

“Supervivencia y esperanza de vida en personas viviendo con VIH”



Generalitat de Catalunya
Departament de Salut

A. - Objetivos de la presentacion

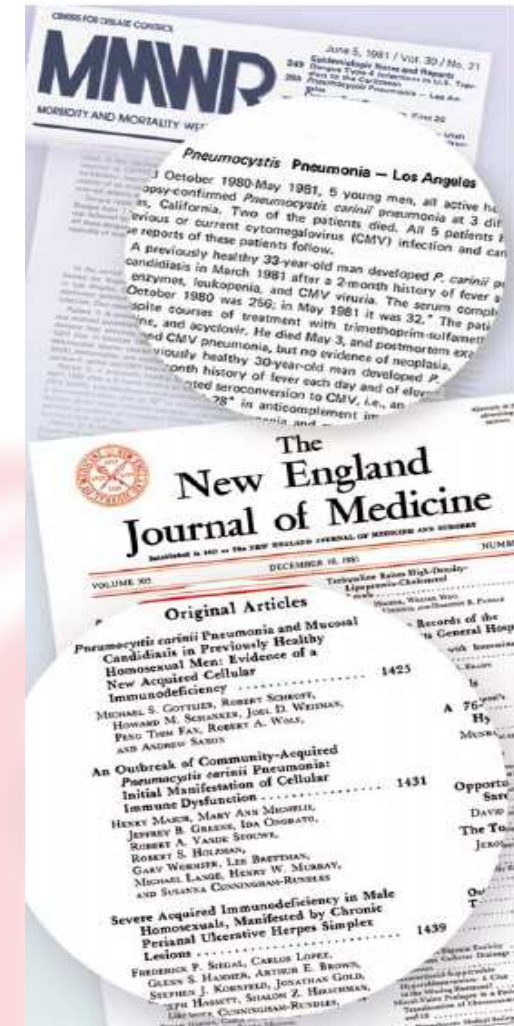
- Resumir la historia natural del VIH
- Repasar la epidemiología actual de la infección
- Resumir las supervivencia histórica y actual de personas viviendo con VIH y sus tendencias

1. - Historia del VIH - i

- Una zoonosis (transmitido de animal a humano)
- HIV-1 resulta de 3 transmisiones independiente
Resultando en los 3 grupos prevalentes (M N O)
- Probablemente ocurro entre 1910 1940
- Primer caso registrado 1959 de un hombre del Congo

