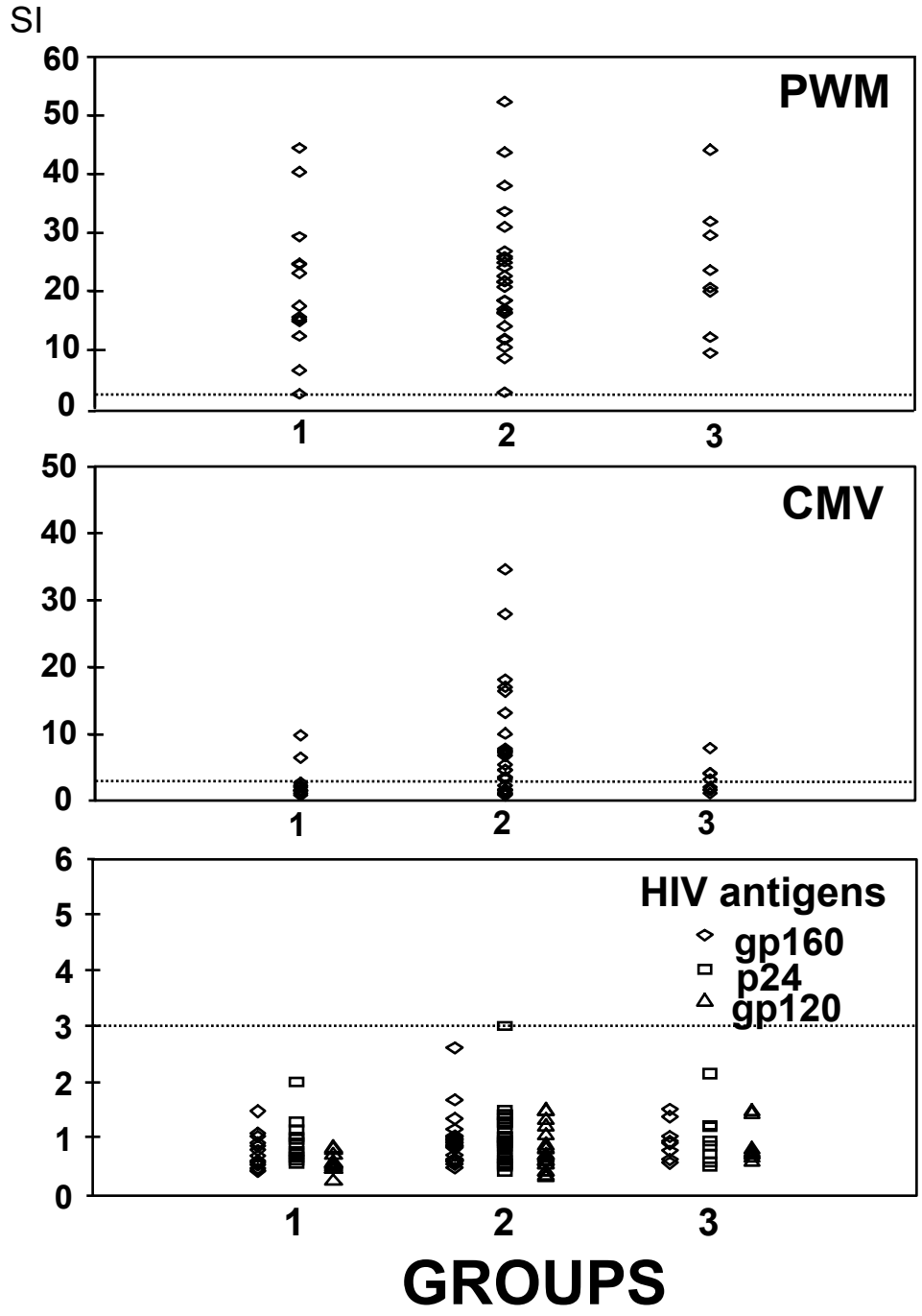
# SPANISH EARTH-1 STUDY (CD4>500 AND VL >10000). STOP THERPAY AFTER 1 YEAR OF D4T+3TC+RIT/IND AND VL<20




Garcia F et al AIDS, 1999

**GROUP 1 (13)**
**HIV +;**
**CD4>500**
**UNTREATED**

**GROUP 3 (8)**
**HIV -**




**GROUP 2 (26)**
**HIV +;**
**CD4>500**
**1 YEAR Rx**

**N = 8**
**TRIPLE**
**VL < 20**

**N=18**
**DOUBLE**
**VL 200-19512**

Lancet, 1998

# Comparación de tres métodos de cálculo de adherencia en pacientes con tratamiento antirretroviral

Carlos Codina[a], Mireia Martínez[a], Montserrat Tuset[c], Elena del Cacho[a], María Teresa Martín[a], José M. Miró[b], Josep Mallolas[b], Elisa De Lazzari[c], Felipe García[b], Esteban Martínez[b], José M. Gatell[b] y Josep Ribas[a]

[a]Servicio de Farmacia. [b]Instituto Clínico de Infecciones e Inmunología. [c]Unidad de Epidemiología y Bioestadística. Hospital Clínic. Instituto de Investigación Biomédica Agustí Pi Sunyer (IDIBAPS). Universidad de Barcelona. Barcelona. España.

El TARGA hay que tomarlo
y evitar las interacciones

EIMC, 2002

# HIV/AIDS 1920-2025:

## The pandemic of XX-XXI centuries: From darkness to sunshine

1. A few basic concepts
2. 1981-85: 5 years of darkness
3. 1986-95: 10 years of moonlight
4. 1996-12: 15 years of sunrise
5. 2013-18: 5 years of sunshine
6. 2025: Where are we now ?
7. Some final considerations

- Treat them all. Limitations of HAART
- We need new and better drugs
- DAA for HCV
- Therapeutic and preventative vaccines

- Life expectancy similar (sometime better) compared with matched general population

# Viral load in asymptomatic patients with CD4+ lymphocyte counts above $500 \times 10^6$/l

Felipe García, Carmen Vidal*, José M. Gatell, José M. Miró, Alex Soriano and Tomás Pumarola*

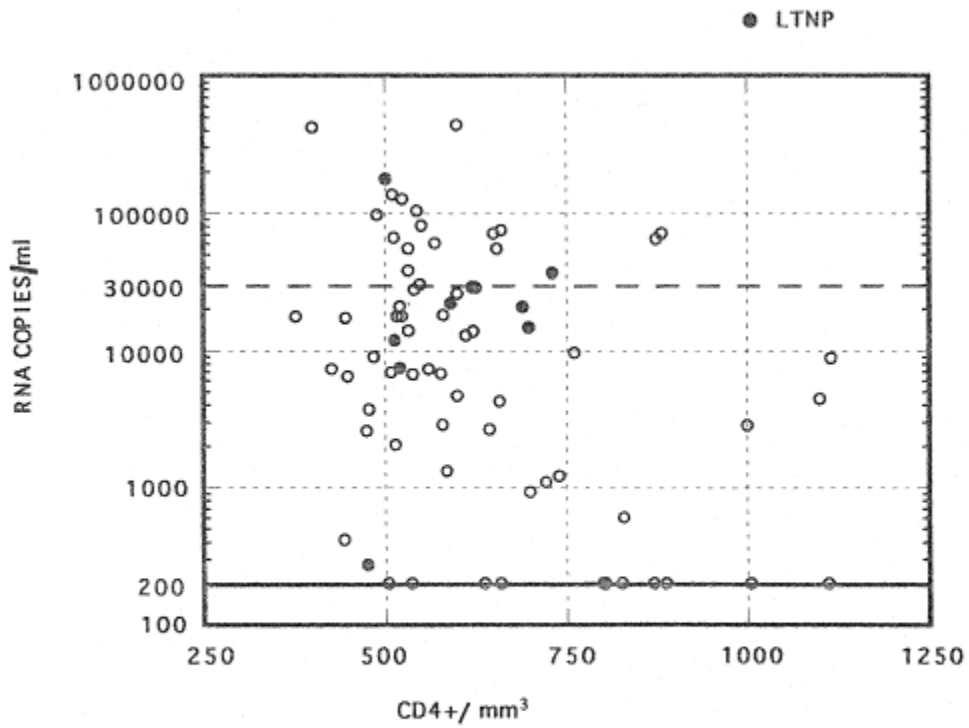



**Fig. 2.** Relationship between baseline CD4+ T-cell counts ($\times 10^6$/l) and plasma HIV-1 RNA concentration ($\log_{10}$ scale). LTNP, long-term non-progressors.

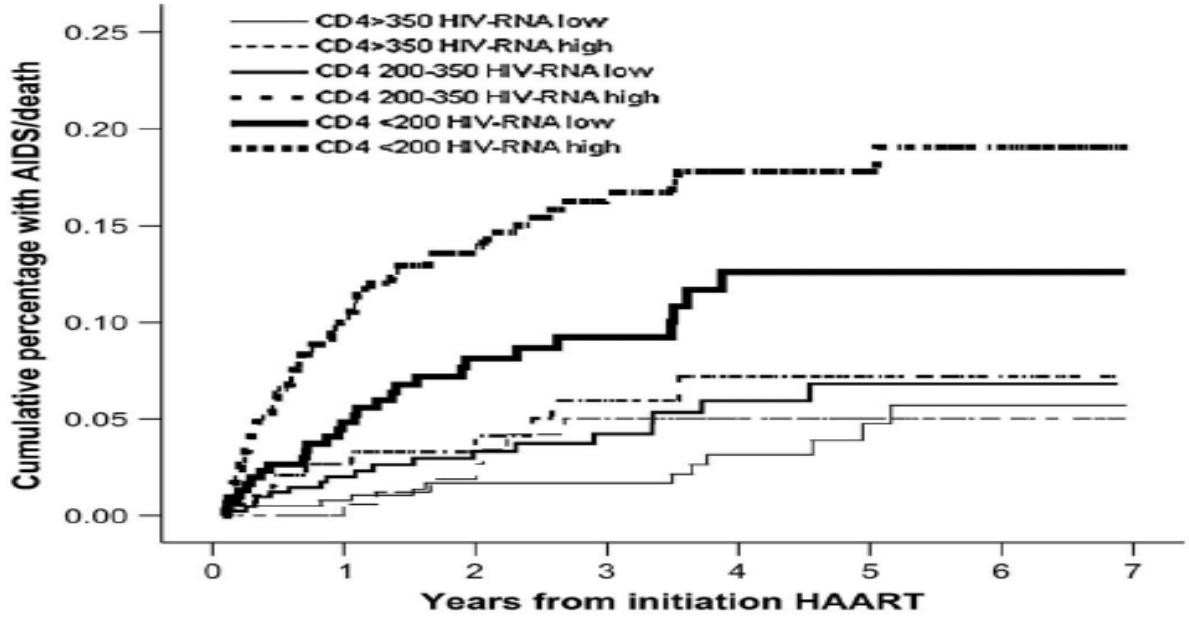
AIDS, 1997

# Determinants of HIV Progression and Assessment of the Optimal Time to Initiate Highly Active Antiretroviral Therapy

## *PISCIS Cohort (Spain)*

*Ángeles Jaén, MD, PhD,*[‖‖] Anna Esteve, PhD,*¶¶ Josep M. Miró, MD, PhD,† Cristina Tural, MD, PhD,‡ Alexandra Montoliu, BSc,*¶¶ Elena Ferrer, MD,§ Melcior Riera, MD, PhD,[‖] Ferran Segura, MD, PhD,¶ Lluis Force, MD, PhD,# Omar Sued, MD, PhD,† Josep Vilaró, MD,** Isabel Garcia, MD,†† Angels Masabeu, MD,‡‡ Jordi Altès, MD,§§ Bonaventura Clotet, MD, PhD,‡ Daniel Podzamczer, MD, PhD,§ Javier Murillas, MD, PhD,[‖] Gemma Navarro, MD, PhD,¶ Josep M. Gatell, MD, PhD,† Jordi Casabona, MD, MPH, PhD,*¶¶## and the PISCIS Study Group*

