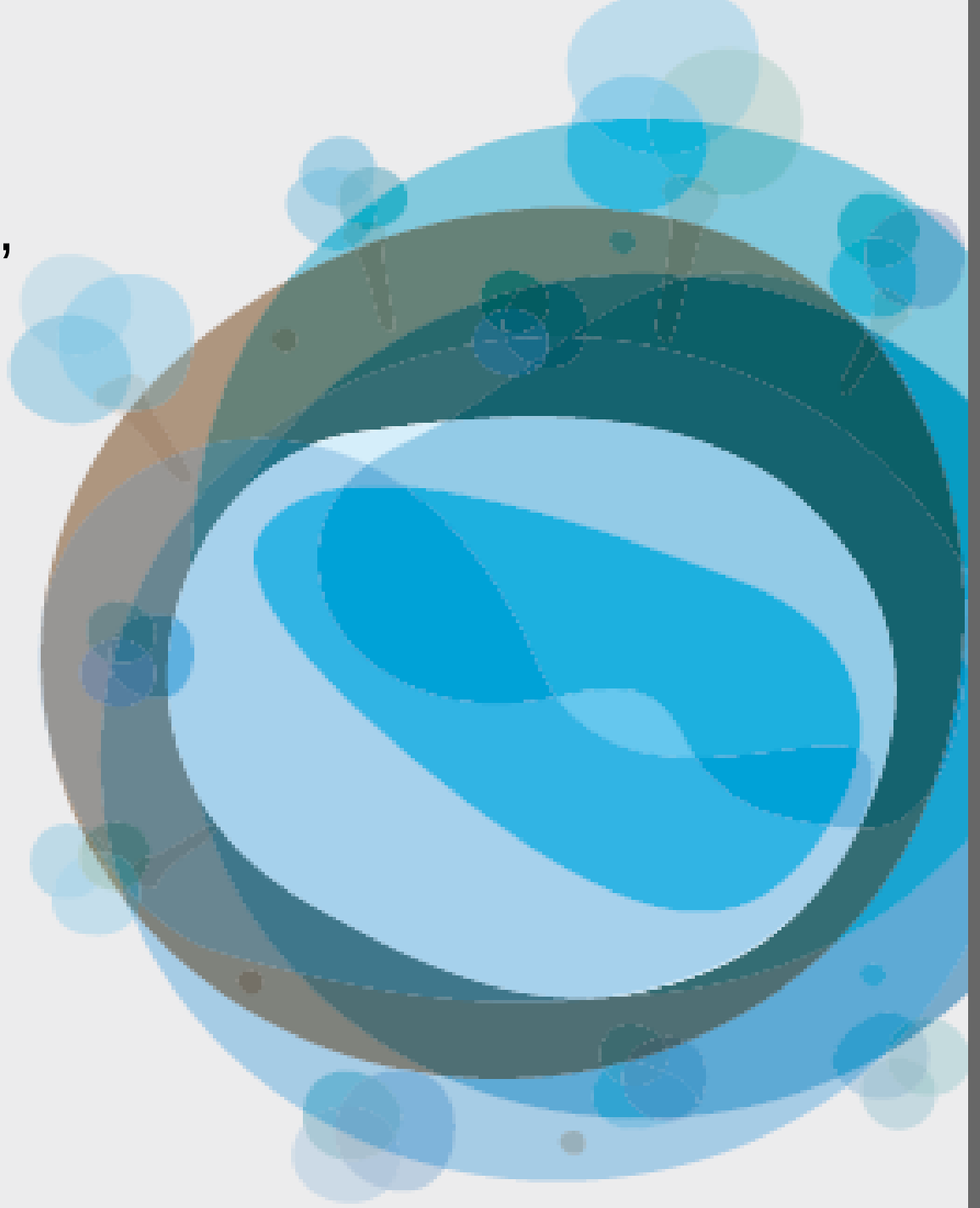
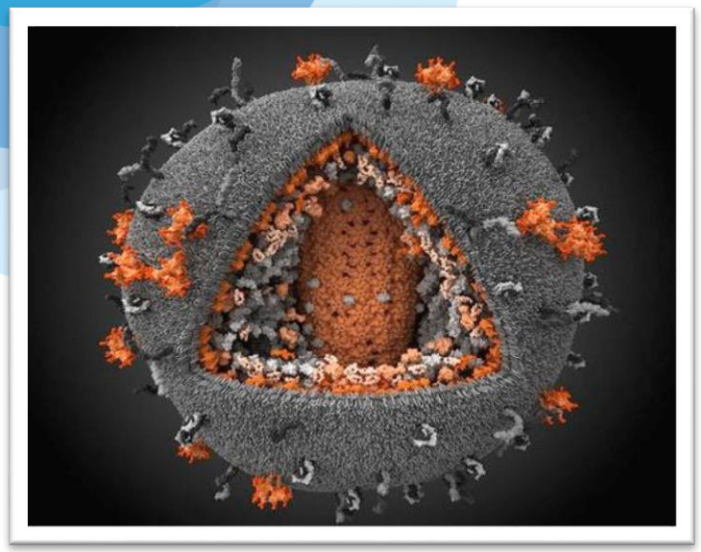
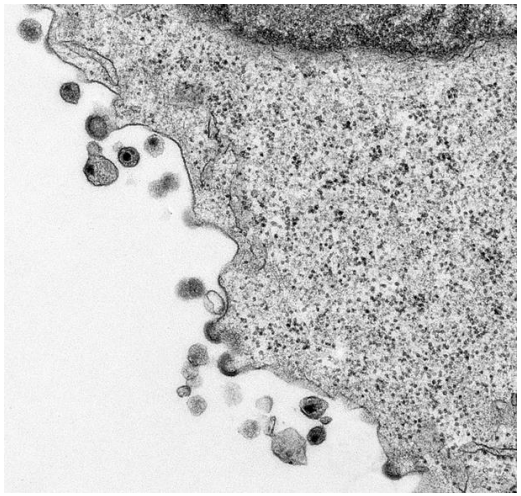
HIV infection: Prevention, treatment and vaccine development



Christian Brander
HIVACAT
Irsicaixa AIDS Research Institute
ICREA Research Professor
UVic-UCC, UAB

Human Immunodeficiency Virus (HIV)





Género: Lentivirus,

Human Immunodeficiency Virus

HIV-1, HIV-2

- Descubiertos en 1983.
- Emparentados con virus de primates (SIV)
- Destruyen sus células diana

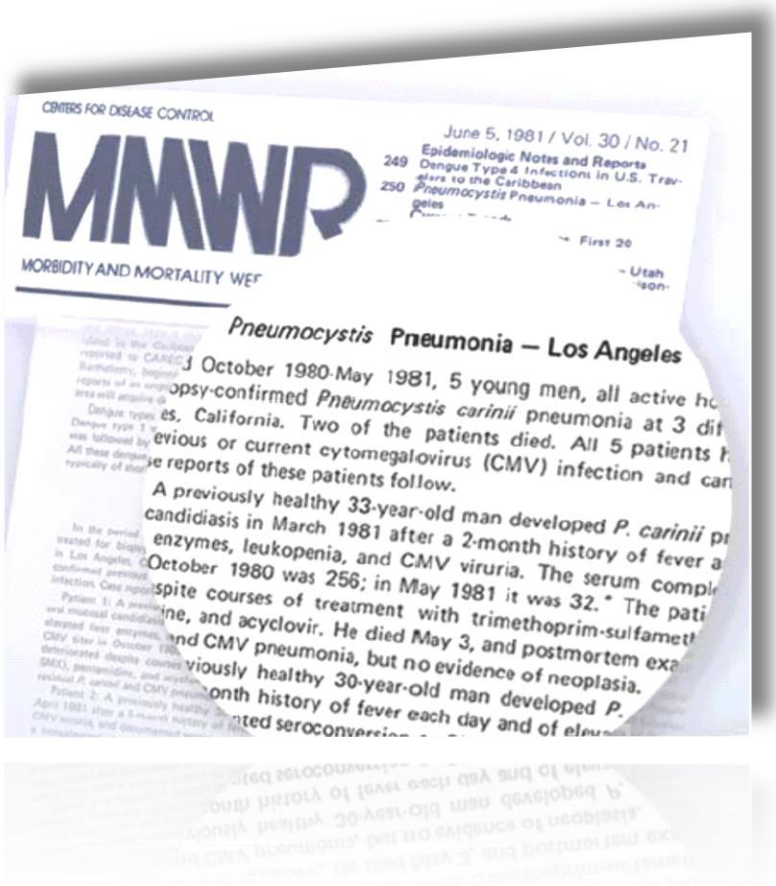
El VIH. Primeras noticias

- 5 de junio de 1981. El CDC notifica 5 casos de *Pneumocystis carinii* en homosexuales de Los Ángeles

- Diseminación de nuevos casos, inmunodeficiencias

- Los datos epidemiológicos apuntan a un AGENTE INFECCIOSO

www.cdc.gov/mmwr/PDF/wk/mm5021.pdf


CENTERS FOR DISEASE CONTROL

MMWR

MORBIDITY AND MORTALITY WEEKLY REPORT

June 5, 1981 / Vol. 30 / No. 21

249 Epidemiologic Notes and Reports
Dengue Type 4 Infections in U.S. Travelers to the Caribbean

250 *Pneumocystis* Pneumonia — Los Angeles

Pneumocystis Pneumonia — Los Angeles

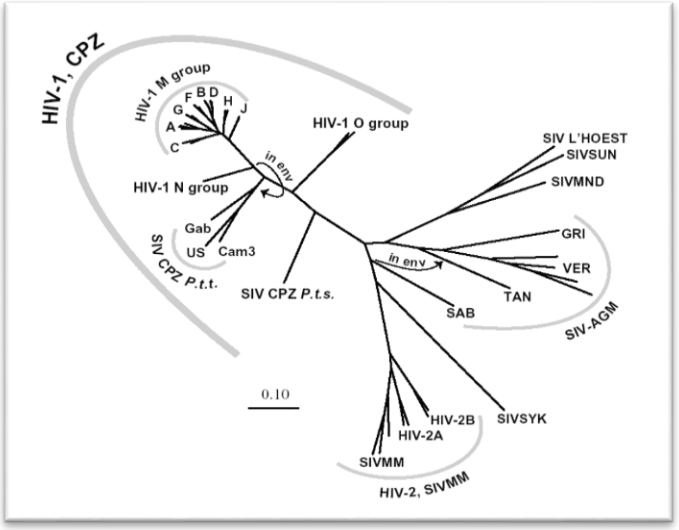
October 1980-May 1981, 5 young men, all active ho
opsy-confirmed *Pneumocystis carinii* pneumonia at 3 dif
es, California. Two of the patients died. All 5 patients h
evious or current cytomegalovirus (CMV) infection and can
e reports of these patients follow.