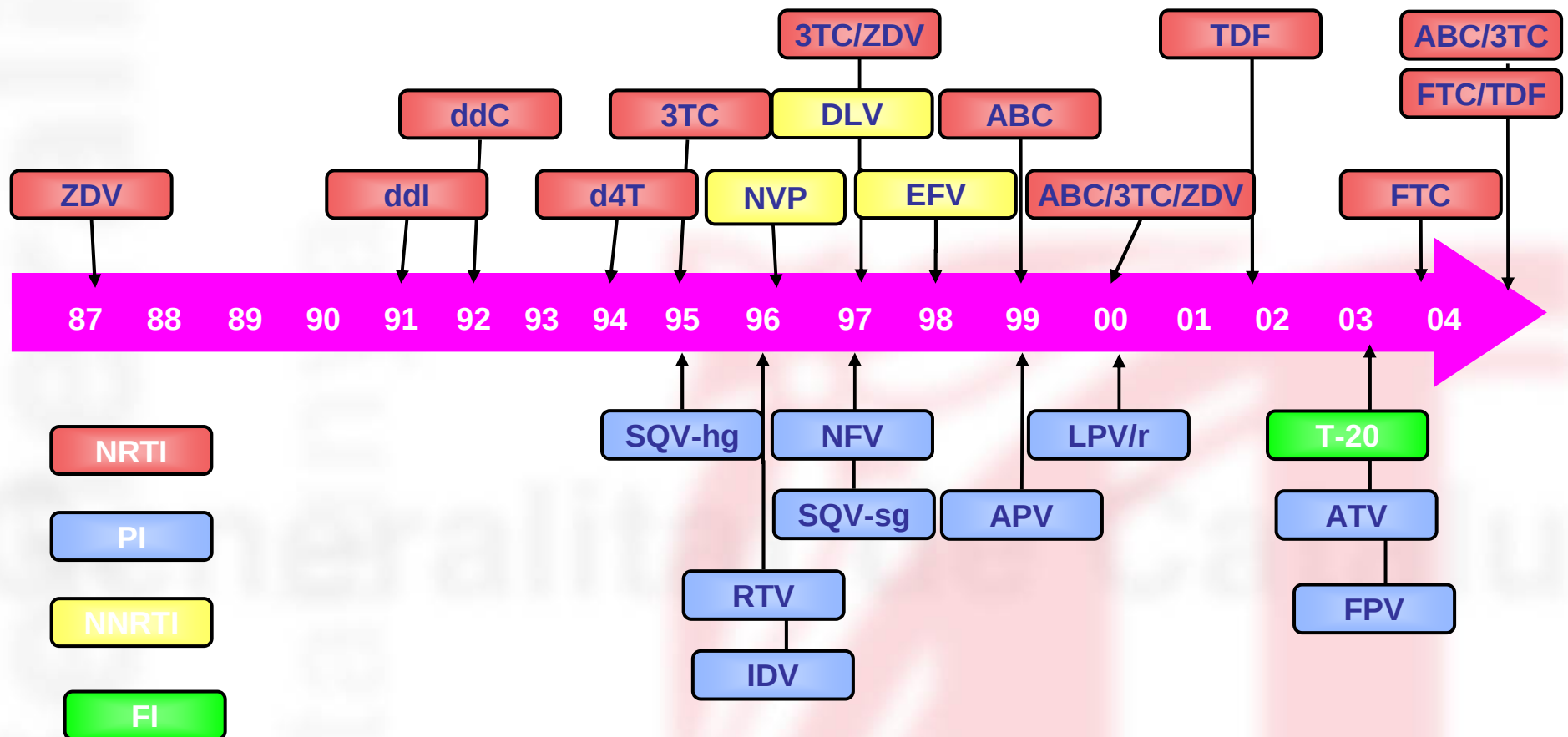
1. - Historia del VIH - ii

- Primer reporte en MMWR en 1981
- “AIDS” nombrado en 1982
- Virus aislado en 1983
- Primera prueba en 1985
- Primer medicamento AZT en 1987
- Biterapia 1994
- TARGA 1996