JAIDS, 2008




| | n | AIDS/death | HR* | 95% CI** | p*** |
|---|---|---|---|---|---|
| **CD4/HIV-1 RNA** | | | | | <0.001 |
| **>350, <100,000** | 399 | 12 | 1 | — | — |
| **>350, ≥100,000** | 204 | 7 | 1.24 | 0.49-3.14 | 0.656 |
| **200-350, <100,000** | 420 | 18 | 1.59 | 0.76-3.30 | 0.215 |
| **200-350, ≥100,000** | 194 | 10 | 1.93 | 0.83-4.47 | 0.124 |
| **<200, <100,000** | 307 | 28 | 3.39 | 1.72-6.67 | <0.001 |
| **<200, ≥100,000** | 417 | 63 | 5.88 | 3.17-10.91 | <0.001 |

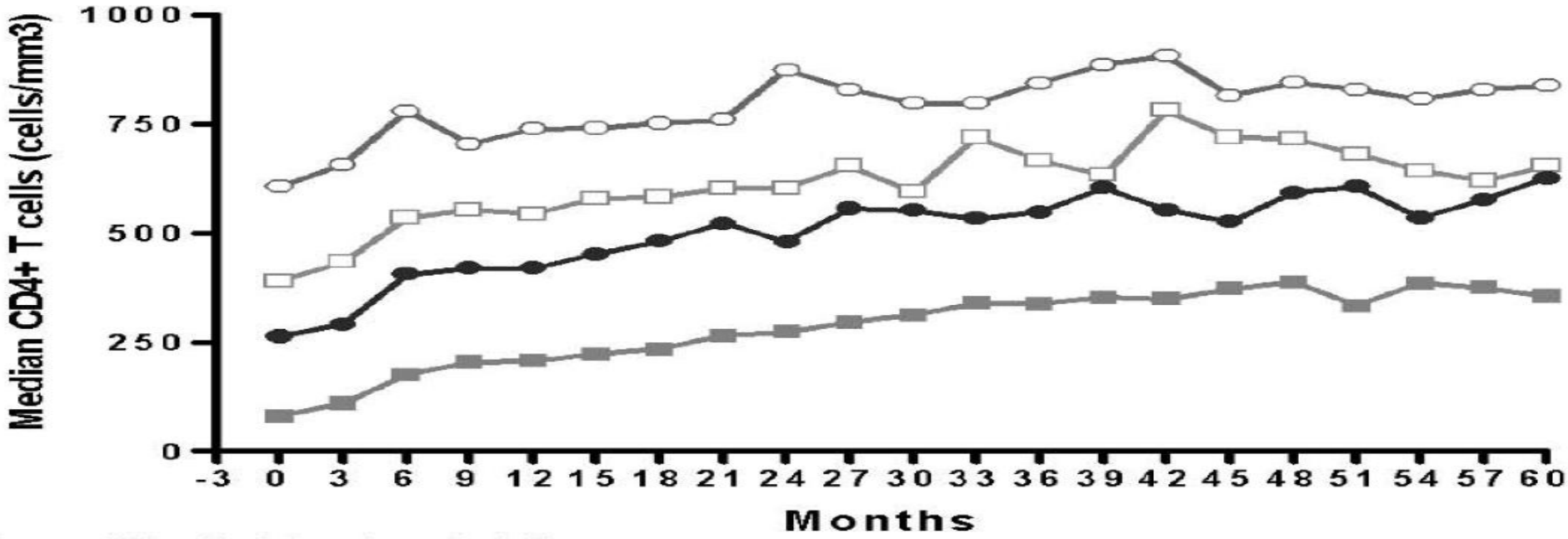
**Hazard ratio (HR); ** 95% confidence interval (95%CI); *** Trend Test

# Long-Term CD4+ T-Cell Response to Highly Active Antiretroviral Therapy According to Baseline CD4+ T-Cell Count

JAIDS, 2004

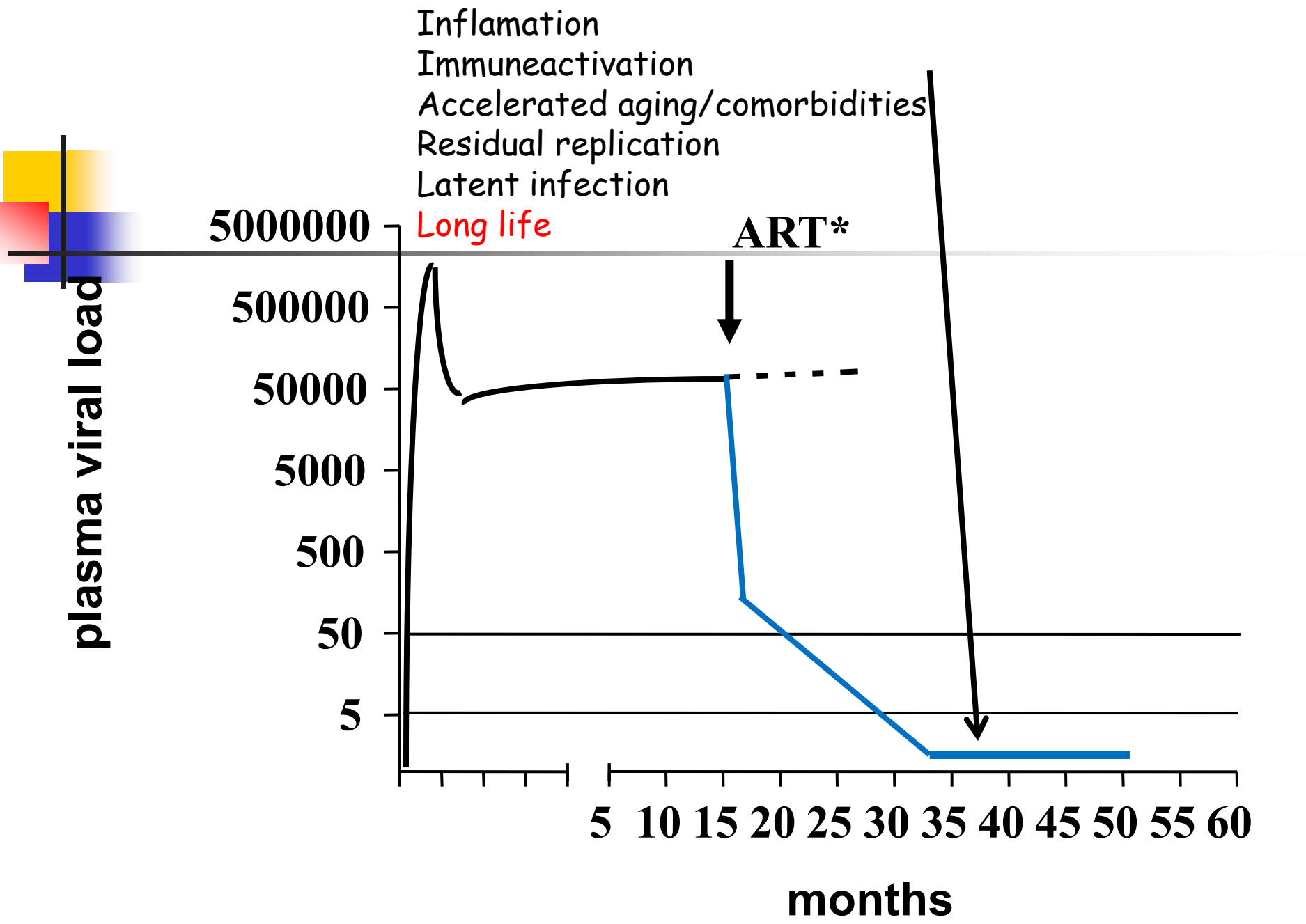
*Felipe García, MD, PhD, Elisa de Lazzari, BSc, Montserrat Plana, MD, PhD, Pedro Castro, MD, Gabriel Mestre, MD, Meritxell Nomdedeu, MD, Emilio Fumero, MD, Esteban Martínez, MD, PhD, Josep Mallolas, MD, PhD, José L. Blanco, MD, PhD, José M. Miró, MD, PhD, Tomás Pumarola, MD, PhD, Teresa Gallart, MD, and José M. Gatell, MD, PhD*

A




Number of individuals at risk

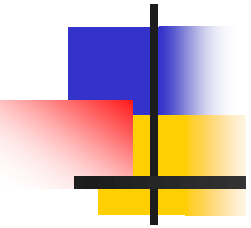
| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| <200 | 408 | 329 | 298 | 250 | 226 | 199 | 161 | 141 | 109 | 73 | 57 |
| 200-349 | 226 | 152 | 152 | 118 | 111 | 102 | 96 | 85 | 70 | 47 | 32 |
| 350-499 | 137 | 109 | 104 | 78 | 64 | 55 | 72 | 50 | 42 | 25 | 19 |
| >=500 | 90 | 69 | 65 | 47 | 46 | 38 | 27 | 24 | 18 | 18 | 14 |




* Often a convenient, single pill & well tolerated regimen

RETIC-RIS | Red Española de Investigación en SIDA (RIS)

SEVENTH FRAMEWORK PROGRAMME



# HIVACAT

## Projecte de Recerca de la Vacuna de la Sida

Generalitat de Catalunya
Departament de Salut

Generalitat de Catalunya
Departament d'Innovació, Universitats i Empresa

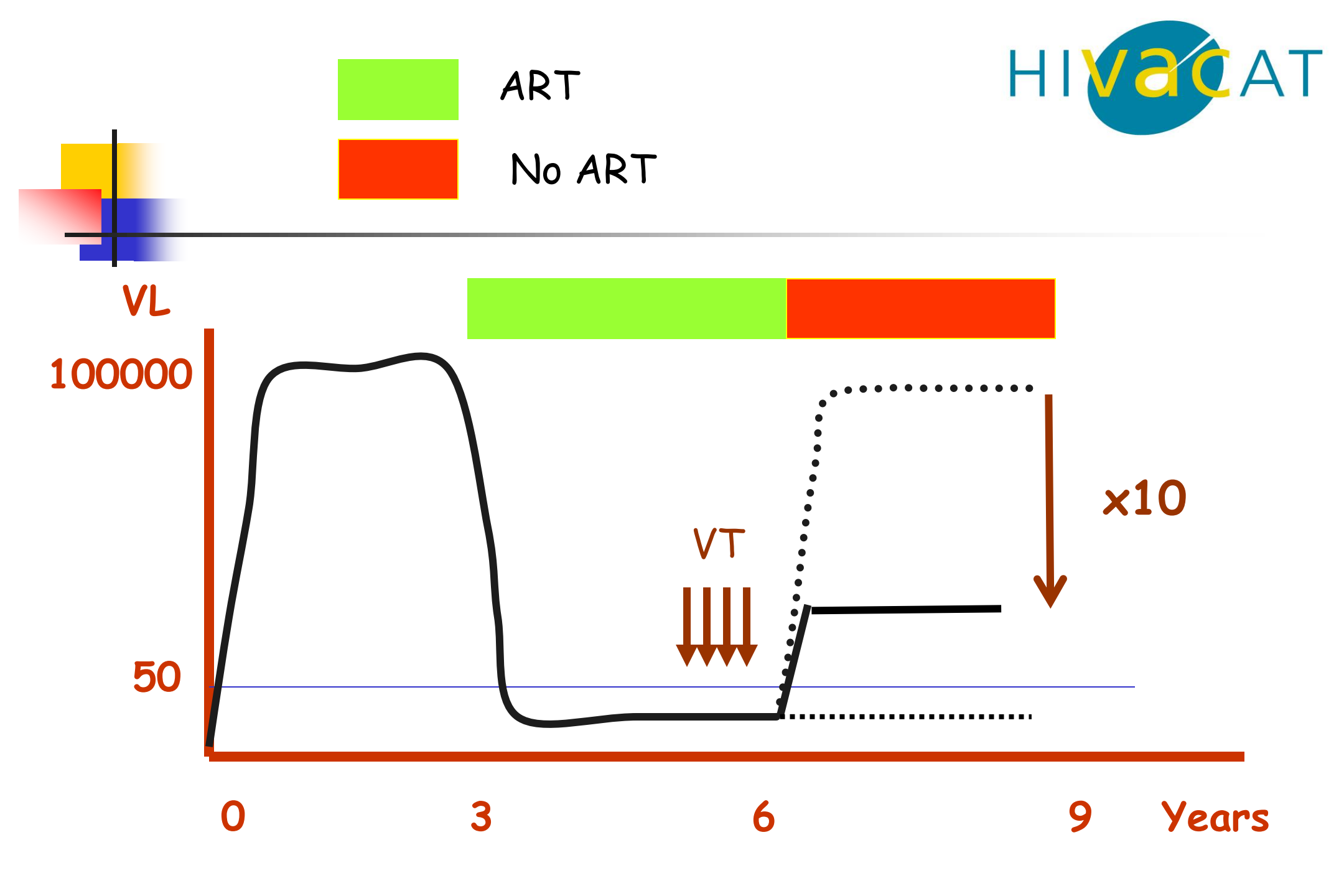
ESTEVE

Obra Social
Fundació "la Caixa"