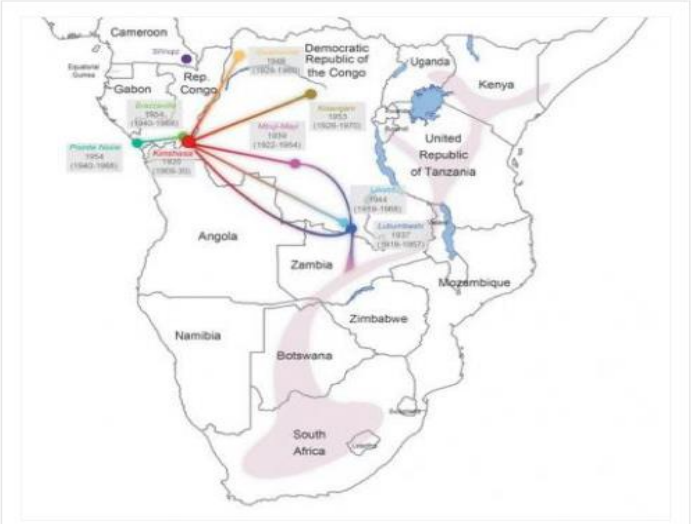
A previously healthy 33-year-old man developed *P. carinii* pr
candidiasis in March 1981 after a 2-month history of fever a
enzymes, leukopenia, and CMV viruria. The serum compl
October 1980 was 256; in May 1981 it was 32.* The pati
spite courses of treatment with trimethoprim-sulfamet
ine, and acyclovir. He died May 3, and postmortem exa
nd CMV pneumonia, but no evidence of neoplasia.
viously healthy 30-year-old man developed *P.*
onth history of fever each day and of elev
ted seroconversion

El VIH. Origen

- Dos zoonosis
  - Chimpancé (HIV-1)

  - Macaco (HIV-2)





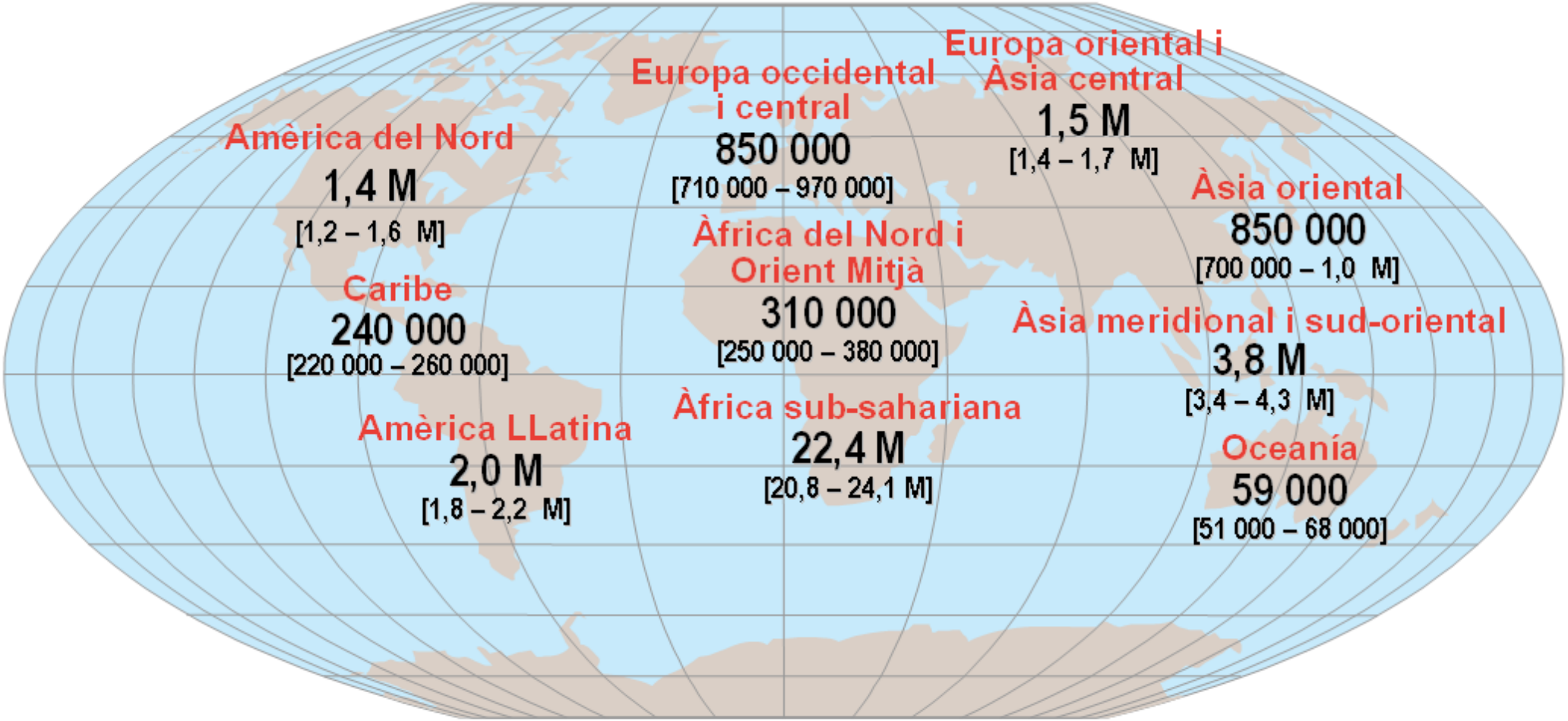
"Our genetic data tells us that HIV very quickly spread across the DRC, traveling with people along railways and waterways to reach Mbuji-Mayi and Lubumbashi in the extreme South and Kisangani in the far North by the end of the 1930s and early 1950s," says Dr. Nuno Faria. Image credit: KU Leuven

Gao F et al. Origin of HIV-1 in the chimpanzee Pan troglodytes troglodytes. Nature. 1999, 397:436-41.

http://www.medicalnewstoday.com/articles/283454.php

HIV infection: state of the epidemic

2009 AIDS EPIDEMIC UPDATE

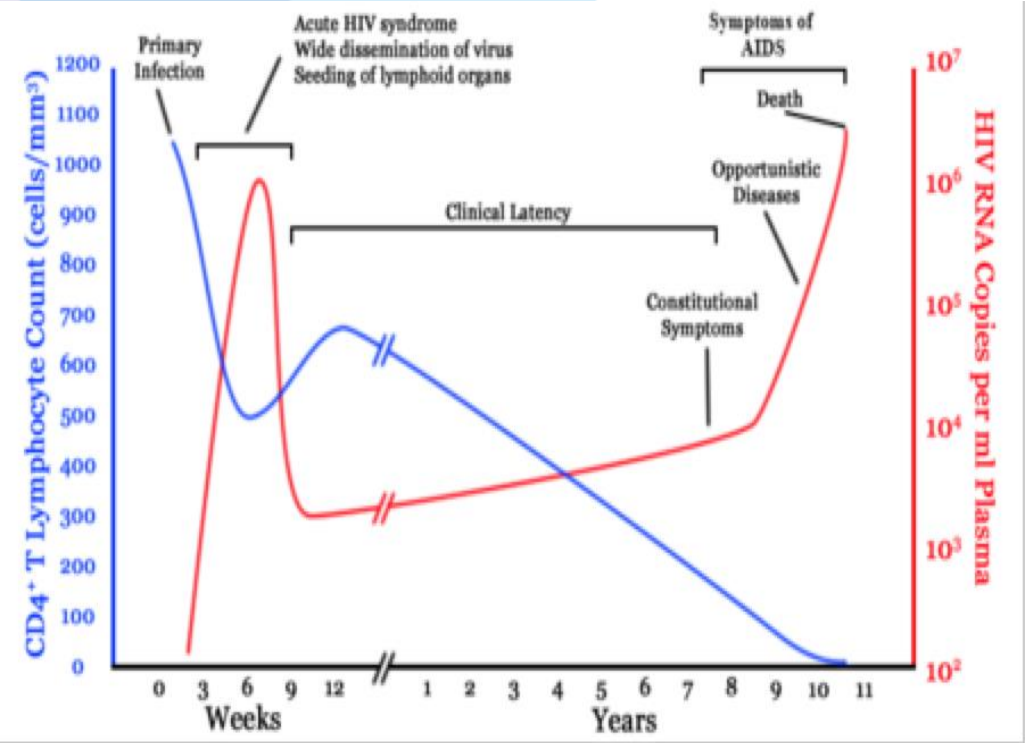


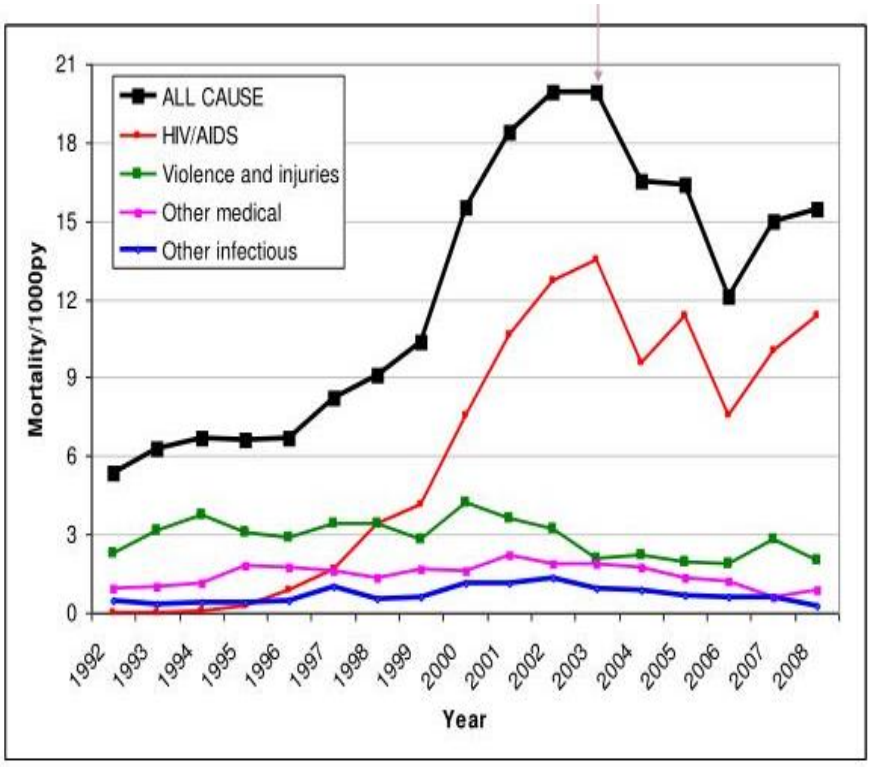
Total: 33,4 milions (31,1 – 35,8 milions)