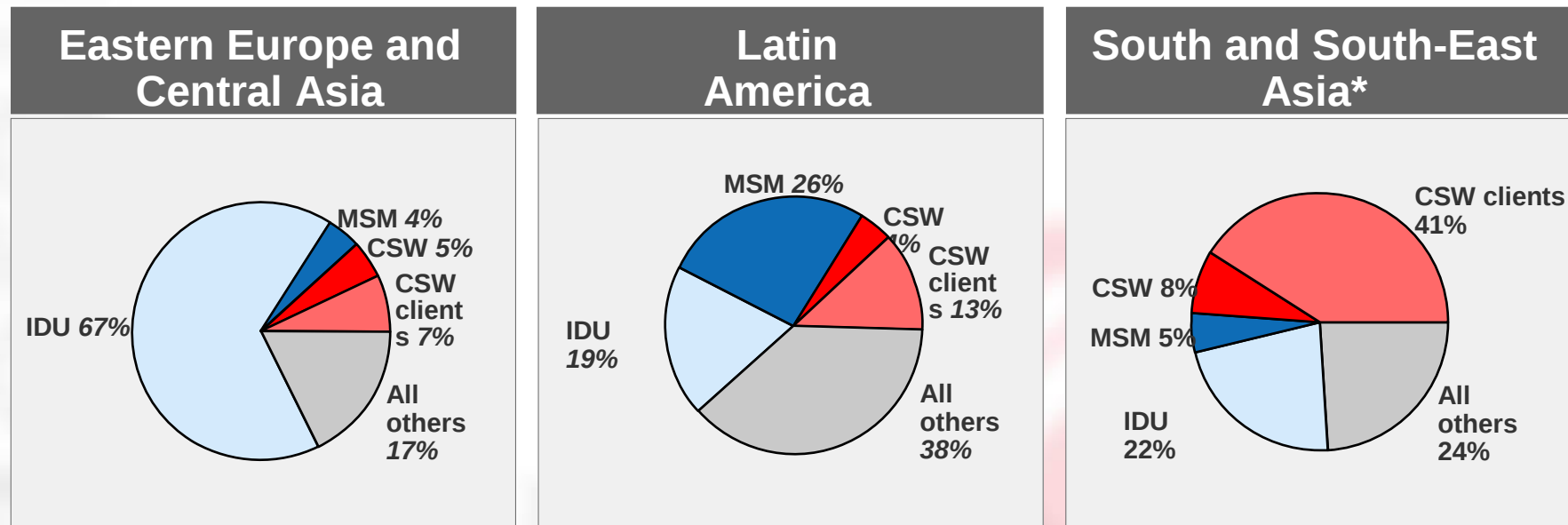


Gottlieb MS NEJM 2001;344:1788-91

Antiretrovirals aprobados



Proportions of HIV infections in different population groups by region, 2005

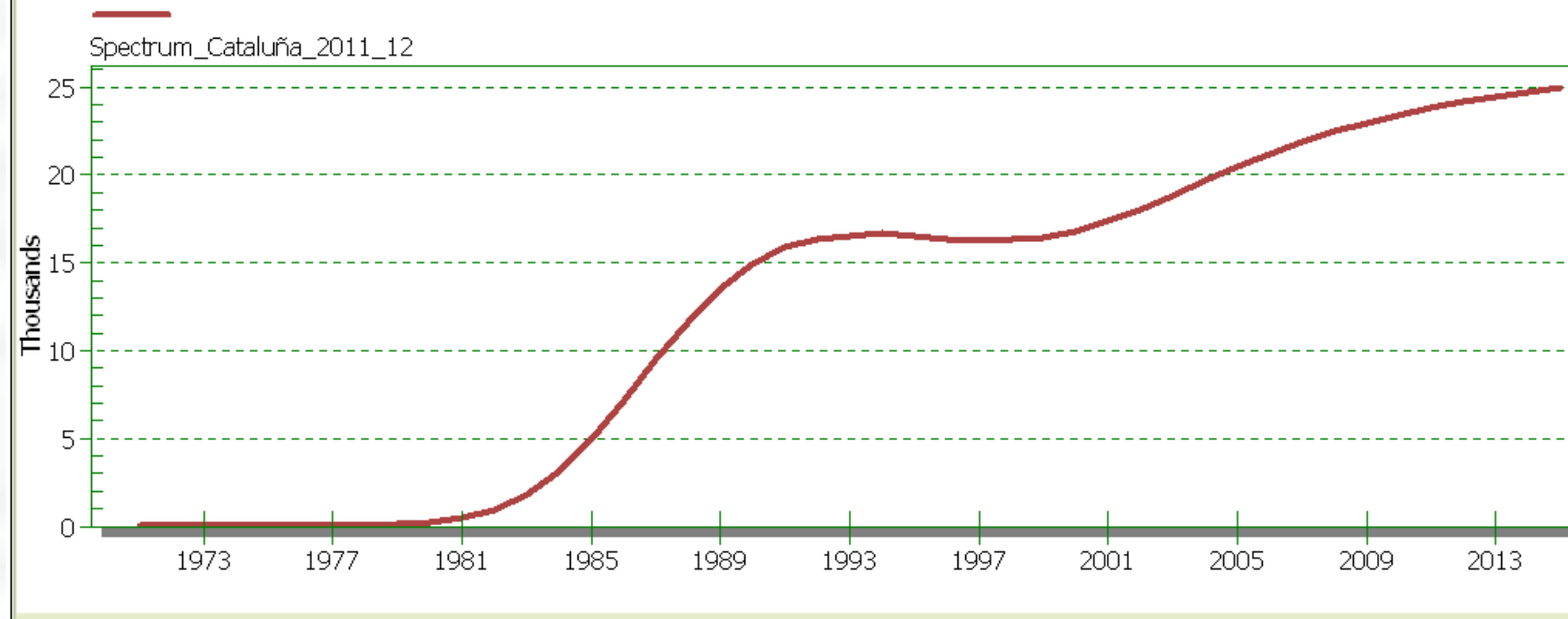


IDU: Injecting Drug Users
MSM: Men having sex with men
CSW: Commercial Sex Workers

* India was omitted from this analysis because the scale of its HIV epidemic (which is largely heterosexual) masks the extent to which other at-risk populations feature in the region's epidemics.

Figure 2

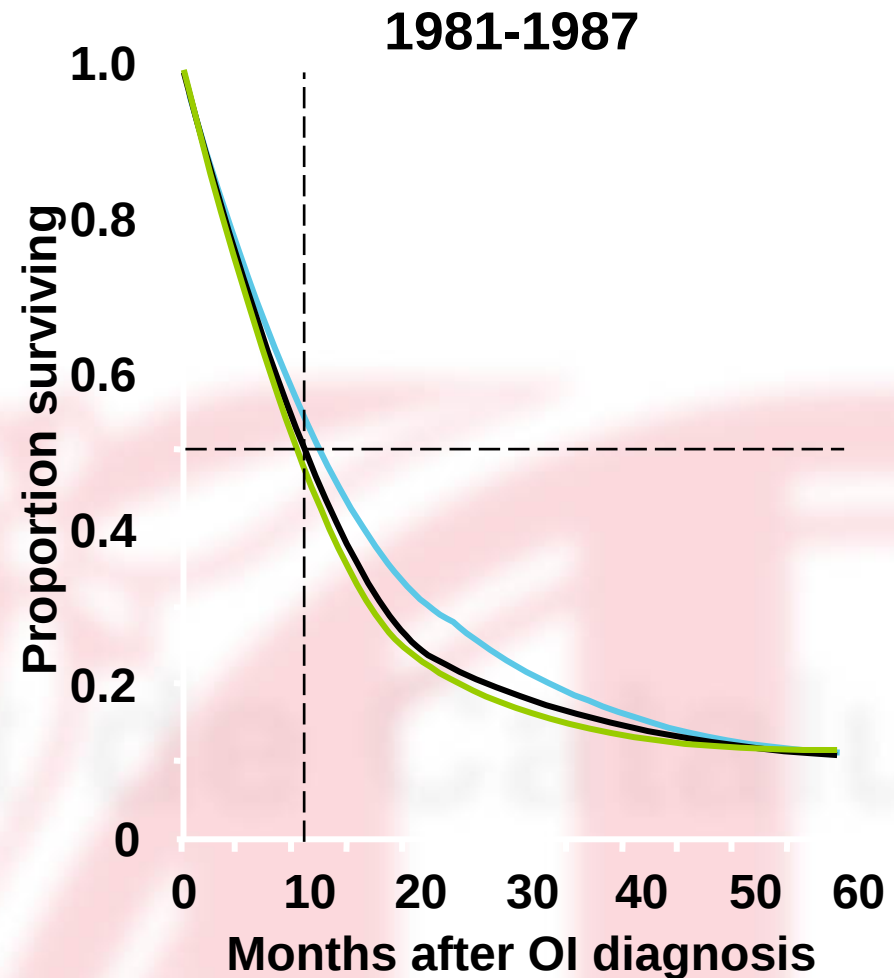
HIV population



2. - Historia natural del VIH

- Supervivencia en los primeros años: 50% fallecidos en 10 meses
- Dr Gottlieb “*..the experience of seeing so many patients die was numbing...I doubted that science would find a way to lower the rate of death in my lifetime*”

Gottlieb, M.S., 2001. AIDS--past and future. *The New England Journal of Medicine*, 344(23), pp.1788-1791.