FUNDACIÓ CLÍNIC BARCELONA

IrsiCaixa
Institut de Recerca de la Sida

IDIBAPS
Institut D'Investigacions Biomèdiques August Pi i Sunyer


ART
No ART
VL
100000
50
VT
x10
0
3
6
9
Years

RESEARCH ARTICLE

HIV

# A Dendritic Cell–Based Vaccine Elicits T Cell Responses Associated with Control of HIV-1 Replication

Felipe García,[1*†] Nuria Climent,[1*] Alberto C. Guardo,[1] Cristina Gil,[1] Agathe León,[1] Brigitte Autran,[2] Jeffrey D. Lifson,[3] Javier Martínez-Picado,[4,5] Judit Dalmau,[4] Bonaventura Clotet,[4] Josep M. Gatell,[1] Montserrat Plana,[1*] Teresa Gallart,[1*] For the DCV2/MANON07-ORVACS Study Group

Combination antiretroviral therapy (cART) greatly improves survival and quality of life of HIV-1–infected patients; however, cART must be continued indefinitely to prevent viral rebound and associated disease progression. Inducing HIV-1–specific immune responses with a therapeutic immunization has been proposed to control viral replication after discontinuation of cART as an alternative to "cART for life." We report safety, tolerability, and immunogenicity results associated with a control of viral replication for a therapeutic vaccine using autologous monocyte-derived dendritic cells (MD-DCs) pulsed with autologous heat-inactivated whole HIV. Patients on cART with $CD4^+$ >450 cells/$mm^3$ were randomized to receive three immunizations with MD-DCs or with nonpulsed MD-DCs. Vaccination was feasible, safe, and well tolerated and shifted the virus/host balance. At weeks 12 and 24 after cART interruption, a decrease of plasma viral load setpoint ≥1 log was observed in 12 of 22 (55%) versus 1 of 11 (9%) and in 7 of 20 (35%) versus 0 of 10 (0%) patients in the DC–HIV-1 and DC-control groups, respectively. This significant decrease in plasma viral load observed in immunized recipients was associated with a consistent increase in HIV-1–specific T cell responses. These data suggest that HIV-1–specific immune responses elicited by therapeutic DC vaccines could significantly change plasma viral load setpoint after cART interruption in chronic HIV-1–infected patients treated in early stages. This proof of concept supports further investigation of new candidates and/or new optimized strategies of vaccination with the final objective of obtaining a functional cure as an alternative to cART for life.

DCV2b/MANON07-ORVACS/RISVAC 01

## Editor's Summary:
## Putting the Vaccine Before the cART

Combination antiretroviral therapy has turned HIV infection from a death sentence to a manageable disease. However, current treatment requires "cART for life," a less than ideal situation for HIV-infected individuals because of drug cost and worries about resistance. New vaccine strategies are attempting to control viral replication after infection, thus allowing discontinuation of cART and a "functional cure." Garcia *et al.* report a dendritic cell (DC)–based vaccine that elicits an HIV-1–specific immune response and may change the setpoint of viral load.

The authors pulsed the patient's own DCs with heat-inactivated whole HIV and then used these DCs as a therapeutic vaccine. The vaccine was safe and well tolerated. They observed a decrease in viral setpoint after cART interruption in vaccinated patients with a concomitant increase in HIV-1–specific T cell responses. Although not yet a functional cure, these results support future studies optimizing a therapeutic vaccine to maintain HIV-1–infected patients.

Enferm Infecc Microbiol Clin. 2011;29(10):721–730

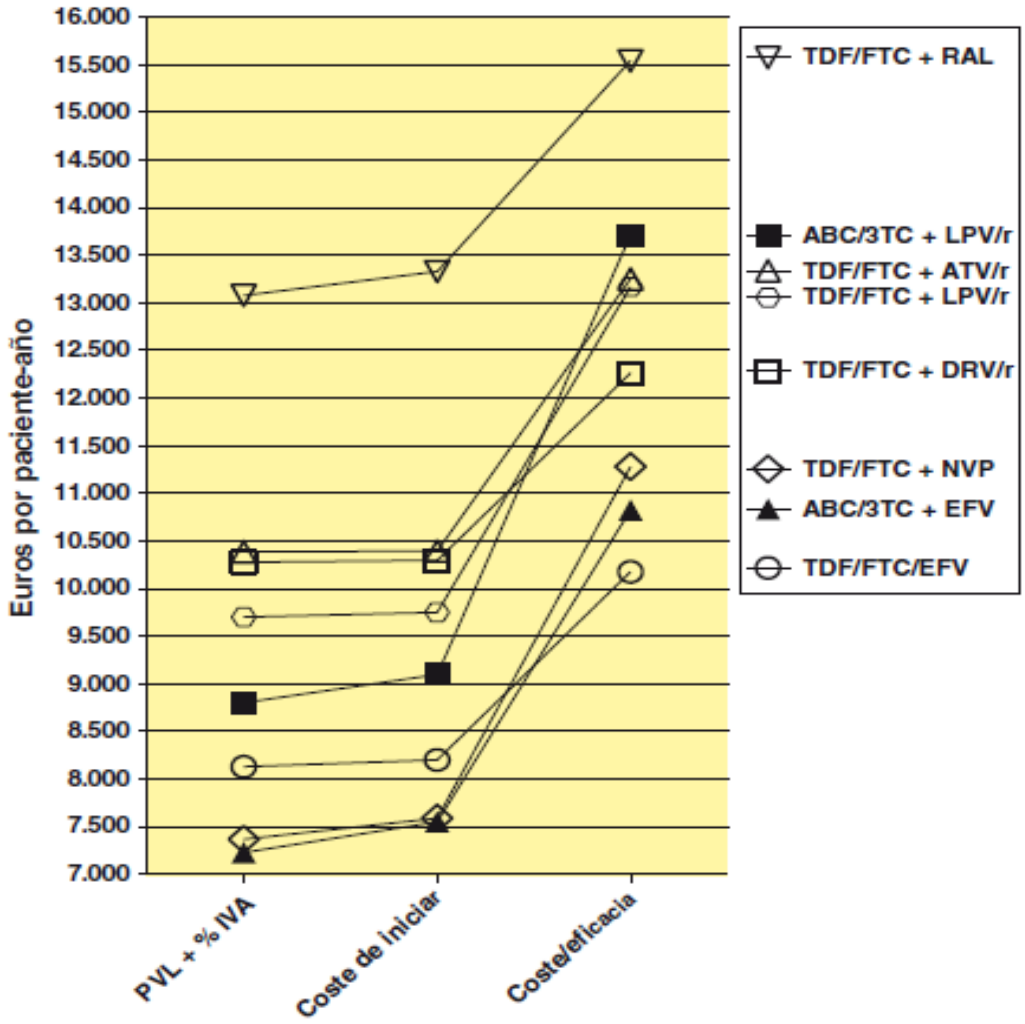
Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc

Original

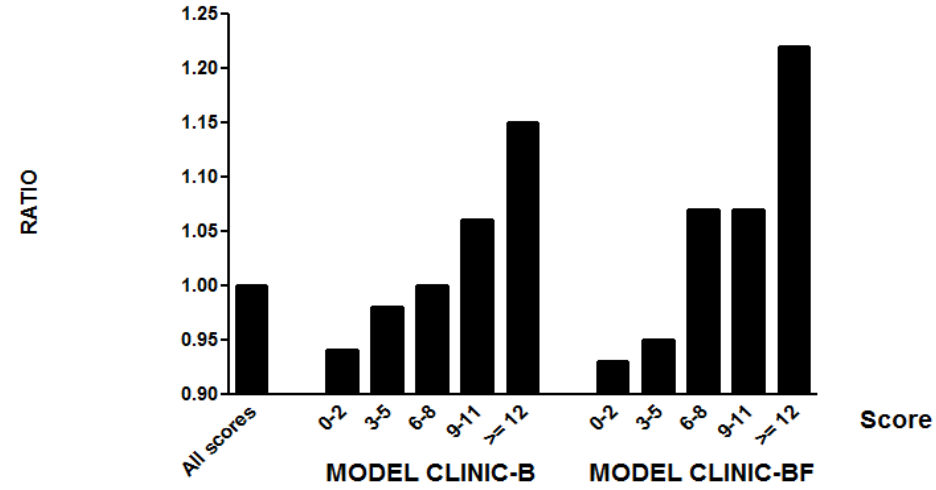
# Análisis de costes y de coste/eficacia de las pautas preferentes de GESIDA para el tratamiento antirretroviral inicial

Antonio Javier Blasco[a], José Ramón Arribas[b], Bonaventura Clotet[c], Pere Domingo[d], Juan González-García[b], Juan Carlos López-Bernaldo[e], Josep M. Llibre[c], Fernando Lozano[f], Daniel Podzamczer[g], Juan Miguel Santamaría[h], Montserrat Tuset[i], Laura Zamora[j], Pablo Lázaro[a] y Josep M. Gatell[j,*]



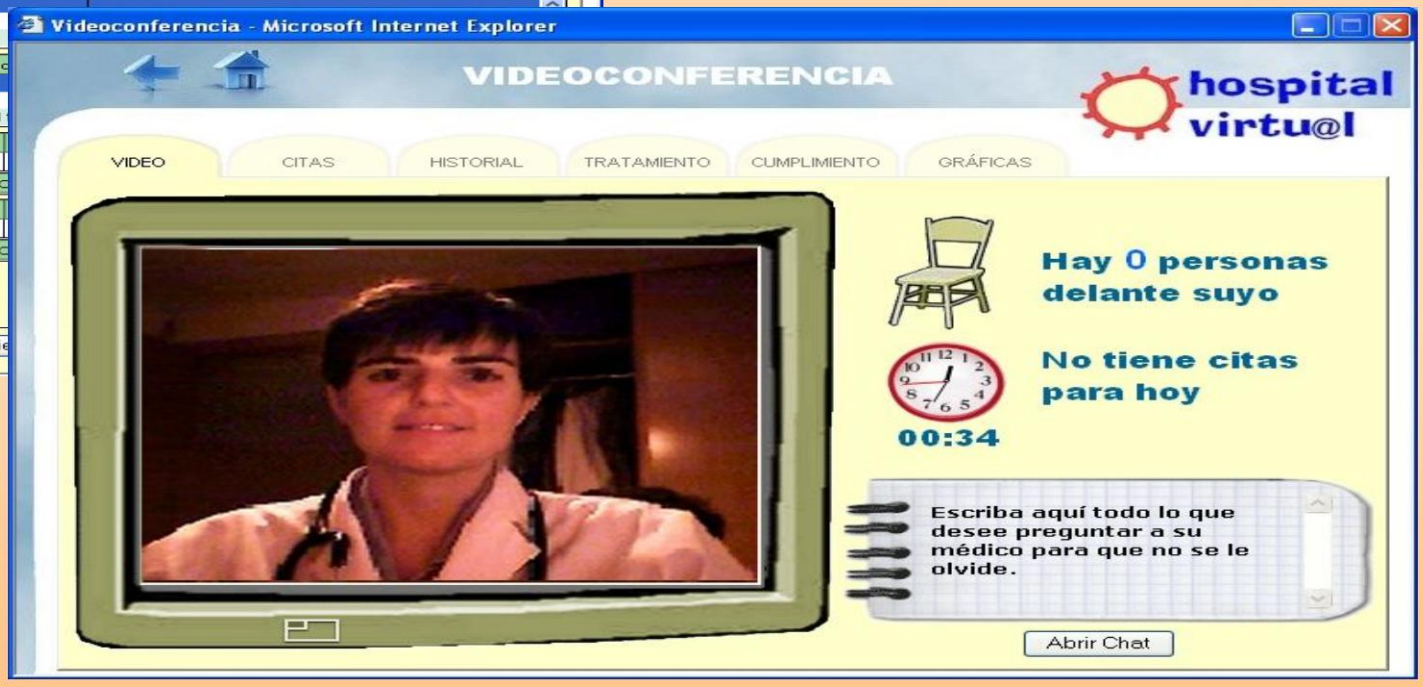

JAIDS, 2014 submitted

**Fig 2c**
**PERCENTUAL INCREMENT COMPARED WITH LOWEST SCORE RANGE OF MEAN NORMALIZED REAL COST OF THE 3758 PATIENTS OF THE Hospital Index (HI) DISTRIBUTED BY SCORE RANGES**