ONUSIDA
PROGRAMA CONJUNTO DE LAS NACIONES UNIDAS SOBRE EL VIH/SIDA

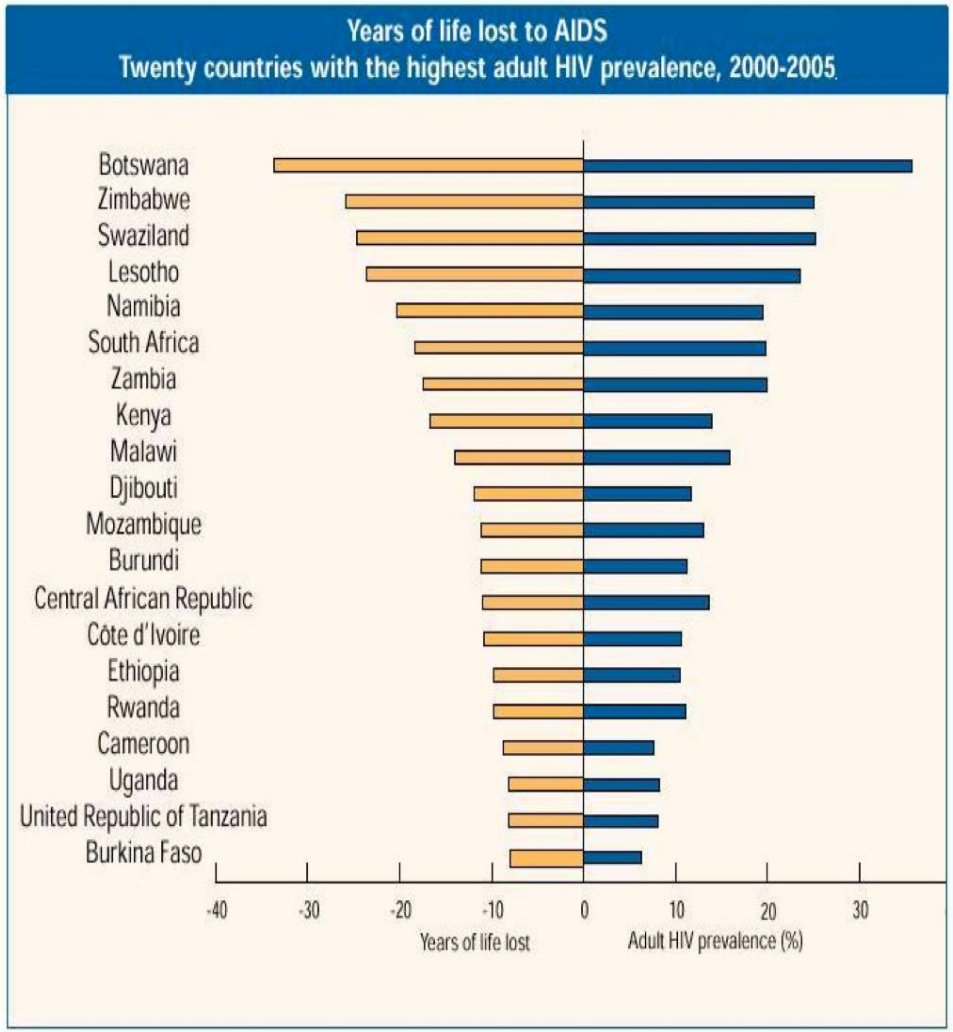
Organización Mundial de la Salud

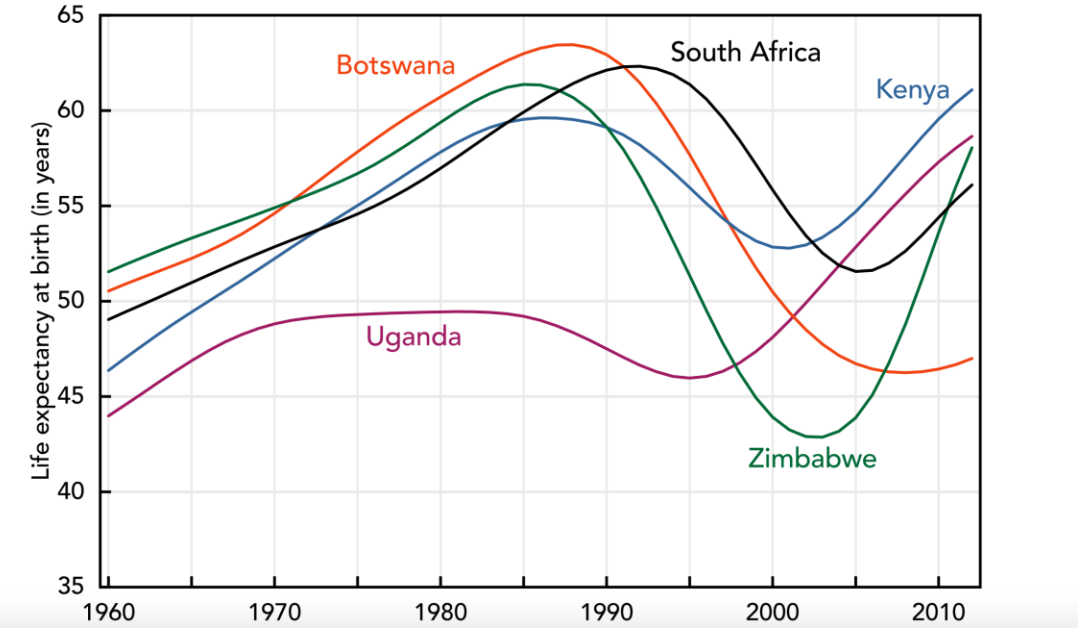
HIV disease course and mortality (South Africa)

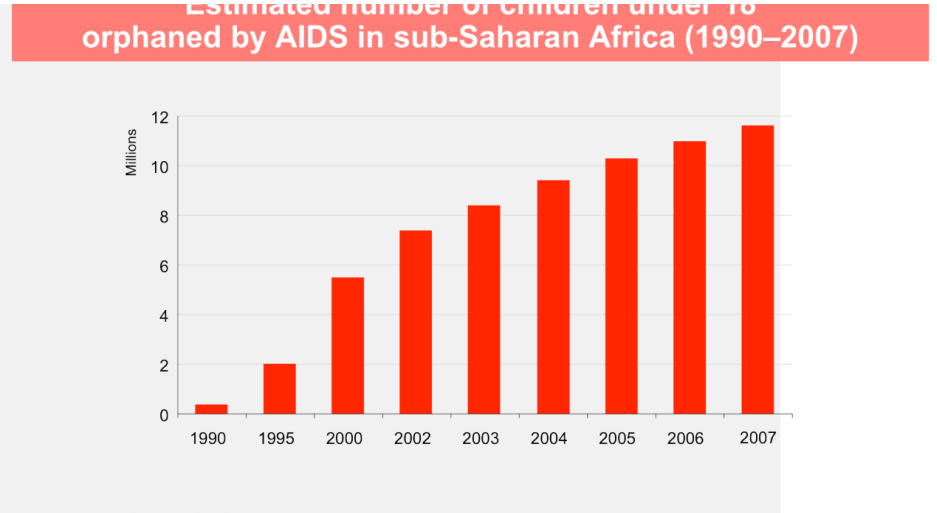




Demographic impact on sub-Saharian populations







How can we fight HIV ?