Fuente : National AIDS case surveillance data, CDC

3. - Cambios en la esperanza de vida - evidencia

TABLE 2. Relative Risk of Death and Morbidity Among Patients with CD4+ T-Lymphocyte Counts of Fewer Than 100 per Cubic Millimeter, According to Type of Antiretroviral Therapy.*

ANTIRETROVIRAL-THERAPY CATEGORY†	ADJUSTED RELATIVE RISK (95% CI)‡	P VALUE
Mortality		
None vs. monotherapy	1.5 (1.2–2.0)	0.002
None vs. combination	2.9 (2.1–4.2)	<0.001
None vs. combination + PI	4.5 (3.3–6.2)	<0.001
Monotherapy vs. combination	1.9 (1.4–2.7)	<0.001
Monotherapy vs. combination + PI	3.0 (2.1–4.1)	<0.001
Combination vs. combination + PI	1.5 (1.0–2.2)	0.03
Morbidity		
None vs. monotherapy	1.9 (1.2–2.8)	0.003
None vs. combination	2.4 (1.5–3.7)	<0.001
None vs. combination + PI	4.5 (2.8–7.2)	<0.001
Monotherapy vs. combination	1.3 (0.8–1.9)	0.26
Monotherapy vs. combination + PI	2.4 (1.5–3.8)	<0.001
Combination vs. combination + PI	1.9 (1.2–3.1)	0.01

*Morbidity was defined for this analysis as a diagnosis of *Pneumocystis carinii* pneumonia, *Mycobacterium avium* complex infection, or cytomegalovirus retinitis.

†Antiretroviral therapy was categorized as follows: no antiretroviral therapy, monotherapy, combination therapy without a protease inhibitor (combination), and combination therapy with a protease inhibitor (combination + PI).

‡For mortality, the relative risks have been adjusted for study center and the CD4+ cell count at the first study visit (0 to 49, 50 to 99, or ≥100 per cubic millimeter); for morbidity, the model included these variables as well as the rate of prophylaxis against *M. avium* complex. CI denotes confidence interval.

Palella, F.J., Jr et al., 1998.
Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. *The New England Journal of Medicine*, 338(13), pp.853-860.

Primeras indicaciones de TAR exitoso

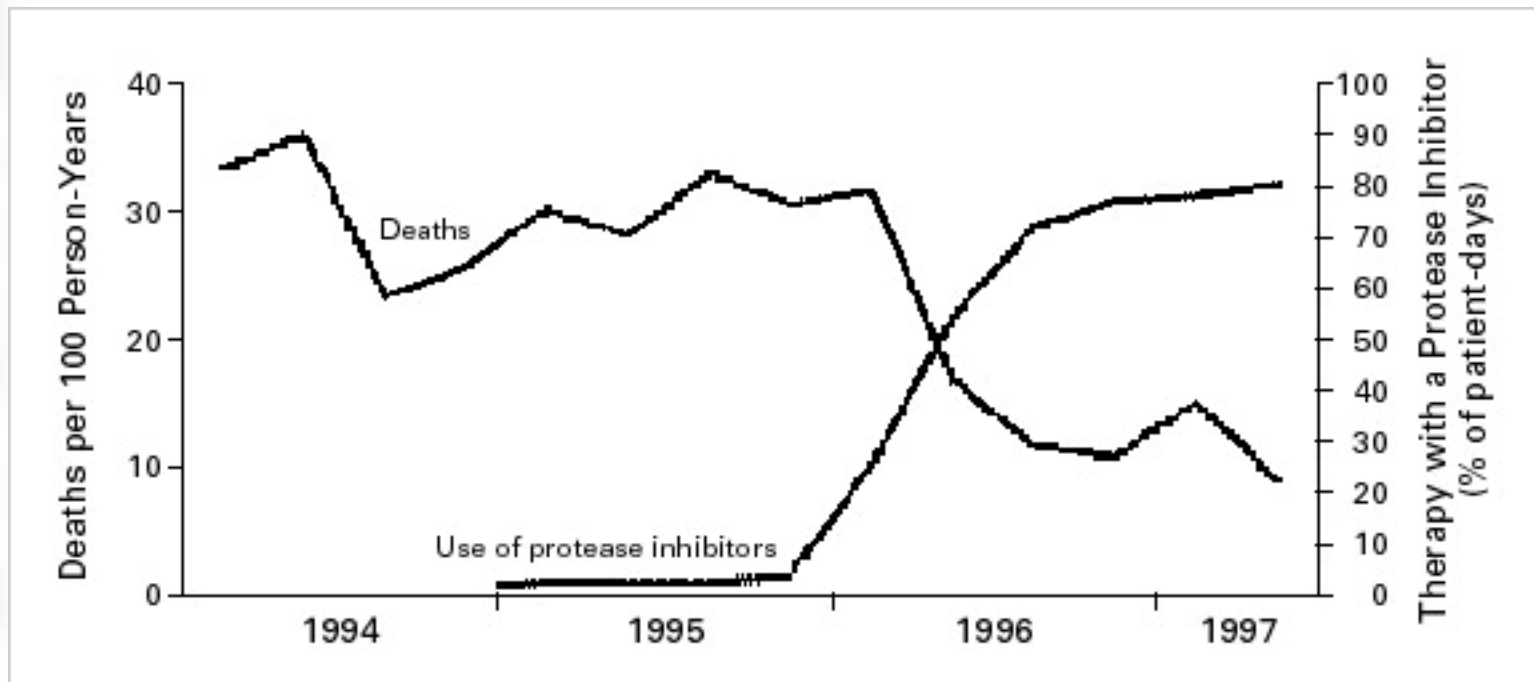


Figure 1. Mortality and Frequency of Use of Combination Antiretroviral Therapy Including a Protease Inhibitor among HIV-Infected Patients with Fewer than 100 CD4+ Cells per Cubic Millimeter, According to Calendar Quarter, from January 1994 through June 1997.