# Users


Professional user



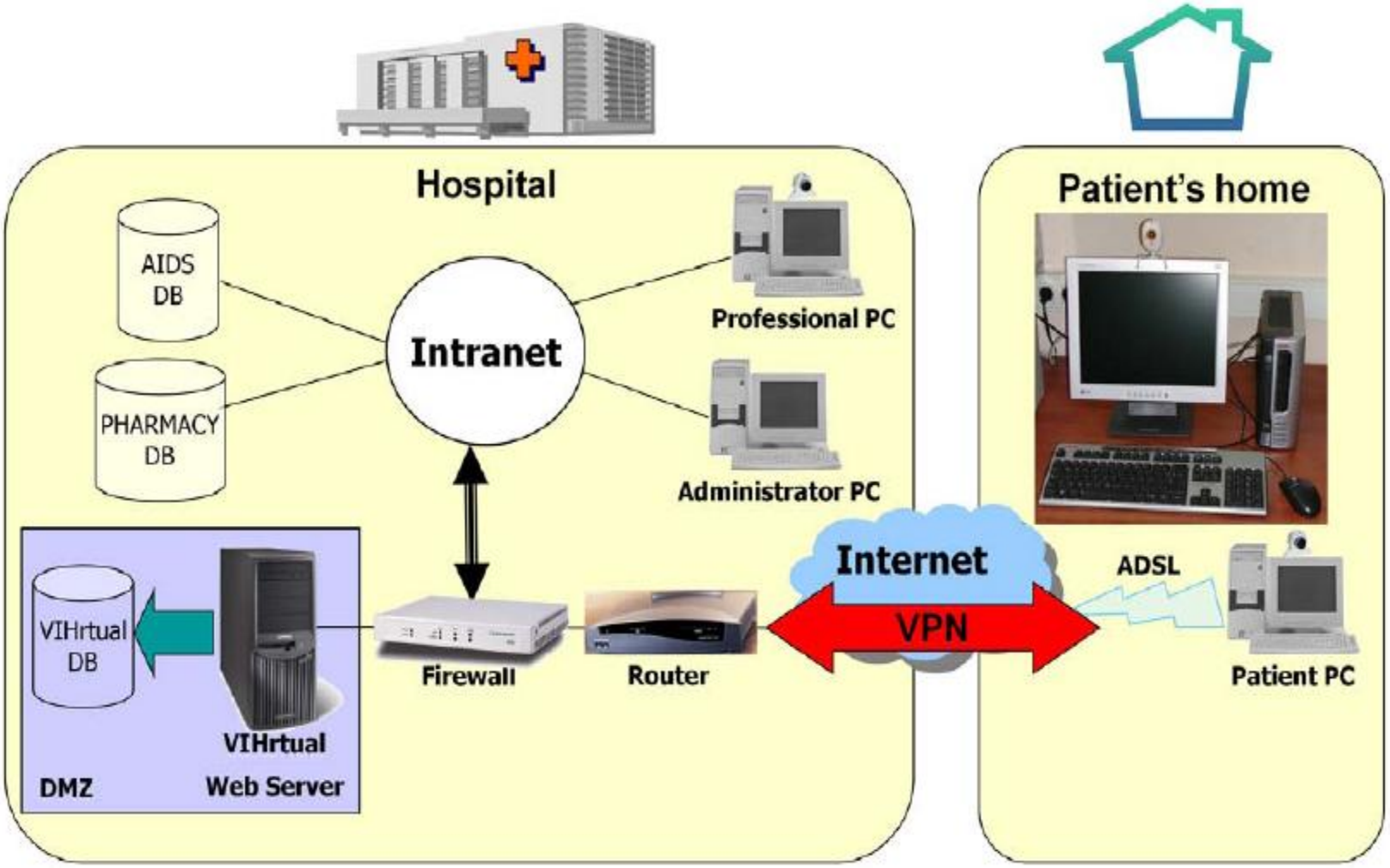

Patient user

OPEN ACCESS Freely available online

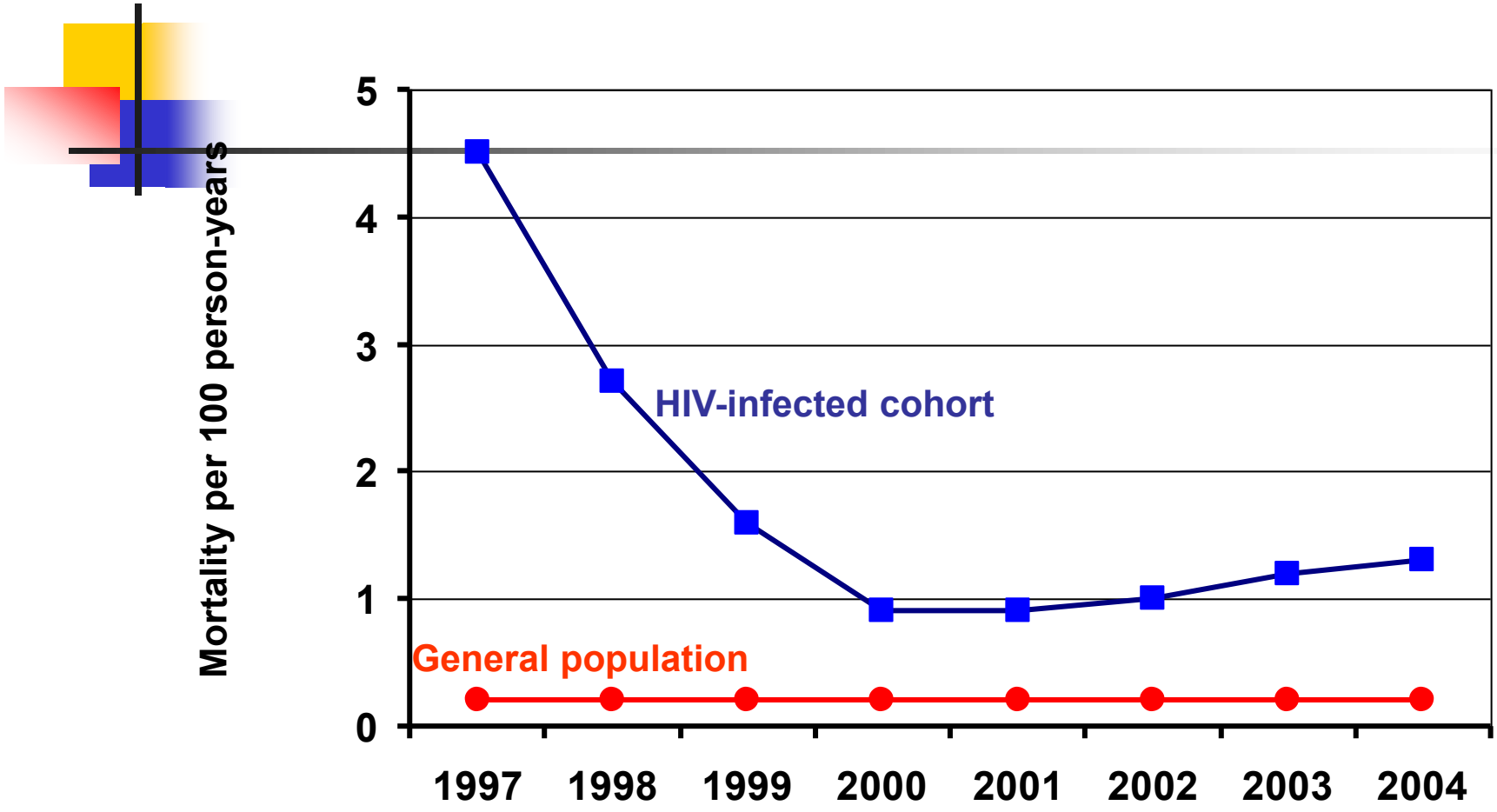
PLoS on

# A New Multidisciplinary Home Care Telemedicine System to Monitor Stable Chronic Human Immunodeficiency Virus-Infected Patients: A Randomized Study

Agathe León[1]*, César Cáceres[2], Emma Fernández[1], Paloma Chausa[2], Maite Martin[3], Carles Codina[3], Araceli Rousaud[4], Jordi Blanch[4], Josep Mallolas[1], Esteban Martinez[1], Jose L. Blanco[1], Montserrat Laguno[1], Maria Larrousse[1], Ana Milinkovic[1], Laura Zamora[1], Neus Canal[5], Josep M. Miró[1], Josep M. Gatell[1], Enrique J. Gómez[2], Felipe García[1]



# Annual incidence of mortality in the HIV-infected cohort compared with general population aged 16-65 years in Catalonia




- Significant reduction in mortality for HIV-infected patients over this period ($P<0.001$; $\chi^2$ test for trend), but not for the general population ($P<0.936$; $\chi^2$ test for trend)

Martinez et al. HIV Medicine 2007

Life expectancy after 2015 of adults with HIV on long-term antiretroviral therapy in Europe and North America: a collaborative analysis of cohort studies

Adam Trickey, Caroline A Sabin, Greer Burkholder, Heidi Crane, Antonella d'Arminio Monforte, Matthias Egger, M John Gill, Sophie Grabar, Jodie L Guest, Inma Jarrin, Fiona C Lampe, Niels Obel, Juliana M Reyes, Christoph Stephan, Timothy R Sterling, [illegible], Jan-Christian Wasmuth, Ferdinand Wit, Linda Wittkop, Robert Zangerle, Michael J Silverberg, Amy Justice, Jonathan A C Sterne

**Summary**

**Background** The life expectancy of people with HIV taking antiretroviral therapy (ART) has increased substantially [illegible]

ATCC+CHIC
N=206,891
N=5780 deaths

**STILL ROOM TO IMPROVE**

**Chronic inflammation and immunoactivation may explain part of the difference**

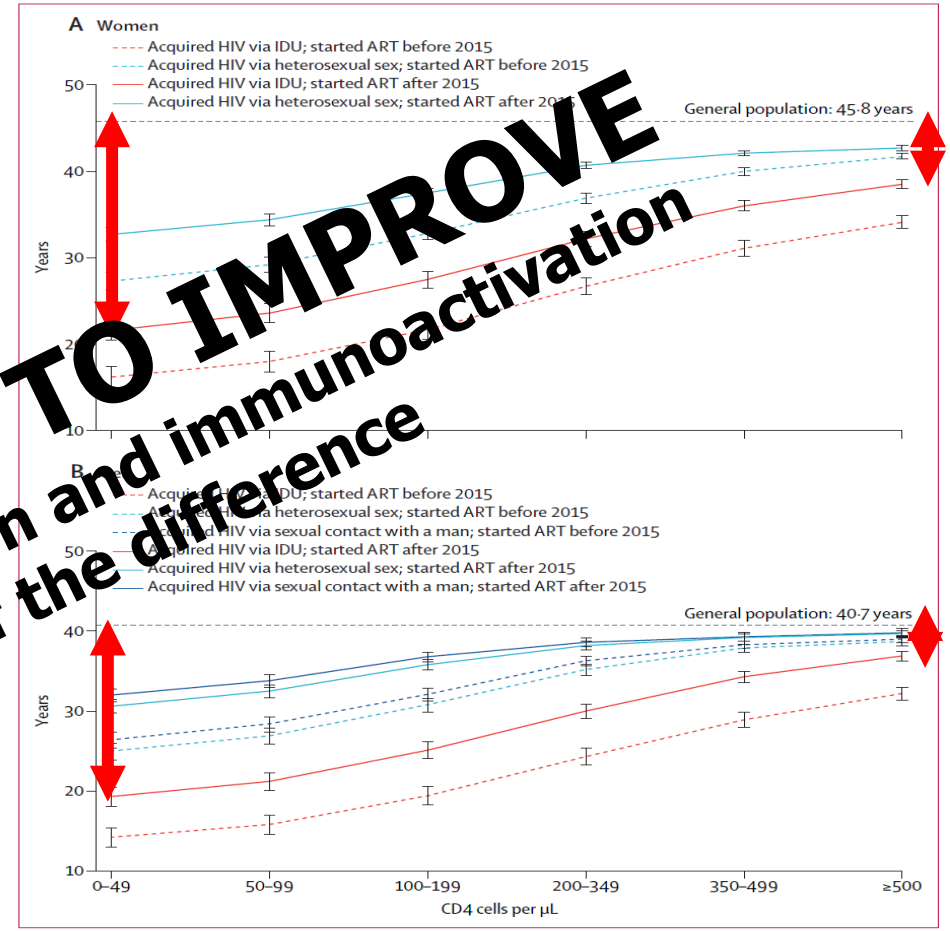



*Figure:* **Estimated years of life left at age 40 years for women (A) and men (B) with HIV on ART who had suppressed viral loads and did not have AIDS at the start of follow-up**
Data are stratified by CD4 cell count, HIV acquisition route, and ART start year. Error bars show 95% CIs. ART=antiretroviral therapy. IDU=injecting drug use.