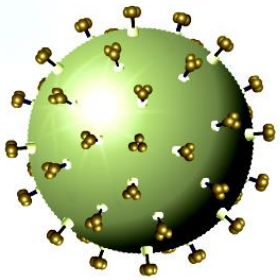
- Reduce transmission rates

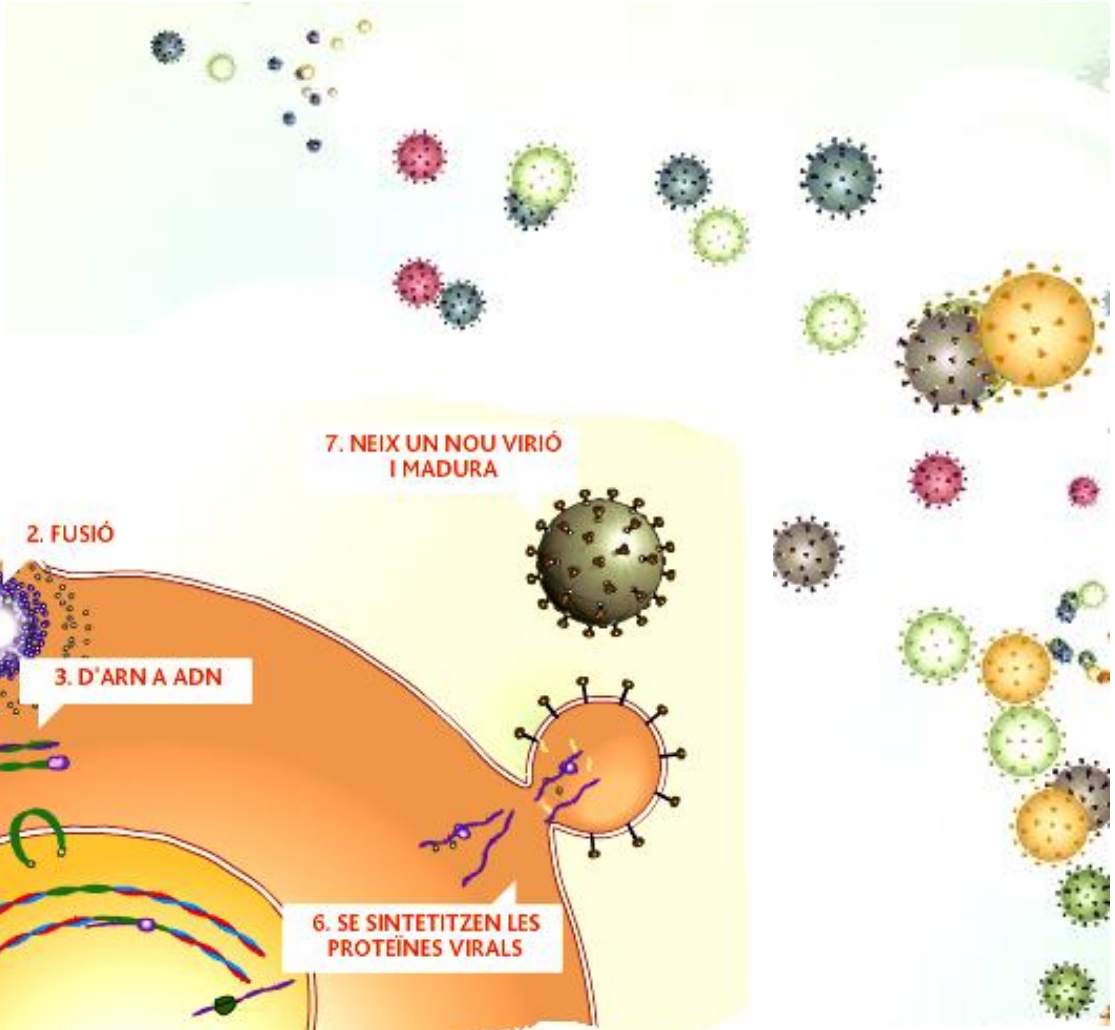
- Reduce mortality and HIV disease

- Antiretroviral drugs

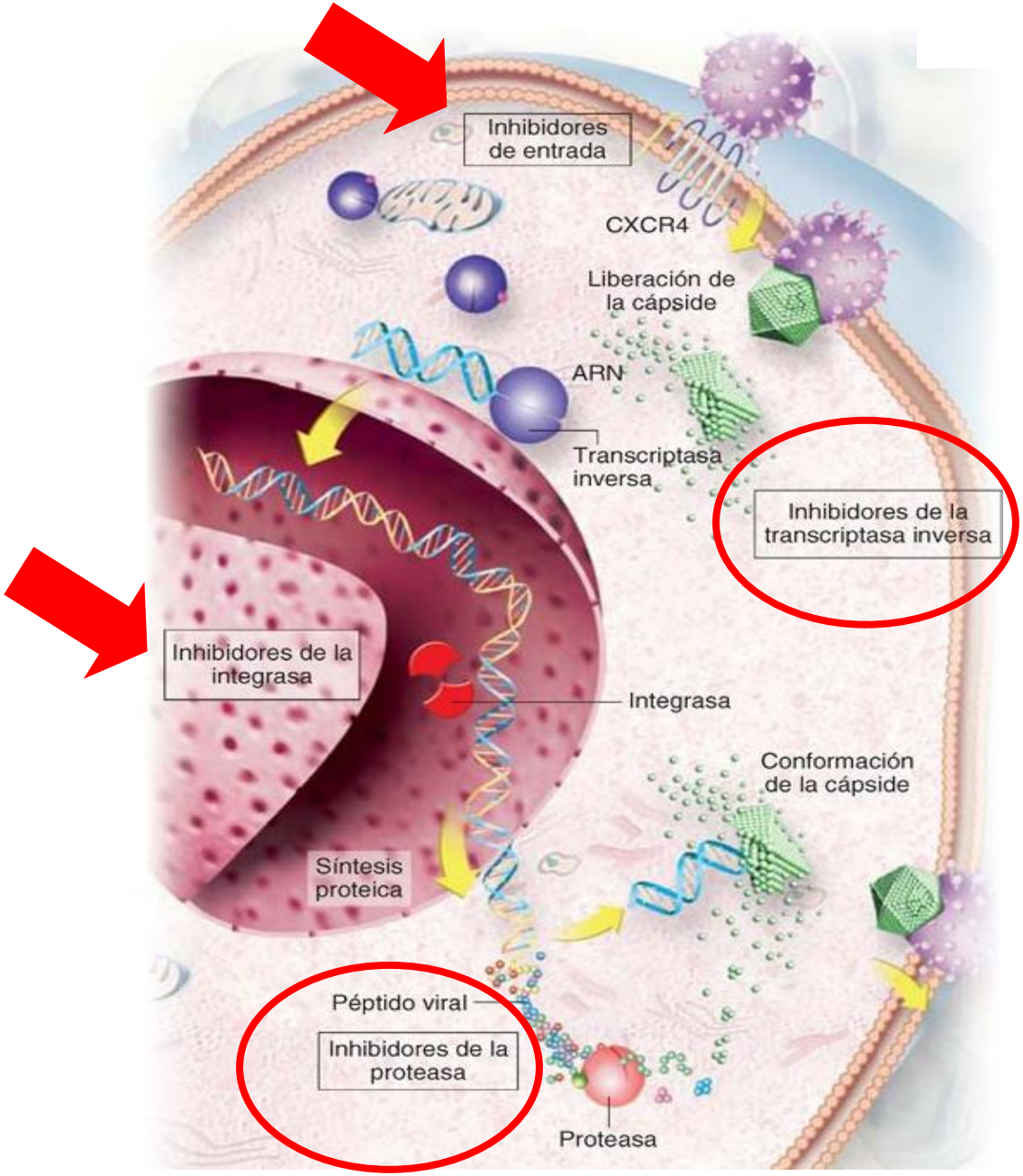
- Vaccines for prevention and therapy

Life cycle and replication of HIV

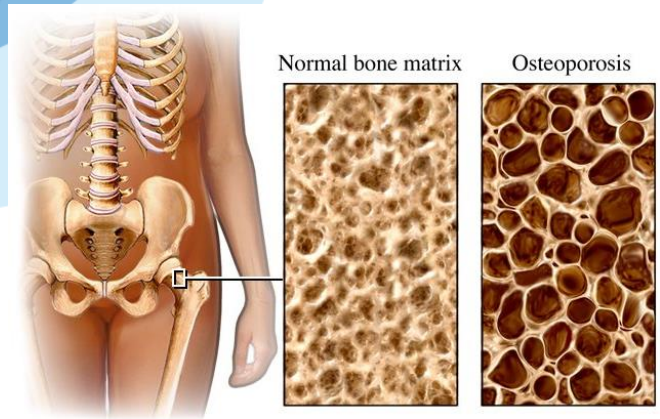




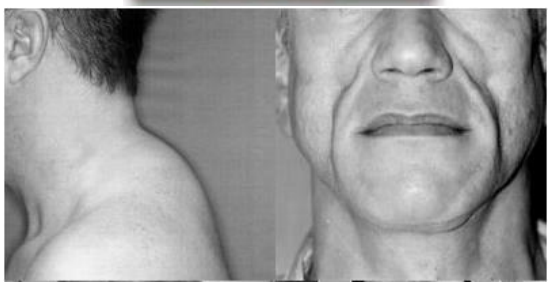
Antiretroviral treatment



Toxicity

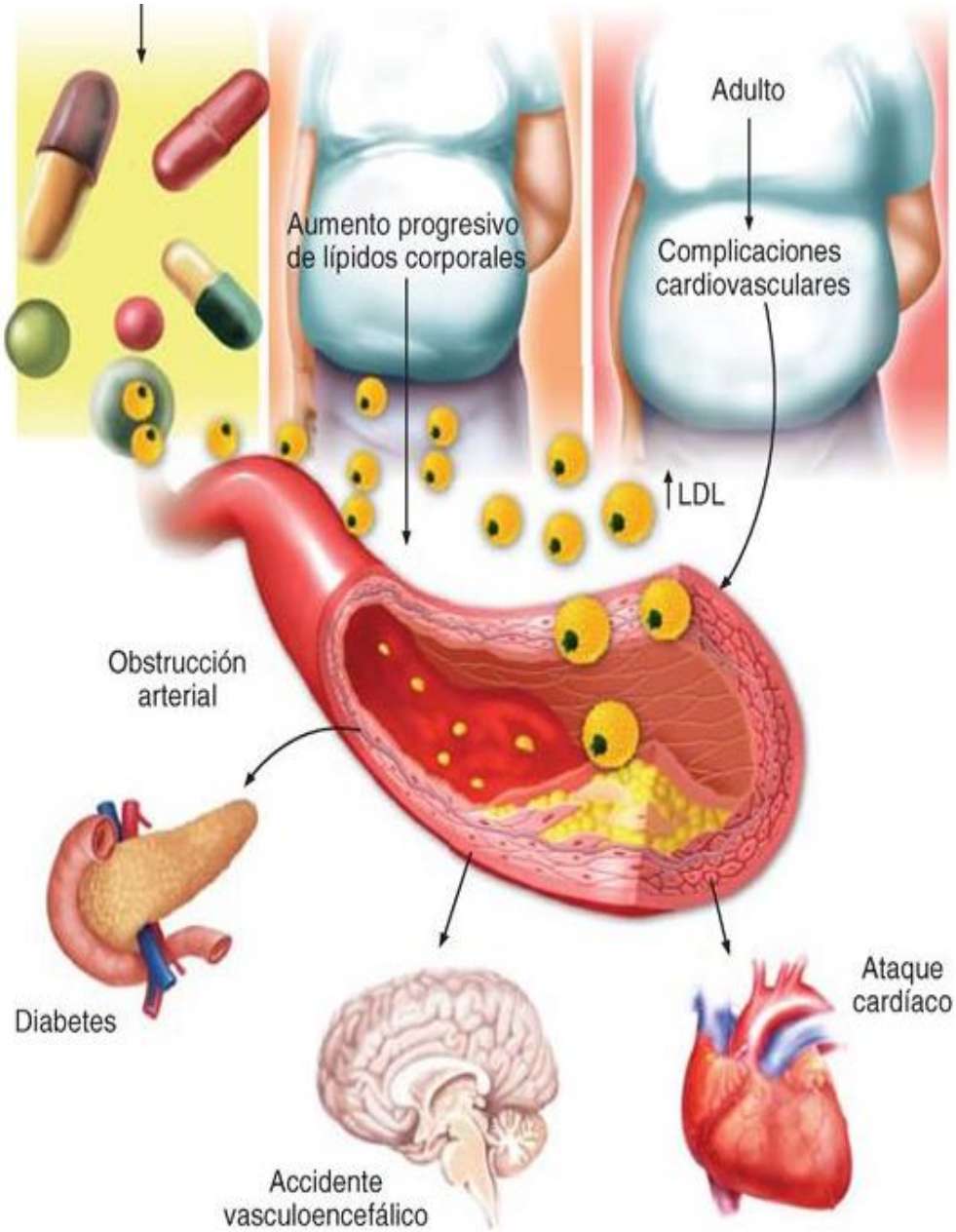

Normal bone matrix
Osteoporosis


Pérdida de grasa
en glúteos