Palella, F.J., Jr et al., 1998. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. *The New England Journal of Medicine*, 338(13), pp.853-860.

3. - Cambios en la esperanza de vida - evidencia

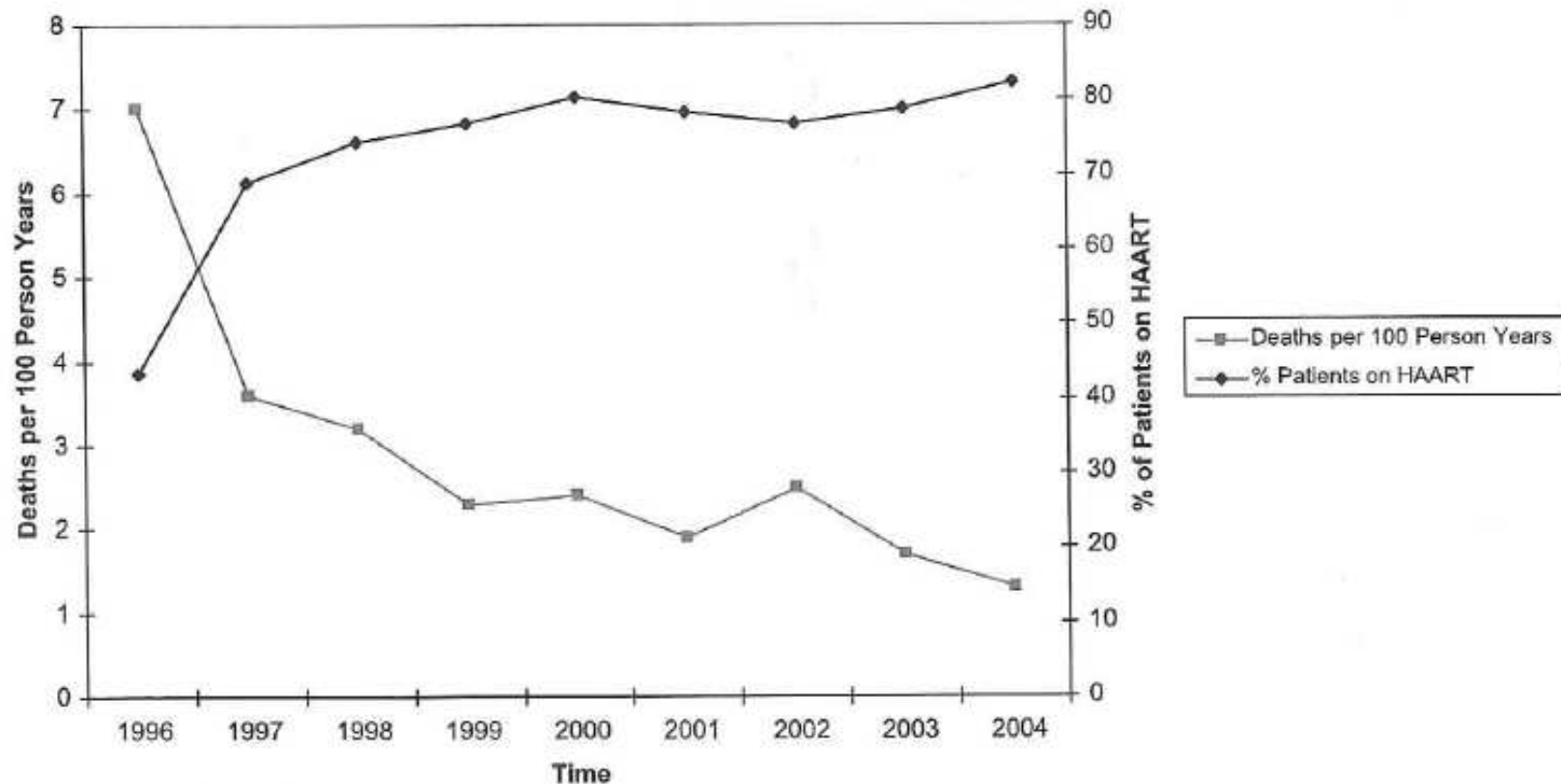


FIGURE 1. Mortality and HAART use over time.

Palella, F.J., Jr et al., 2006. Mortality in the highly active antiretroviral therapy era: changing causes of death and disease in the HIV outpatient study. *Journal of Acquired Immune Deficiency Syndromes* (1999), 43(1), pp.27-34.