# HIV/AIDS 1920-2025:

## The pandemic of XX-XXI centuries: From darkness to sunshine

1. A few basic concepts
2. 1981-85: 5 years of darkness
3. 1986-95: 10 years of moonlight
4. 1996-12: 15 years of sunrise
5. 2013-18: 5 years of sunshine
6. 2025: where are we now ?
7. Some final considerations

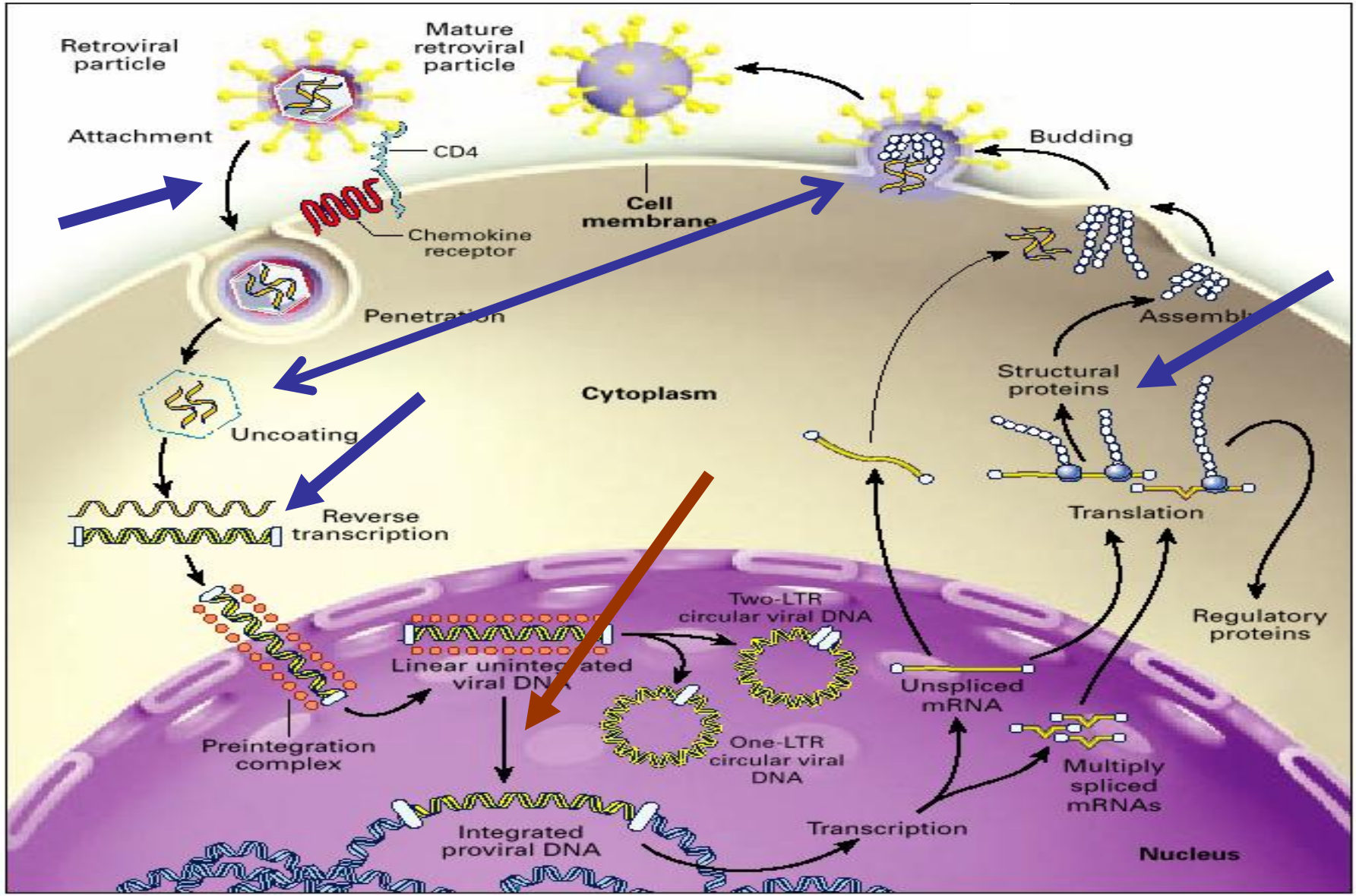
# HIV/AIDS 1920-2025:

## The pandemic of XX-XXI centuries: From darkness to sunshine

### 6. 2025: where are we now ?

ART based on INSTIs
ART based on dual therapies
ART based on dual long acting (LA) therapies (q2mo)

AIDS free world feasible ?. By 2020, 2030, 2050 ……


Retroviral particle
Mature retroviral particle
Attachment
CD4
Chemokine receptor
Cell membrane
Budding
Penetration
Assembly
Structural proteins
Cytoplasm
Uncoating
Reverse transcription
Translation
Two-LTR circular viral DNA
Linear unintegrated viral DNA
Regulatory proteins
Unspliced mRNA
Preintegration complex
One-LTR circular viral DNA
Multiply spliced mRNAs
Integrated proviral DNA
Transcription
Nucleus

# PASO-DOBLE study: Design

Phase IV, open-label, multicentre, randomised clinical trial[1]

**30 sites across Spain**

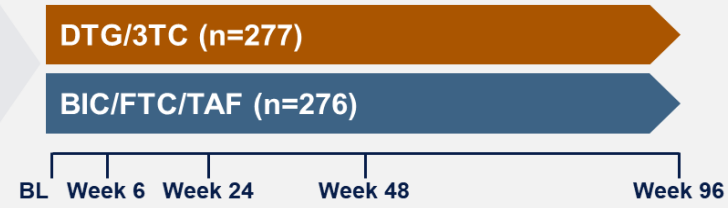
Collaborative study between **Fundación SEIMC-GeSIDA** and ViiV Healthcare

**Screening**

- HIV-1 RNA <50 c/mL for ≥24 weeks
- Current ART containing >1 pill/day, cobi booster, EFV or TDF
- No prior VF or known/suspected resistance
- No prior DTG or BIC
- No chronic hepatitis B

**Randomised 1:1**

Stratified by BL TAF use and sex at birth



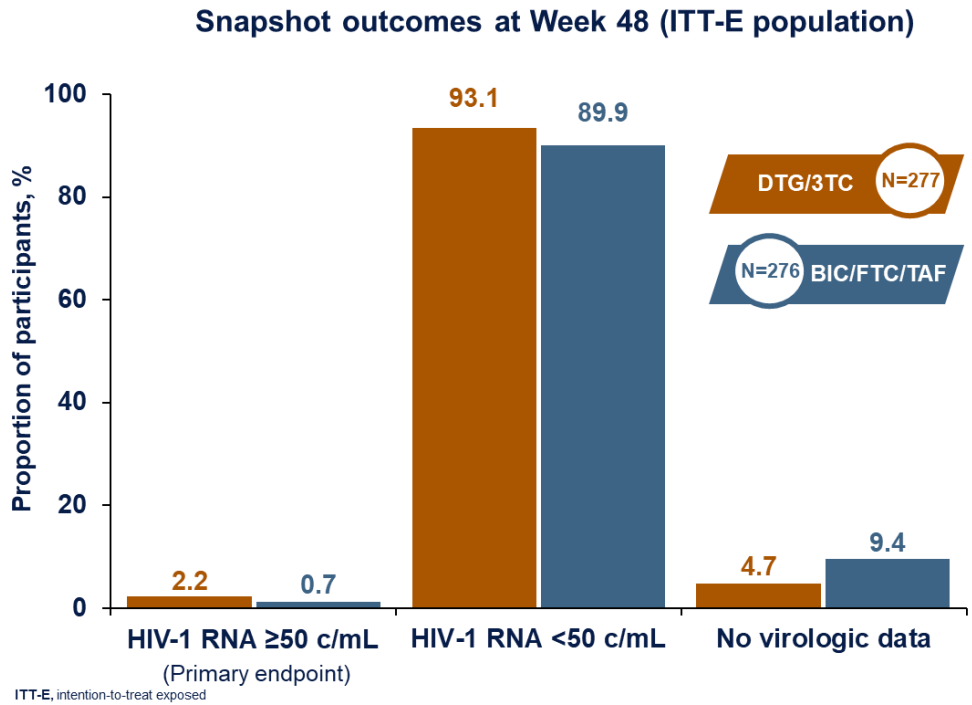

**Primary endpoint:** Participants with plasma HIV-1 RNA ≥50 c/mL (FDA Snapshot; non-inferiority margin 4%)

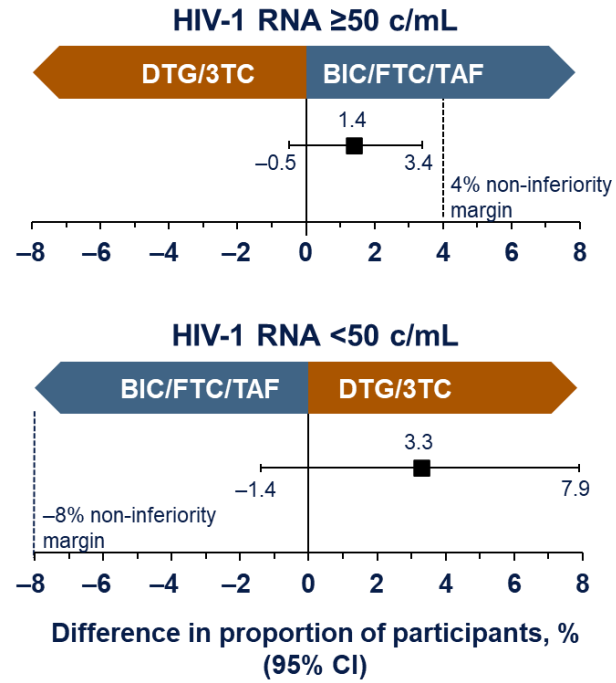
**Key secondary endpoints: efficacy, safety, tolerability, immune recovery, weight, metabolic parameters, kidney function, blood pressure, body and bone composition, PROs, and genotypic resistance in case of virological failure**

**Four sub-studies:** Omics | Senescence | Fat biopsies | Liver steatosis

**1.** PASO DOBLE. Available at: https://clinicaltrials.gov/ct2/show/NCT04884139.

# PASO-DOBLE study: Virologic efficacy



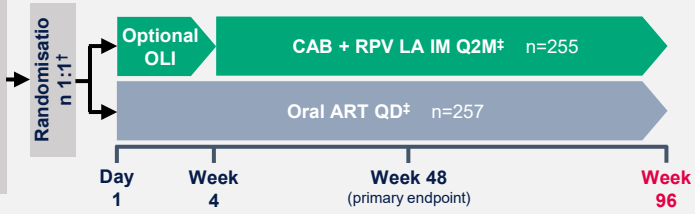
CROI 2025

# CARES: CAB + RPV LA demonstrates non-inferior long-term efficacy in diverse populations and settings through 2 years, compared to oral ART