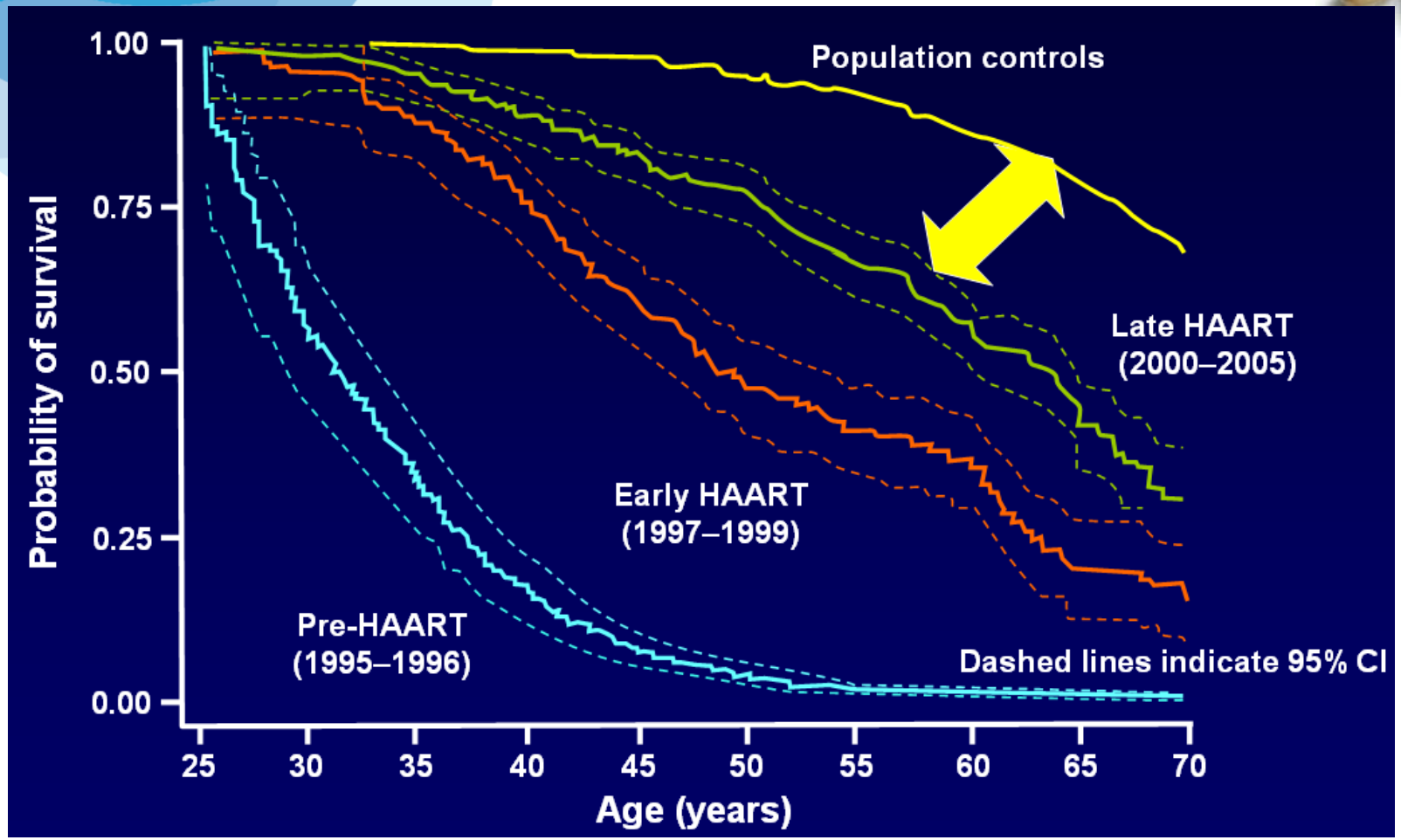



Esteatosis
hepática


Nefropatía


Adulto
Aumento progresivo
de lípidos corporales
Complicaciones
cardiovasculares
LDL
Obstrucción
arterial
Diabetes
Accidente
vasculoencefálico
Ataque
cardíaco

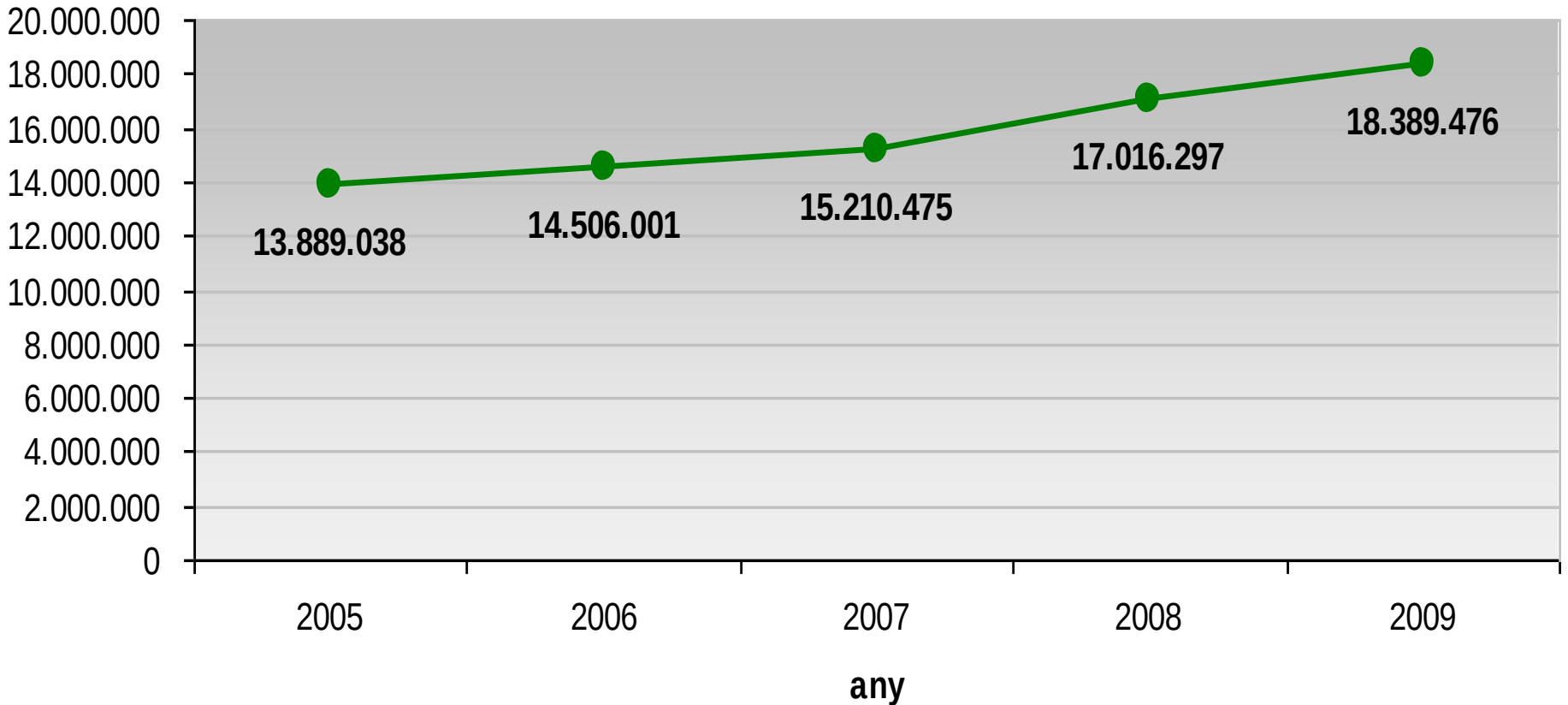
Antiretroviral treatment



Elevated costs are not sustainable

Despesa farmàcia Unitat VIH

Germans Trias i Pujol Hospital



PREVENTION !

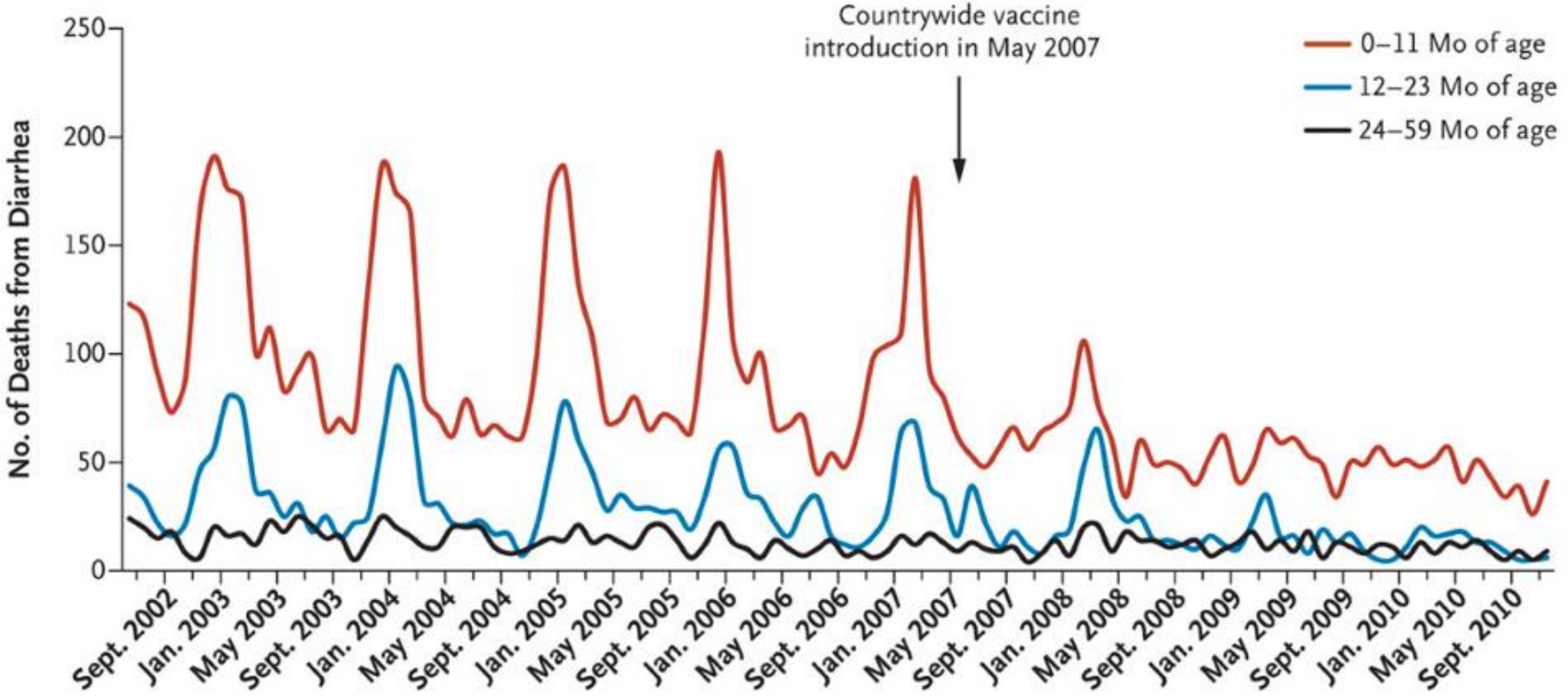
SIDA / HIV

Influenza

PREVENTION !

We need a HIV Vaccine !!!