3. - Cambios en la esperanza de vida - evidencia

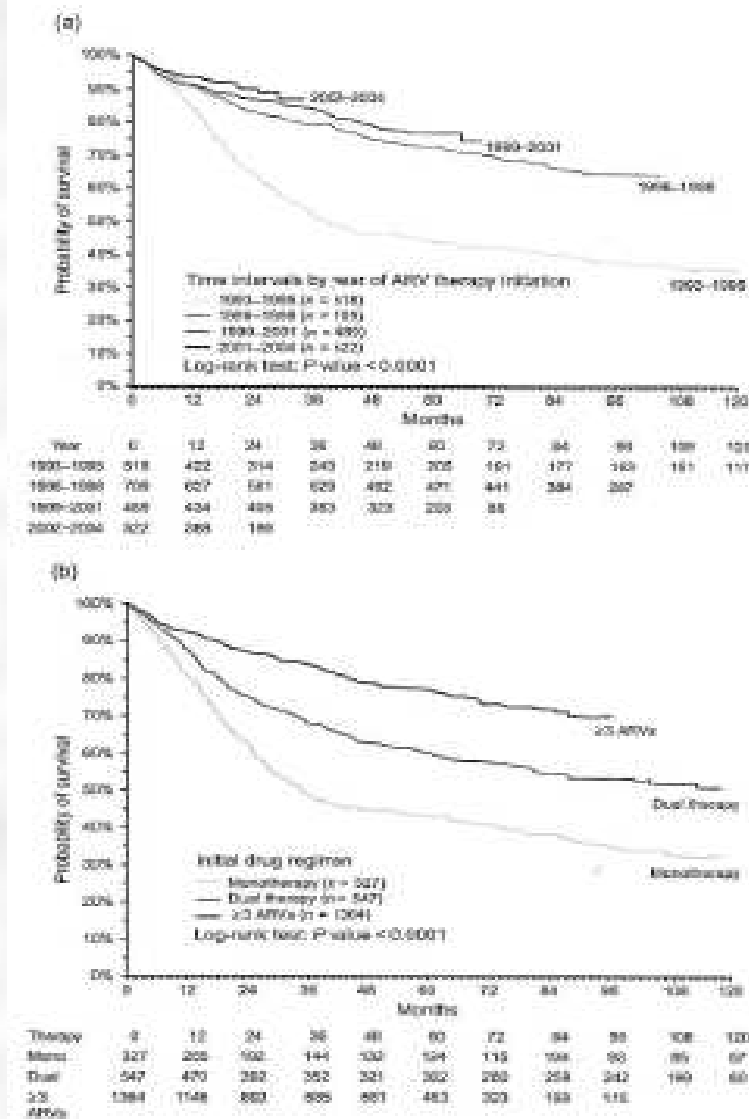


Fig. 1. Life expectancy and probability of survival among 2238 HIV-positive participants who initiated antiretroviral therapy between 1 January 1993 and 30 September 2004. (a) Probability of survival stratified by time period of therapy initiation (1993-1995, 1996-1998, 1999-2001, and 2002-2004). (b) Probability of survival stratified by type of therapy (mono, dual, and three or more antiretroviral drugs). The diminishing number of participants in the study at each subsequent interval, in (a) and (b), is the result of mortality events or limited follow-up.

Lima, V.D. et al., 2007. Continued improvement in survival among HIV-infected individuals with newer forms of highly active antiretroviral therapy. *AIDS (London, England)*, 21(6), pp.685-692.