## Study design and population[1,2]

**Inclusion criteria**

- Aged ≥18 years
- Receiving ART* for ≥6 months
- No history of treatment failure
- Confirmed VL <50 c/mL




**Multi-country RCT completed in Uganda, Kenya and South Africa (N=512):**

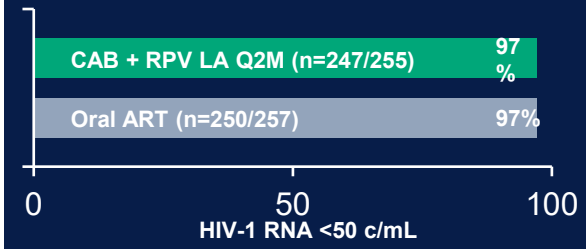
- **Women**: 58%
- **Black** race: 99.6%
- BL **BMI ≥30 kg/m²**: 21%
- **INSTI** use at BL: 92%
- Prior exposure to **NNRTIs**: 74%

Assessed retrospectively at W48:

- **Viral subtype A1**: 55%
- BL archived **RPV RAMs§**: 8%
- BL archived **CAB RAMs§**: 4%

**Routine VL monitoring was done at BL, 6, 12, 18 and 24 months**

## Efficacy[1]




**1.6%** (4/255) on CAB + RPV LA experienced CVF¶

3 participants had viral sequences available at failure; 3/3 had RAMs to RPV and CAB. 3 resuppressed on DTG/TDF/3TC, 1 died due to HIV-unrelated reason[2]

## Adherence, safety, tolerability and PROs[1]

- **High adherence to injections**
  96% (3,142/3,261) of scheduled injections administered within the ±7-day window
- **CAB + RPV LA was well tolerated**
  <1% (2/255) Grade 1–4 AEs led to treatment discontinuation in the CAB + RPV LA arm and 2% (5/257) in the oral ART arm#
- **Strong preference for CAB + RPV LA and significant increase in treatment satisfaction with CAB + RPV LA vs oral ART**
  >99% (243/244) preferred CAB + RPV LA vs oral ART (CAB + RPV LA arm)
  HIVTSQs mean change +27.1 vs +17.9 (p<0.0001), respectively**

See slide notes for footnotes and abbreviations


1. Kityo C, et al. CROI 2025. Oral 202
2. Kityo C, et al. Lancet Infect Dis. 2024:S1473-3099(24)00289-5 (and suppl. appendix)

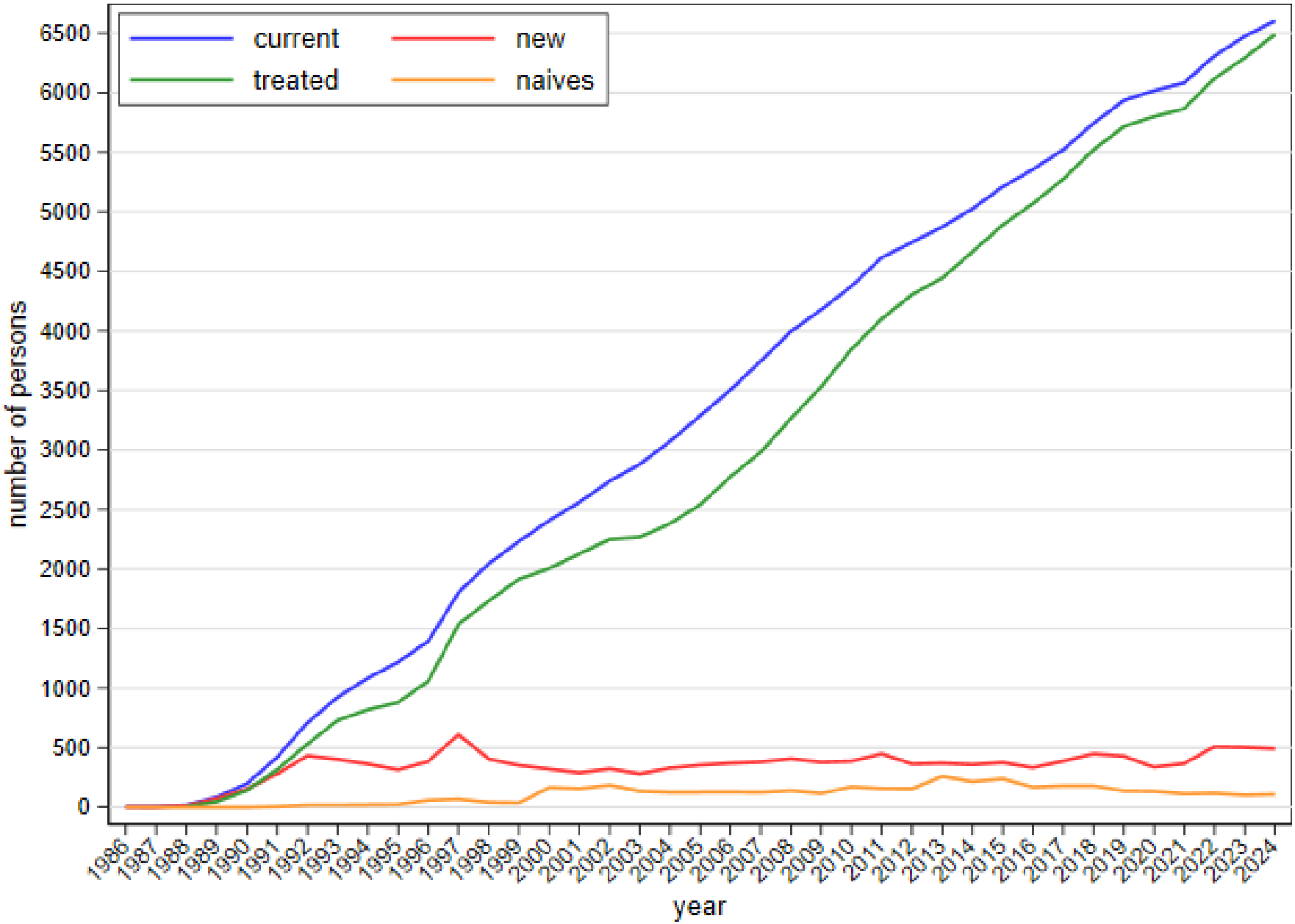
# An AIDS free generation ……2050 ?



*Few could have imagined that we'd be talking about the real possibility of an AIDS-free generation. But that's what we're talking about…make no mistake, we are going to win this fight.*

*President Obama, December 1, 2011*

*PS: By the end of 2013, PEPFAR will directly support more than 6 M people on HAART– 2M more than previously targeted.*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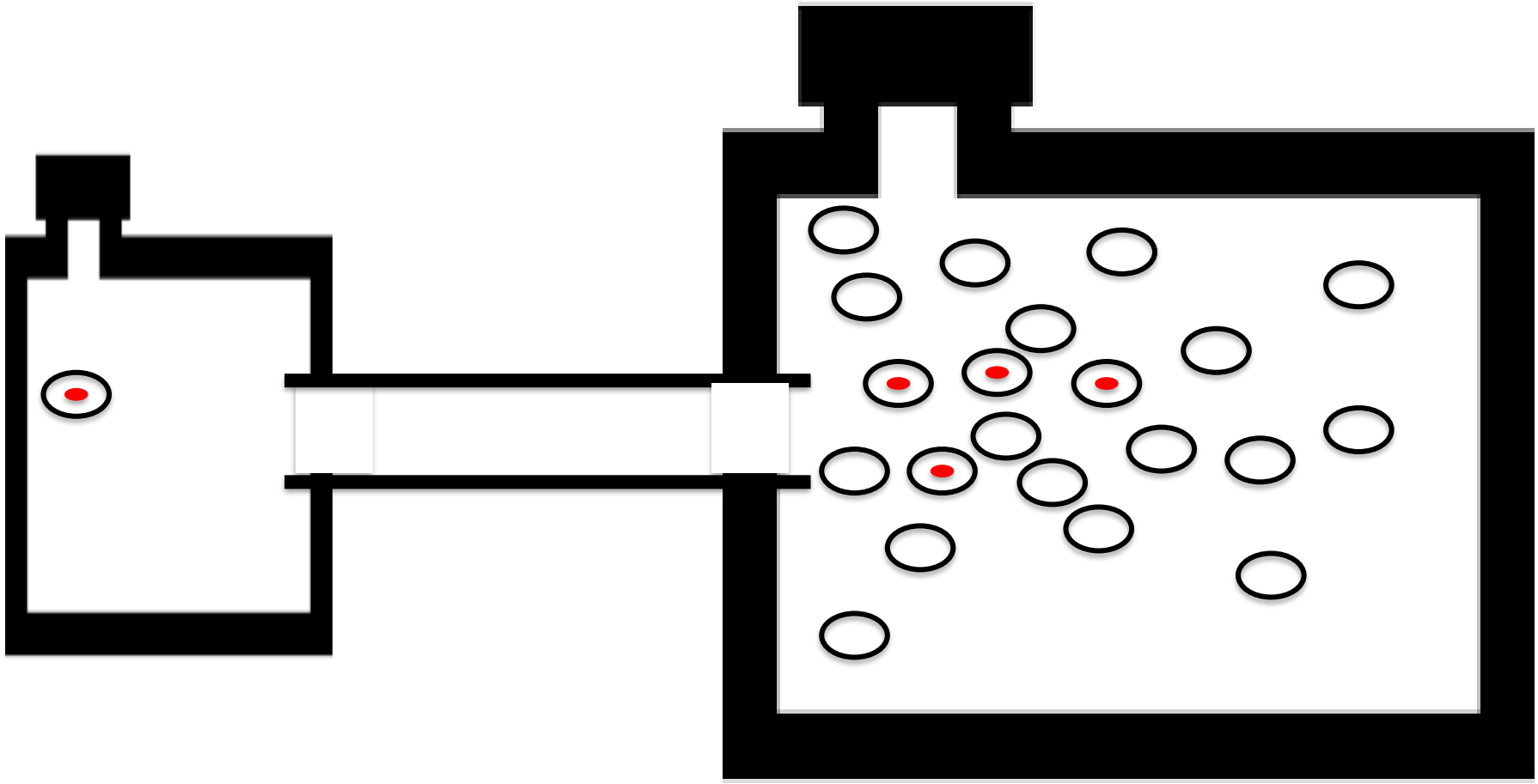
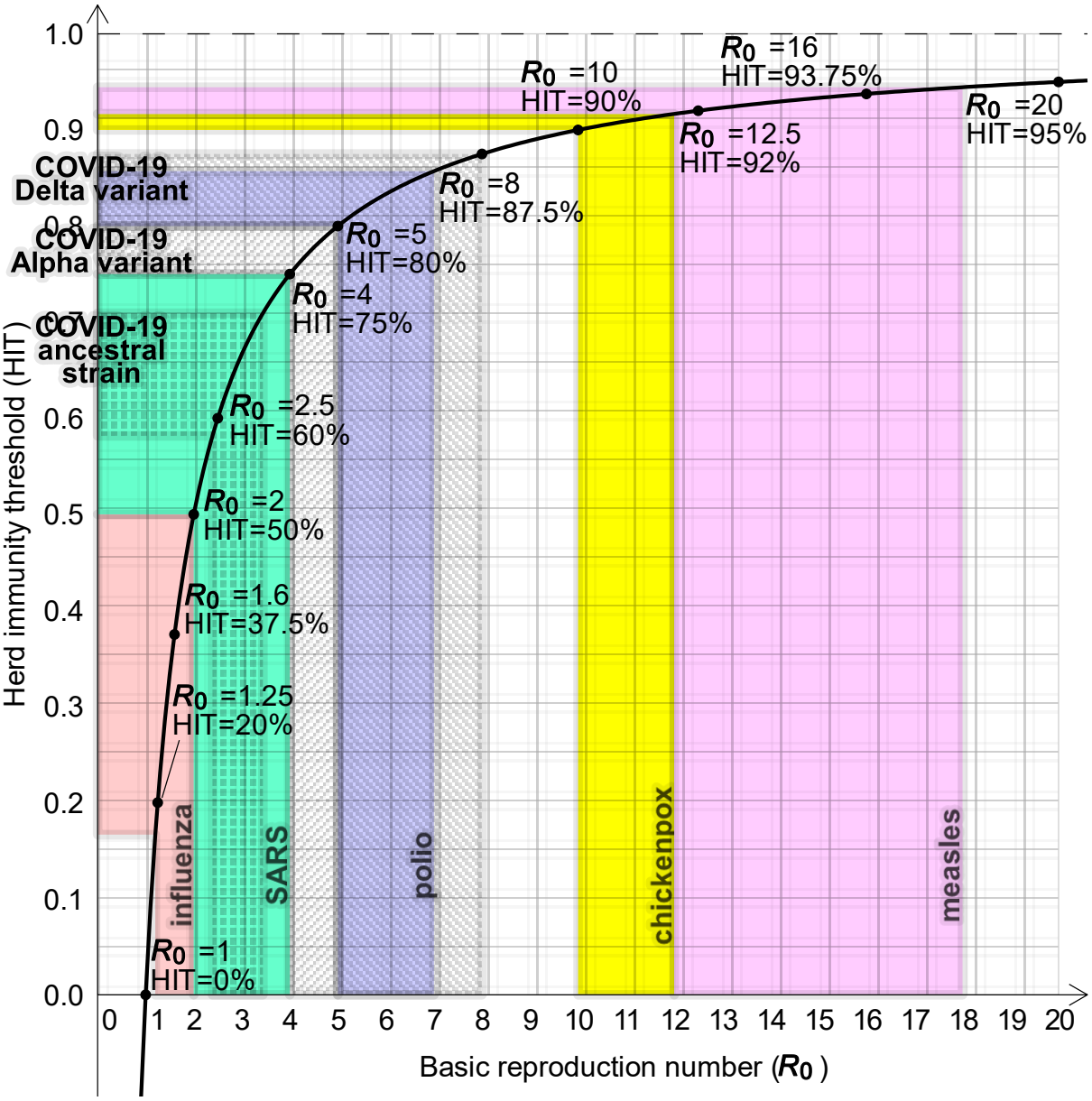
**Ro:** number of secondary infections derived from one primary infection over the infected person´s lifetime in a fully susceptible population (Ro=C*P*D)