Effect of vaccination for HIV-unrelated infections (Rotavirus, Mexico)



Effect of vaccination for HIV-unrelated infections

Reduction of number of cases for vaccine-preventable diseases in the United States before and after the introduction of the vaccine – Roush and Murphy (2007)[4]

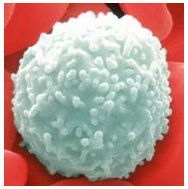
Disease	Number of Annual Prevaccine Cases	Number of Annual Postvaccine Cases	Reduction of Cases after Vaccine Introduction (in %)
Diphteria	21,053	0	100%
Measles	530,162	55	99.90%
Mumps	162,344	6,584	95.90%
Pertussis	200,752	15,632	92.20%
Poliomyeltis, acute	19,794	0	100%
Poliomyeltis, paralytic	16,316	0	100%
Rubella	47,745	11	99.90%
Congenital rubella syndrome	152	1	99.30%
Smallpox	29,005	0	100%
Tetanus	580	41	92.90%
Hepatitis A	117,333	15,298	87%
Acute hepatitis B	66,232	13,169	80.10%
Invasive (Haemophilus influenza type b)	20,000	<50	>99.8%
Invasive (pneumococcal disease)	63,067	41,550	34.10%
Varicella	4,085,120	612,768	85

Reduction of number of deaths for vaccine-preventable diseases in the United States before and after the introduction of the vaccine – Roush and Murphy (2007)[5]

Disease	Number of Annual Prevaccine Deaths	Number of Annual Postvaccine Deaths	Reduction of Deaths after Vaccine Introduction (in %)
Diphteria	1822	0	100%
Measles	440	0	100%
Mumps	39	0	100%
Pertussis	4034	27	99.30%
Poliomyeltis, acute	1393	0	100%
Poliomyeltis, paralytic	1879	0	100%
Rubella	17	0	100%
Congenital rubella syndrome	--	0	--
Smallpox	337	0	100%
Tetanus	472	4	99.20%
Hepatitis A	137	18	86.90%
Acute hepatitis B	237	47	80.20%
Invasive (Haemophilus influenza type b)	–	<5	>99.5
Invasive (pneumococcal disease)	6500	4850	25.4
Varicella	105	19	81.9

Com funcionen les vacunes?

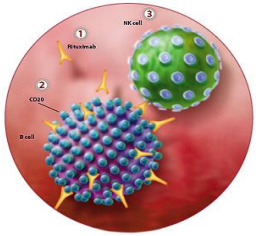
The vaccine provides parts and pieces of the microoroganism to stimulate an immune response

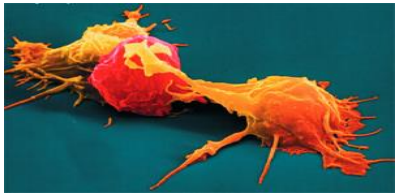


B and T cells in the blood and tissue become activated and persist for many years

Memory T and B cells can react quicker and stronger when the body sees the pathogen again

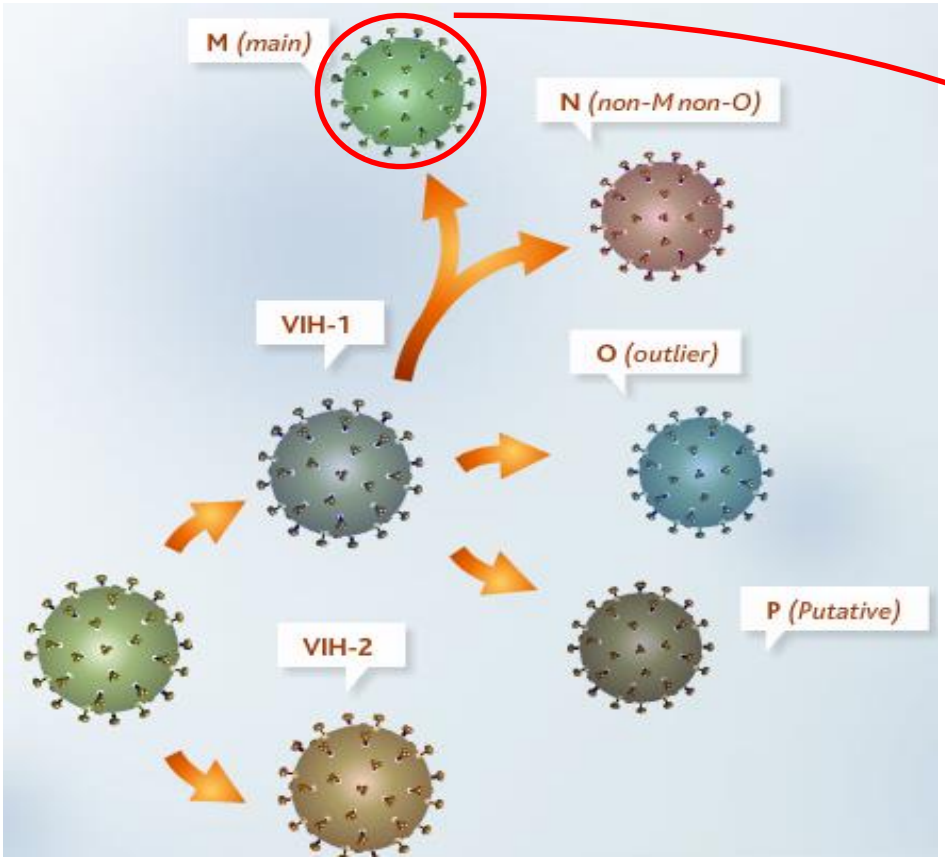
B cells produce antibodies which bind the pathogen and dis-activate it

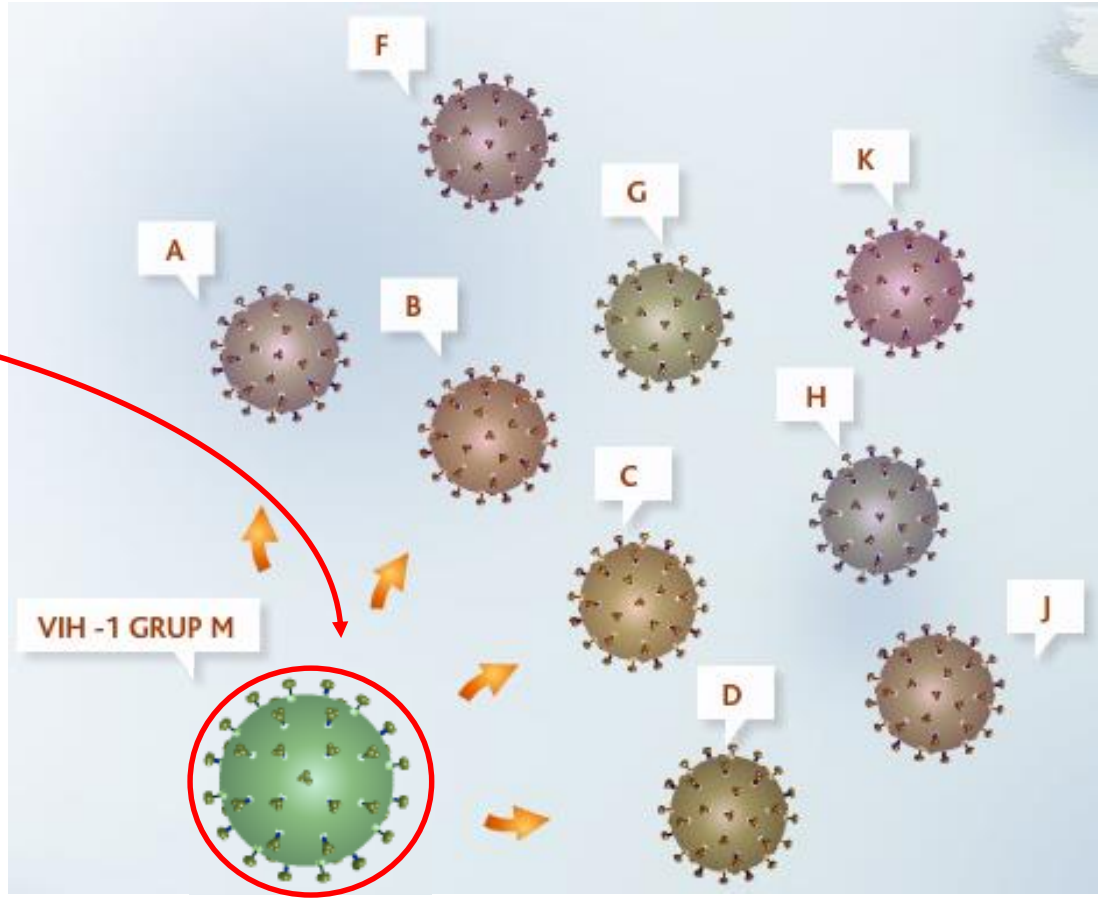




CD4+ T cells help the production of antibodies and support the expansion and activation of killer CD8 T cells which eliminate infected cells