3. - Cambios en la esperanza de vida - evidencia

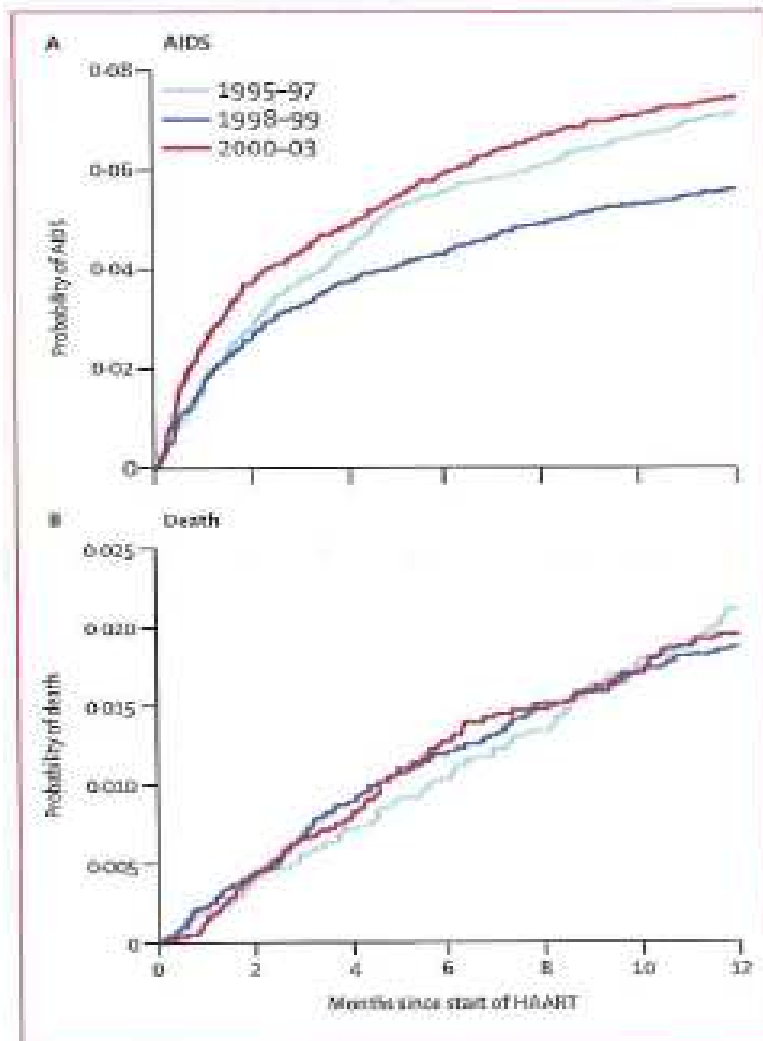


Figure: Kaplan-Meier estimates of cumulative proportion of (A) AIDS and (B) death by calendar year of starting HAART, ART-CC, 2004

May, M.T. et al., 2006. HIV treatment response and prognosis in Europe and North America in the first decade of highly active antiretroviral therapy: a collaborative analysis. *Lancet*, 368(9534), pp.451-458.

3. - Cambios en la esperanza de vida - evidencia

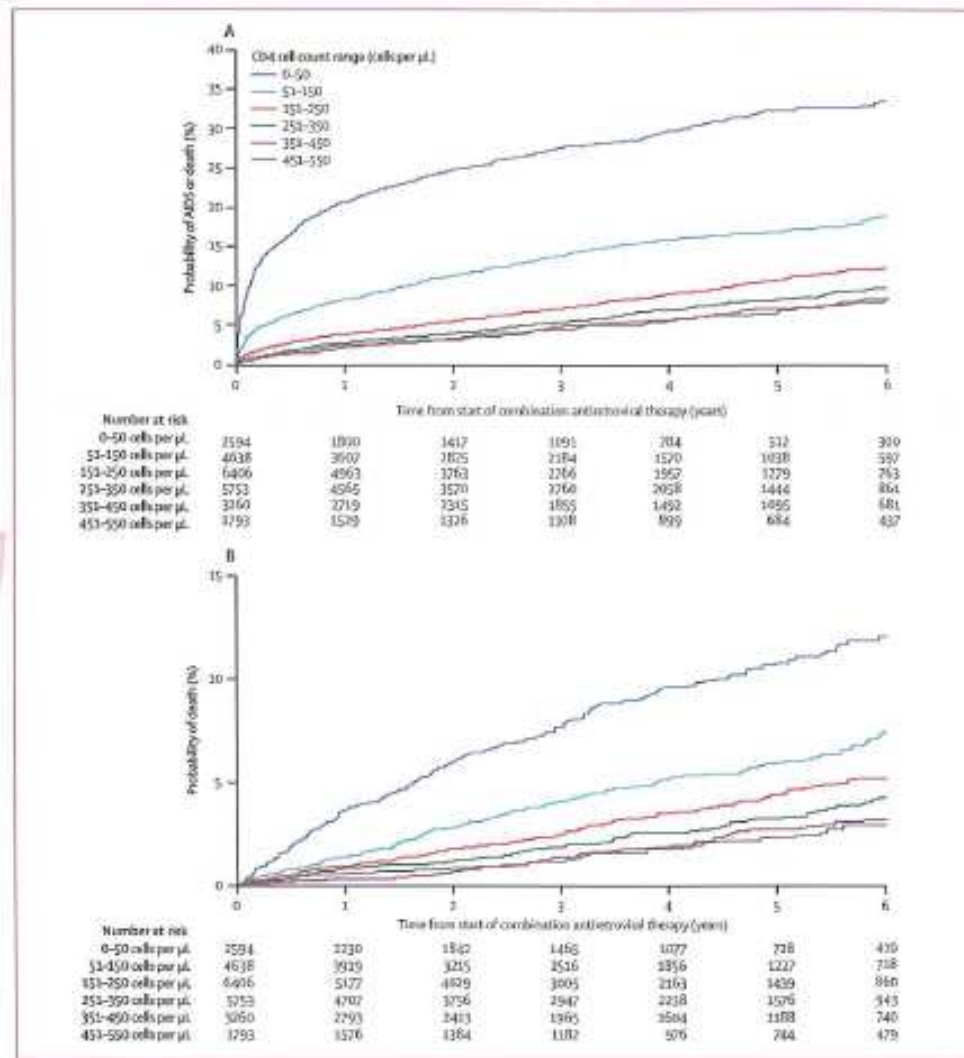


Figure 2: Cumulative probability of (A) AIDS or death or (B) death alone after initiation of combination antiretroviral therapy, according to range of CD4 cell count at the time of treatment initiation

Sterne, J.A.C. et al., 2009.
Timing of initiation of
antiretroviral therapy in AIDS-
free HIV-1-infected patients: a
collaborative analysis of 18 HIV
cohort studies. *Lancet*,
373(9672), pp.1352-1363.