Ro:

| | |
|---|---|
| Measles | 10-18 |
| Chickenpox | 10-12 |
| Polio | 5- 7 |
| HIV | 2- 5 |
| SARS | 2- 4 |
| Ebola | 2 |
| Flu | 1- 2 |

HIT=1-(1/Ro)

# Transmisson

IV drug users sharing needles and equipment

Contaminated needles and syringes

Hospital personnel and people working with blood products (transmission risk low)

**SEX**

**Heterosexual/homosexual**

Genital ulceration has been shown to enhance transmission

Blood and blood products

Organ transplantation

**Vertical Transmission**

*In utero*

At birth

Breast milk?

**No evidence**

Insects

Saliva

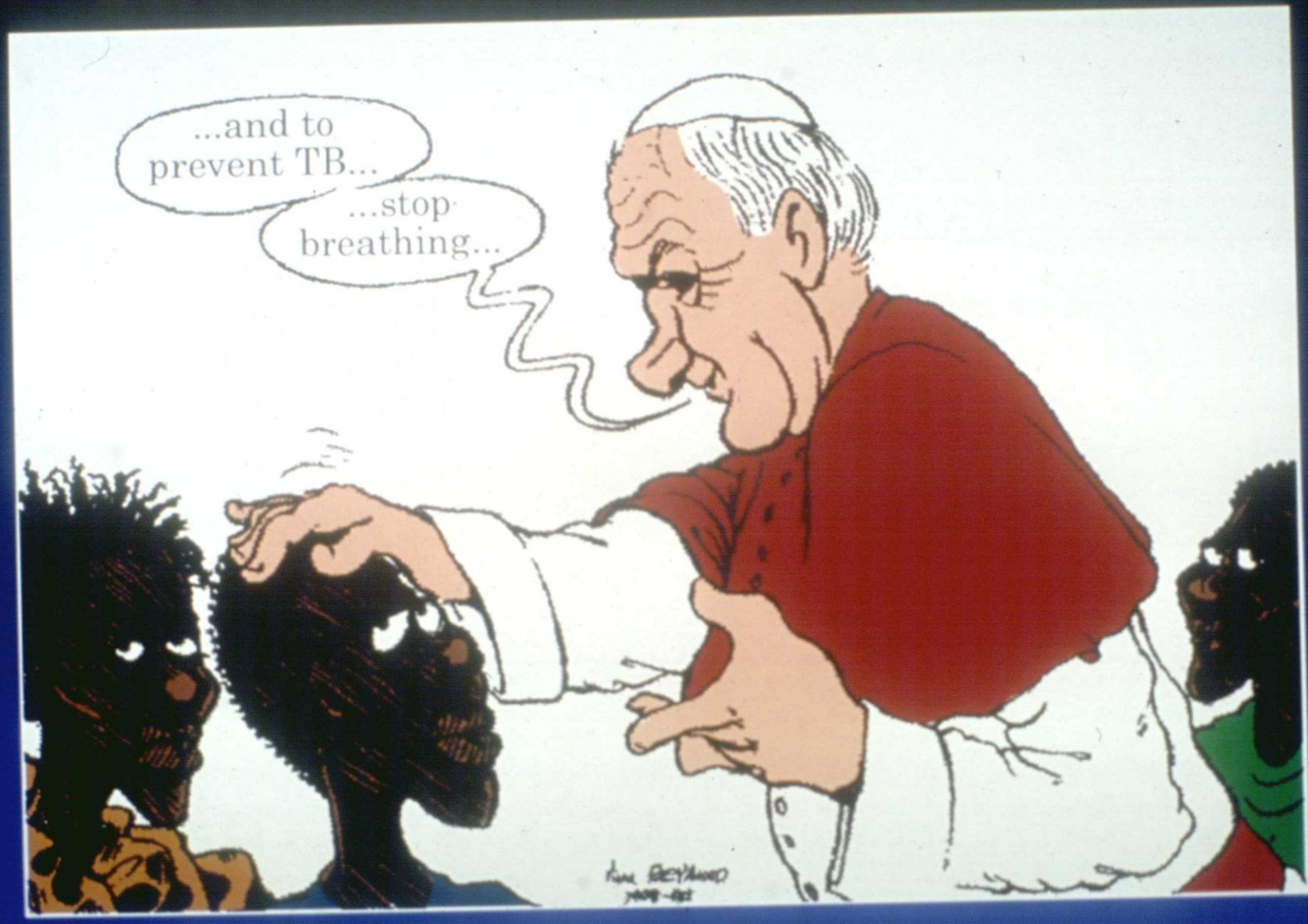
Casual/social contact etc

Sharing eating/ drinking utensils



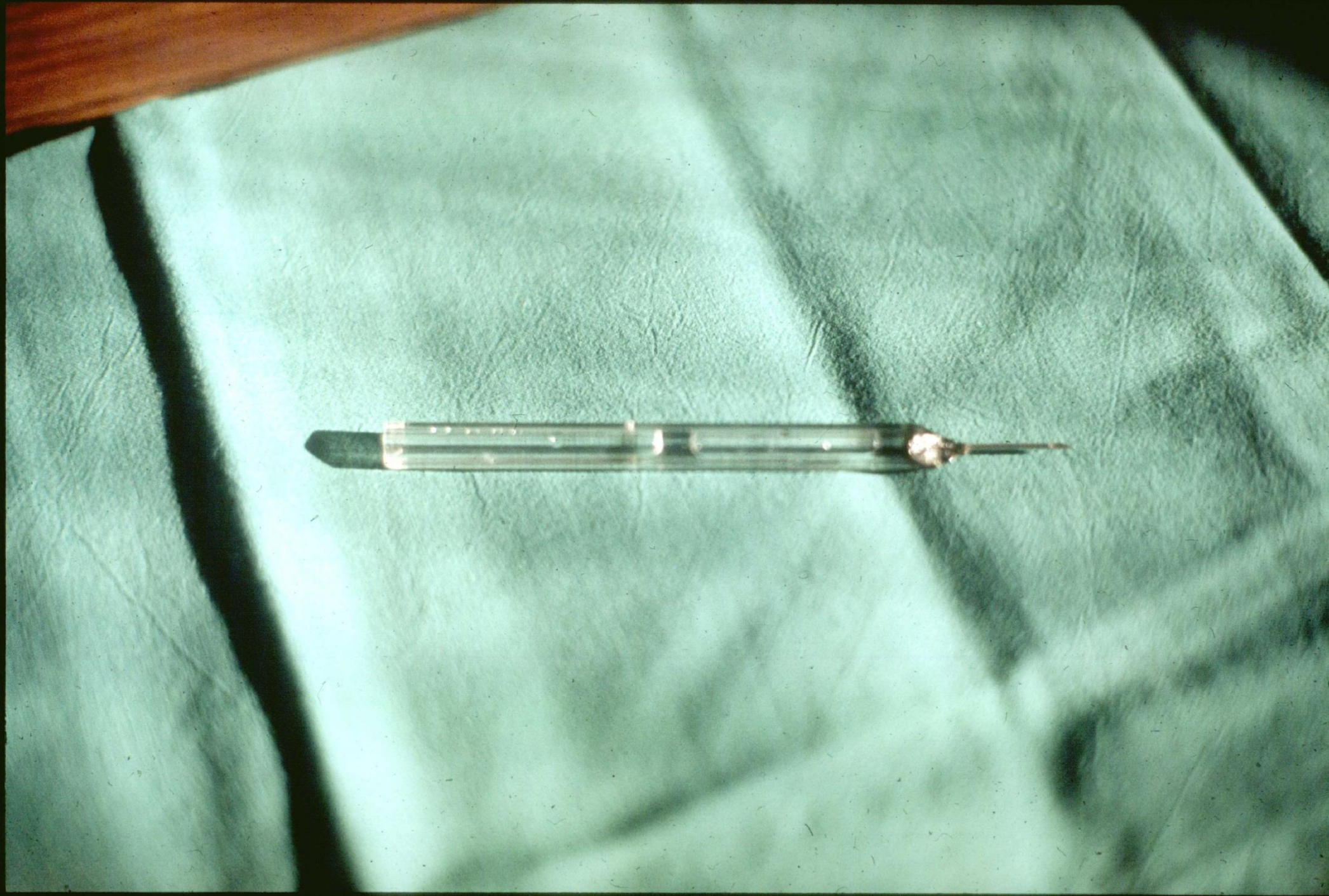
GM30.5/11.91/10.0/R

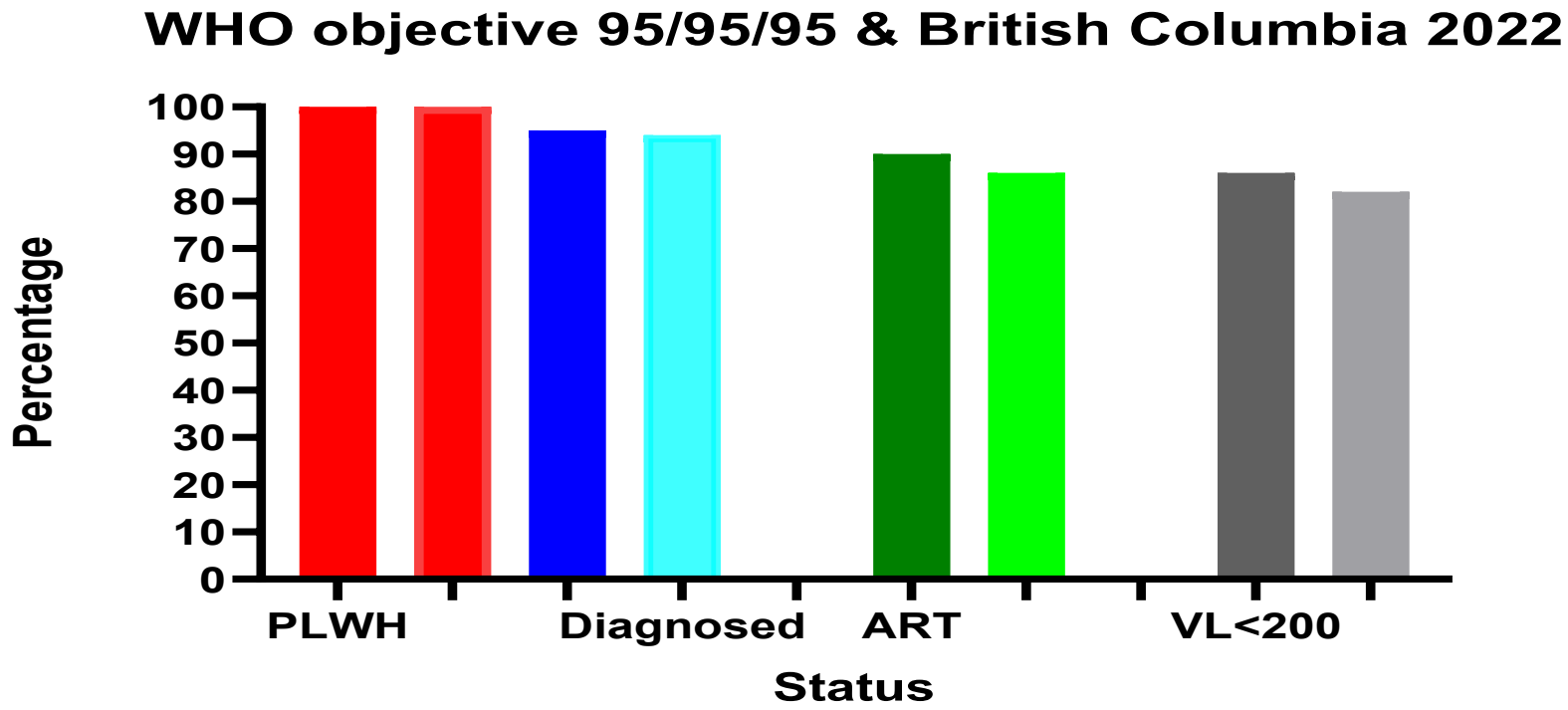
# To Prevent Aids: Chastity...



# Hi ha coses que

COM MÉS
LES PRACTIQUES,
MÉS T´AGRADEN.






Dark blue, green and gray bars are WHO objectives
Light blue, green and gray bars are the situation in British Columbia

# HIV/AIDS 1920-2025:

## The pandemic of XX-XXI centuries: From darkness to sunshine

1. A few basic concepts
2. 1981-85: 5 years of darkness
3. 1986-95: 10 years of moonlight
4. 1996-12: 15 years of sunrise
5. 2013-18: 5 years of sunshine
6. 2025: where are we now ?
7. Some final considerations

# HIV/AIDS 1920-2025:

## The pandemic of XX-XXI centuries: From darkness to sunshine

## 1. Some final considerations

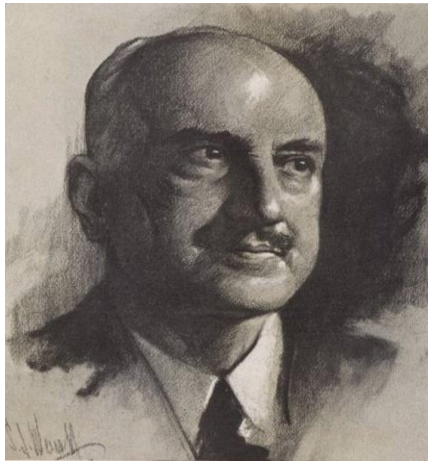
HIV infection is a manageable disease with a life expectancy similar to general population

Antiretroviral therapy is for life

A preventative vaccine may not be feasible

Yet, a world free of AIDS is an achievable goal. However, disruptions associated with funding cuts (USAID, PEPFAR) of present USA administration may substantially delay this end point

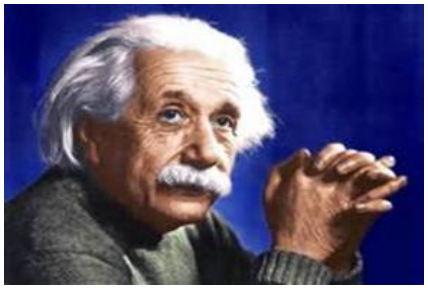
# “Those who cannot remember the past are condemned to repeat it.”



**George Santayana (1863-1952)**
(born Jorge Agustín Nicolás Ruiz de Santayana y Borrás)

*Life of Reason, Reason of Common Sense*
Charles Scribner’s Sos, New York, 1905. p294

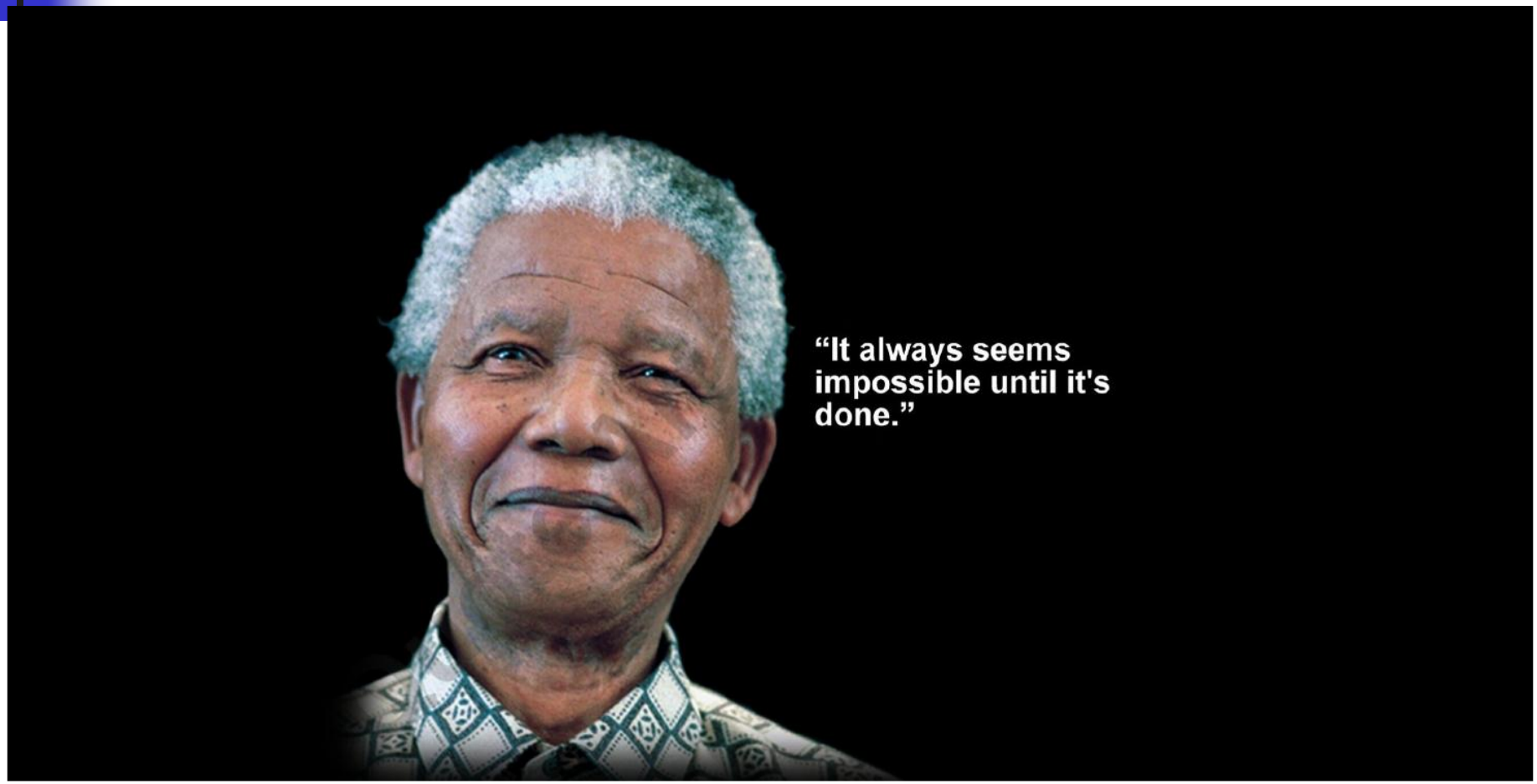