Main hurdles in the development of a HIV vaccine



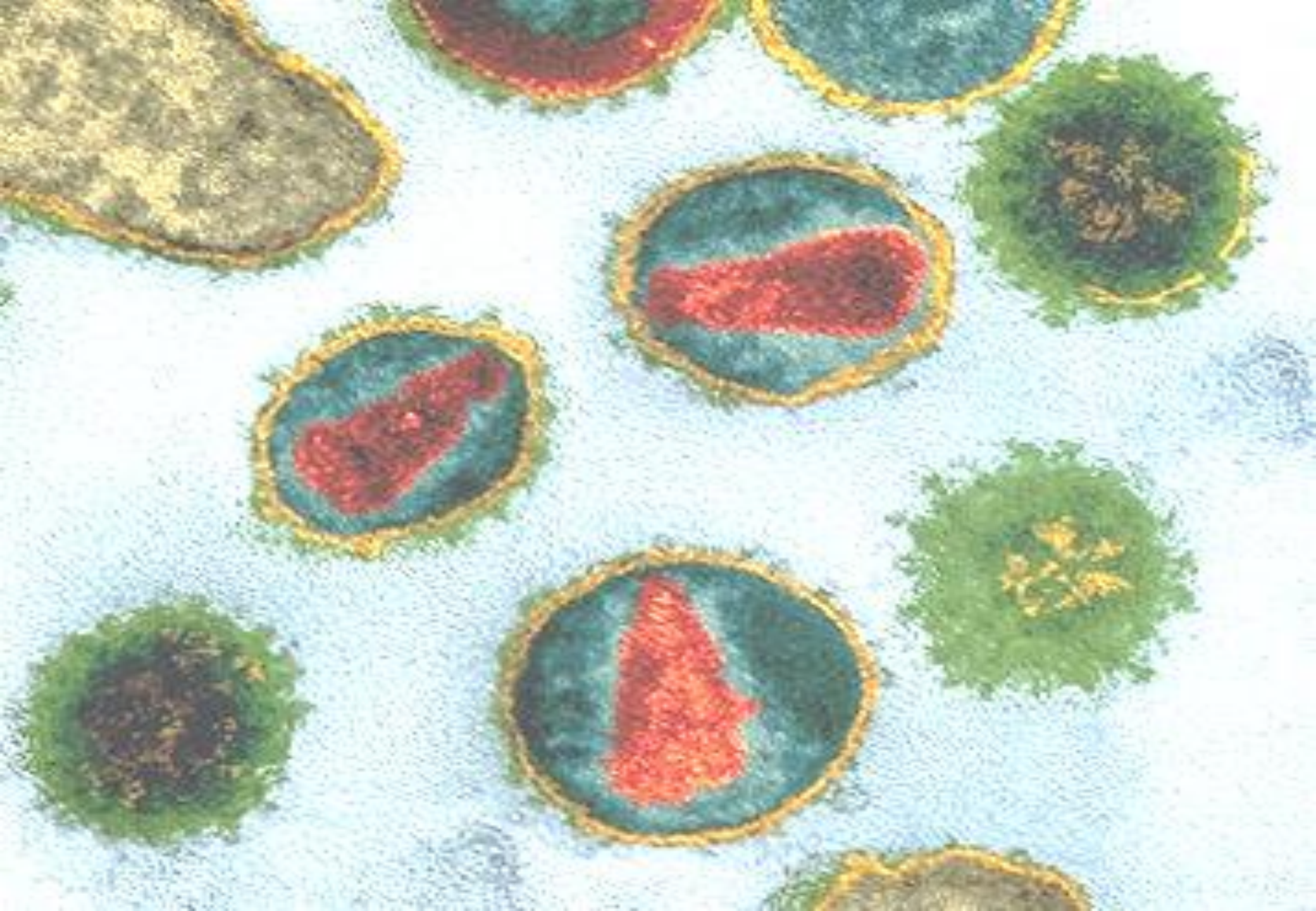


HIVACAT
Projecte de Recerca de la Vacuna de la Sida

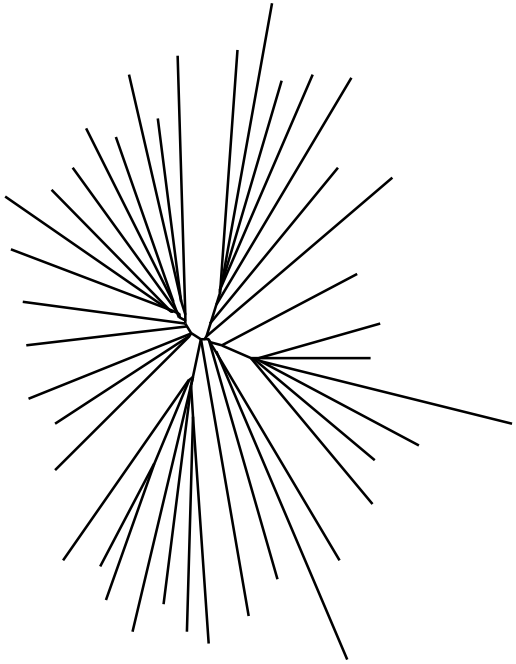
Main hurdles in the development of a HIV vaccine

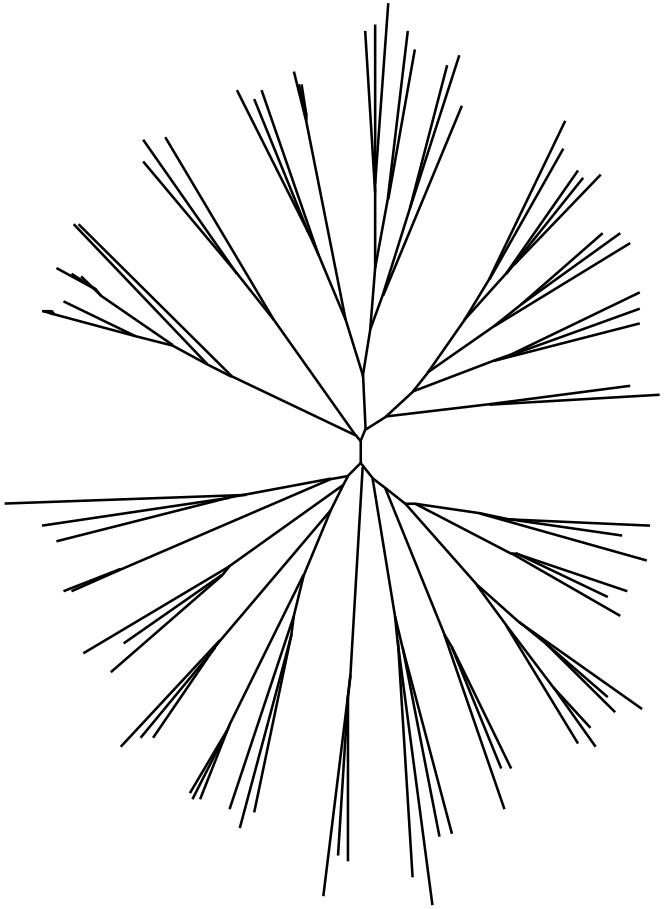
L'elevada taxa de mutació del VIH fa que les persones infectades hagin de prendre precaucions tota la vida, donat que es podrien reinfectar amb altres variants, cosa que complicaria més poder trobar tractaments eficaços.

HIVACAT
Projecte de Recerca de la Vacuna de la Sida



Main hurdles in the development of a HIV vaccine





Virus de la grip a nivell mundial

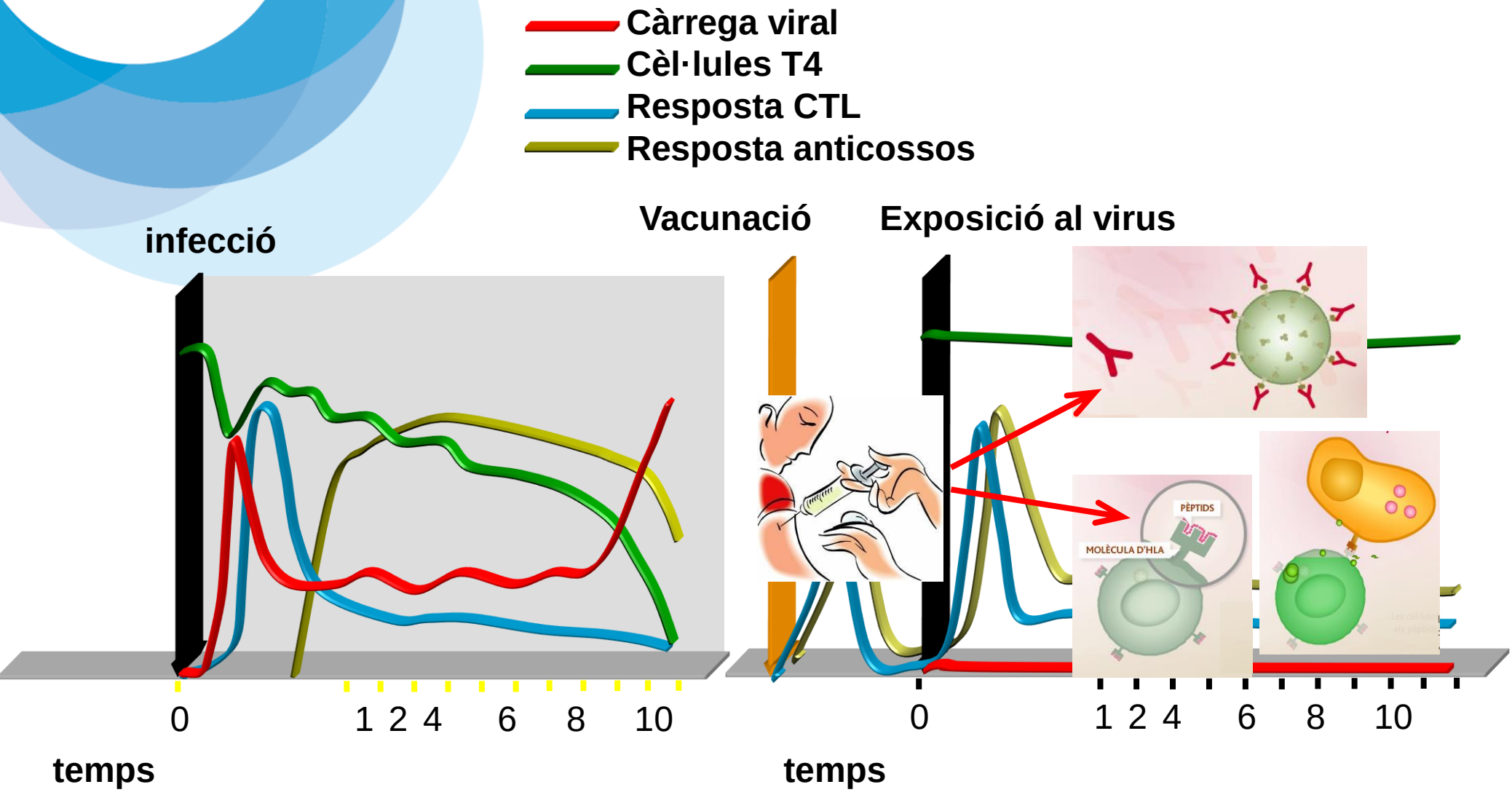
Virus del VIH en un SOL pacient

Virus del VIH en una regió

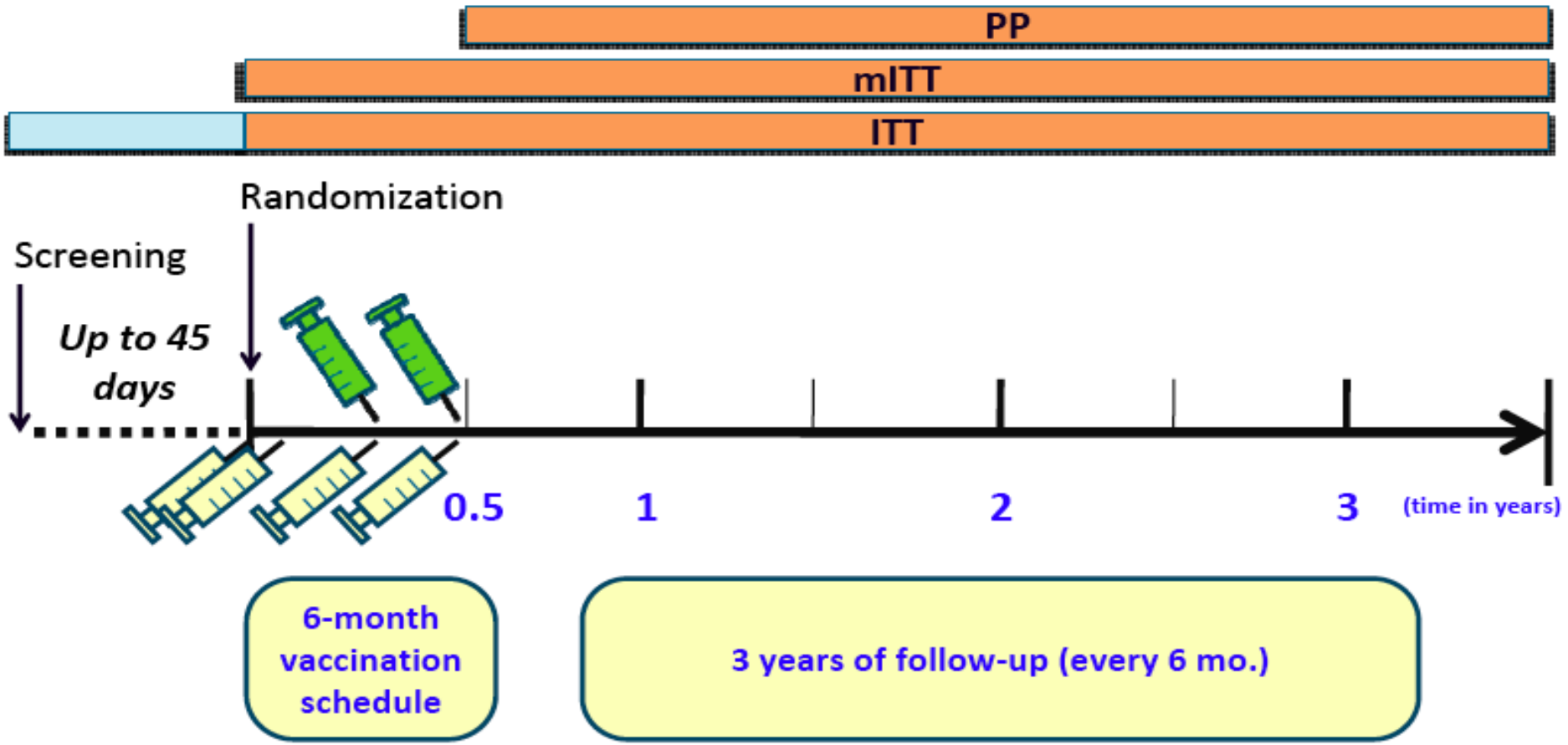
Virus del VIH a nivell mundial

Adapted from Francine McCutchan and from Korber B, et al. Brit Med Bull 2001; 58:19-42.

What has been achieved so far



Endpoint Accrual Timeframes



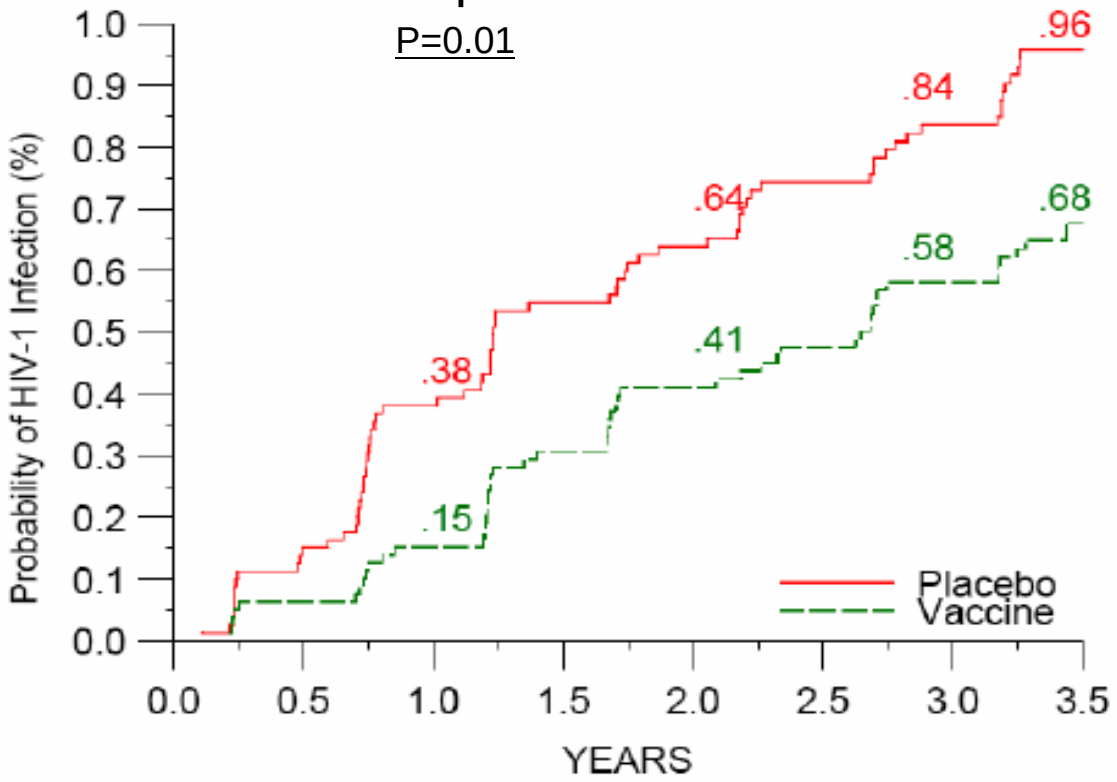
ALVAC®-HIV (vCP1521) priming at week 0, 4, 12, 24

AIDSVAX® B/E gp120 boosting at week 12, 24

HIVACAT
Projecte de Recerca de la Vacuna de la Sida

Efficacy (mITT)

Cumulative # Infections	Placebo	30	50	65	74
	Vaccine	12	32	45	51



52,985 person-years

125 infections

Vaccine infections: 51
Placebo infections: 74

VE: 31.2%
p=0.04
95% CI: 1.1, 52.1
(O'Brien-Fleming-adjusted)

HIV Vaccine development in HIVACAT

HIVACAT

Projecte de Recerca de la Vacuna de la Sida

IrsiCaixa

Institut de Recerca de la Sida

Obra Social

Fundació "la Caixa"

FUNDACIÓ CLÍNIC BARCELONA

Generalitat de Catalunya
Departament de Salut

GOBIERNO DE ESPAÑA
MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD

ESTEVE

Generalitat de Catalunya
Departament d'Innovació, Universitats i Empresa

CUTHIVAC
CUTANEOUS HIV VACCINATION

SEVENTH FRAMEWORK PROGRAMME

icrea

Institució Catalana de Recerca i Estudis Avançats

NIDCR National Institutes of Health
National Institute of Dental and Craniofacial Research

catSIDA

Càtedra de SIDA i Malalties Relacionades - UVic-UCC

HIV Vaccine development in HIVACAT

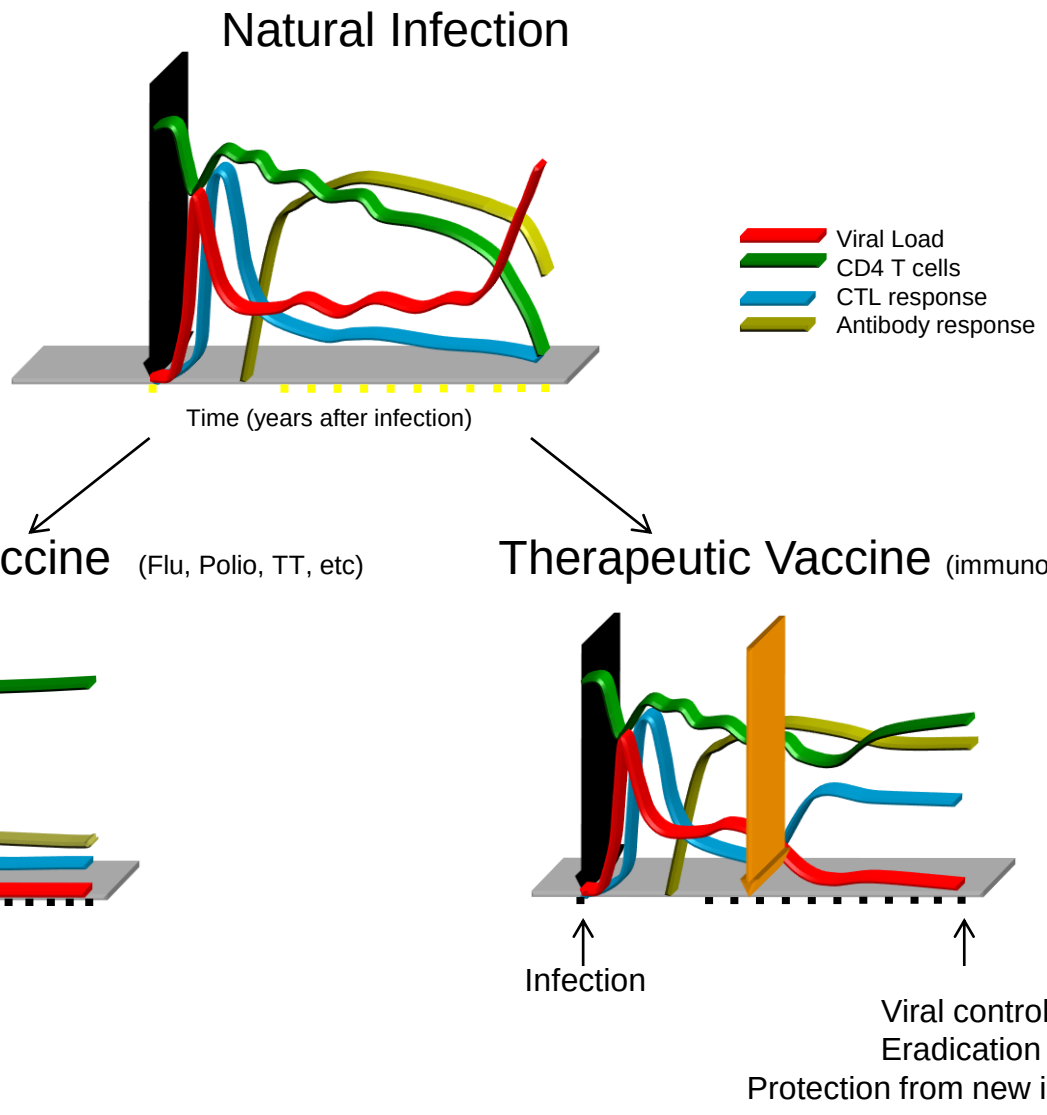
HIVACAT

Projecte de Recerca de la Vacuna de la Sida

AELIX

THERAPEUTICS

Concepts of preventive and therapeutic HIV vaccines



Take home message

- HIV continues to spread across the globe, including all segments of the population and all countries !
- Prevention is in most cases (and in theory) simple
- HIV infection can be treated and made into a chronic infection with extensive life expectancy; however risks of resistance mutations and drug-related side effects exist
- Interventions in HIV infected individuals may offer ways to eliminate the virus from the body, but this is in the far future
- A preventive vaccine is the only sustainable way to halt the pandemic
- If you are at risk of HIV infection, get tested ! Regularly.