**Insanity:** “doing the same thing over and over again and expecting different results”
***(attributed to Albert Einstein)***



# Potential conflicts of interest:

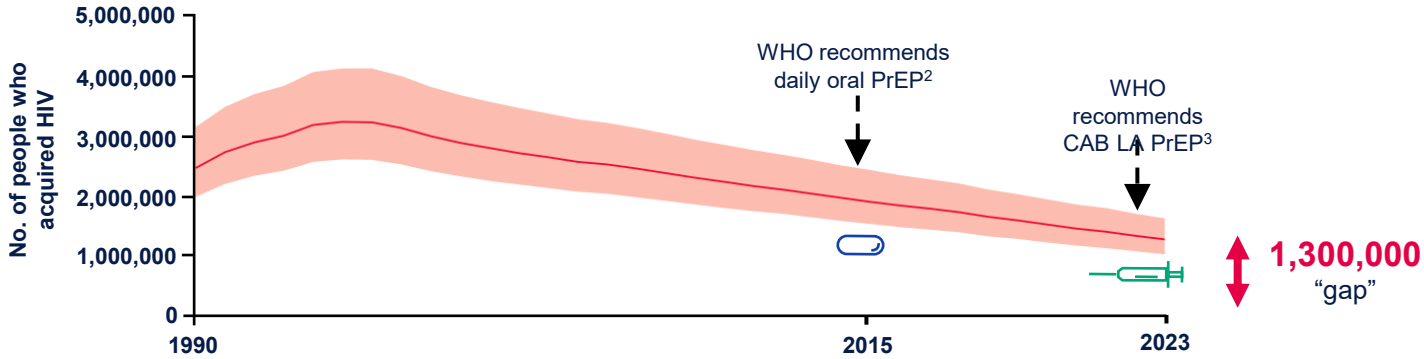
**Since May 1st 2018 I am fulltime employee (Senior Global Medical Director) of ViiV Healthcare**

- **ViiV healthcare does not approve of or recommend the use of medicines in any way other than that stated in the approved package inserts.**
- **For full prescribing information, refer to the package inserts approved by TFDA.**


“It always seems
impossible until it's
done.”

# Despite availability of PrEP, an estimated 1,300,000 people newly acquired HIV in 2023

**Number of people who acquired HIV globally, 1990–2023[1]**




**PrEP remains underutilized[4–6]**

**PrEP uptake in at-risk individuals in the US in 2022*[4]**


- Barriers to oral PrEP use can include stigma, pill fatigue, factors of daily life, or influence from partners[6–8]
- **CAB LA PrEP can address** many of the **challenges associated with taking daily oral PrEP,** and **providing choice** may be an important step toward ending the HIV epidemic[9–12]

*PrEP coverage was calculated as the number of individuals aged ≥16 years who had been prescribed PrEP divided by the estimated number of persons who had indications for PrEP

**WHO,** World Health Organization; **UNAIDS,** The Joint United Nations Programme on HIV/AIDS


**1.** UNAIDS. The Urgency of Now. AIDS at a Crossroads. Available at: https://crossroads.unaids.org/wp-content/uploads/2024/09/Executive-summary_En.pdf (accessed Feb 2025)
**2.** WHO. Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV 2015; **3.** WHO. Guidelines on long-acting injectable cabotegravir for HIV prevention, Jul 2022
**4.** CDC. Expanding PrEP coverage in the United States to achieve EHE goals. Available at: https://www.cdc.gov/nchhstp/director-letters/expanding-prep-coverage.html (accessed Feb 2025)
**5.** Bernier A, et al. IAS 2017. WEAC0101; **6.** Sidebottom D, et al. BMC Infect Dis 2018;18:581; **7.** Landovitz RJ, et al. Lancet HIV 2023;10:e767–78
**8.** Delany-Moretlwe S, et al. Lancet 2022;399:1779–89; **9.** Mills AM, et al. IDWeek 2024. Oral 508
**10.** Ramgopal M, et al. IDWeek 2024. Oral 505; **11.** Heise MJ, et al. HIVR4P 2024. Abstract 0A0503; **12.** Blisset R, et al. AIDS 2022. Poster EPC145