3. - Cambios en la esperanza de vida - UDVP

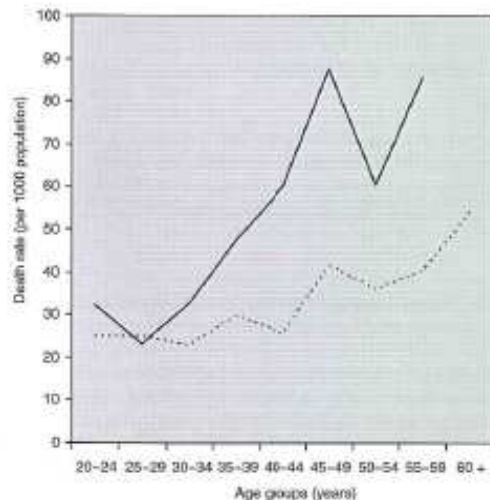


Fig. 1. Age-specific death rates for HOMER (---) and BART (—) cohorts.

Lloyd-Smith, E. et al., 2006. Impact of HAART and injection drug use on life expectancy of two HIV-positive cohorts in British Columbia. *AIDS (London, England)*, 20(3), pp.445-450.

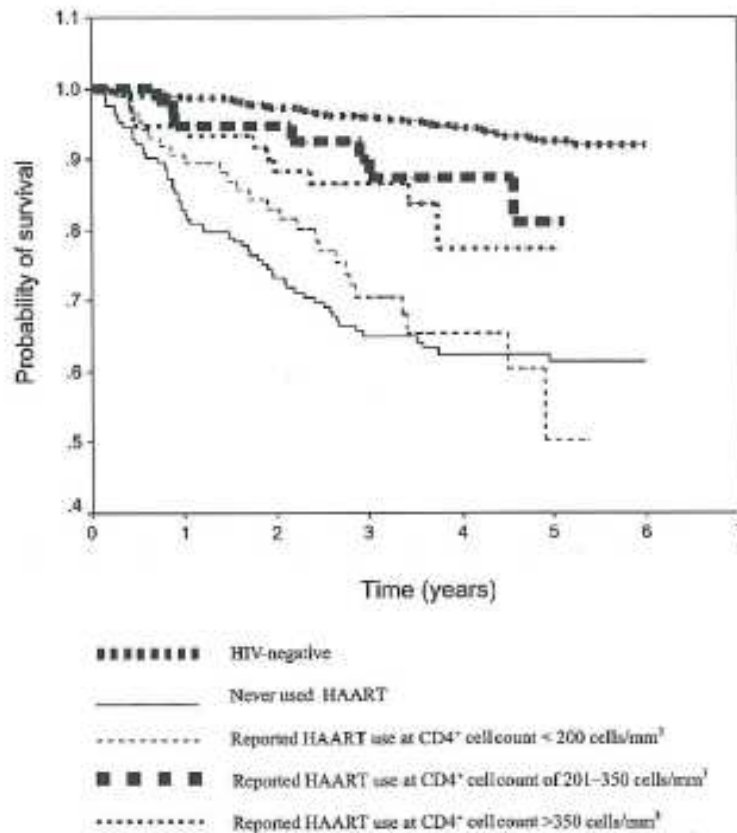
Table 3. Life expectancy of members of HOMER and BART cohorts.

Cohort	Person-years	Absolute No. deaths	Age-specific mortality rate ^a	Life expectancy at exact age 20	Potential years of life lost (per 100 000 population)
HOMER					
All	9175	289	31.5	50.0	96 376
HCV-positive	4786	195	40.7	23.0	125 731
HCV-negative	5019	94	18.4	38.9	56 535
BART					
All	2746	135	49.2	20.5	169 792
Taking antiretroviral therapy	1227	56	45.6	24.5	150 367
No antiretroviral therapy	1519	79	52.0	19.1	185 484

HCV, hepatitis C virus.

^aAge range 20–65 years and per 1000 population.

3. - Cambios en la mortalidad - UDVP



Kohli, R. et al., 2005.
Mortality in an urban cohort of HIV-infected and at-risk drug users in the era of highly active antiretroviral therapy. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*, 41(6), pp.864-872.

Figure 3: Kaplan-Meier survival curves, by HIV serostatus, HAART use, and CD4⁺ lymphocyte count, at initiation of HAART. $P = .60$ for CD4⁺ lymphocyte count of ≤ 200 cells/mm³ versus no HAART; $P = .01$ for CD4⁺ lymphocyte count of ≤ 200 versus 201–350 cells/mm³; $P = .03$ for CD4⁺ lymphocyte count of ≤ 200 versus > 350 cells/mm³; and $P = .49$ for CD4⁺ lymphocyte count of 201–350 versus > 350 cells/mm³. All P values were determined with use of the log-rank test.

3. - Cambios en la esperanza de vida - evidencia

The effect of combined antiretroviral therapy on the overall mortality of HIV-infected individuals

The HIV-CAUSAL Collaboration*

Design: A collaboration of 12 prospective cohort studies from Europe and the United States (the HIV-CAUSAL Collaboration) that includes 62 760 HIV-infected, therapy-naïve individuals followed for an average of 3.3 years. Inverse probability weighting of marginal structural models was used to adjust for measured confounding by indication.

Conclusion: We estimated that cART halved the average mortality rate in HIV-infected individuals. The mortality reduction was greater in those with worse prognosis at the start of follow-up.

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Anon, 2010. The effect of combined antiretroviral therapy on the overall mortality of HIV-infected individuals. *AIDS (London, England)*, 24(1), pp.123-137.

3. - Cambios en la esperanza de vida - evidencia

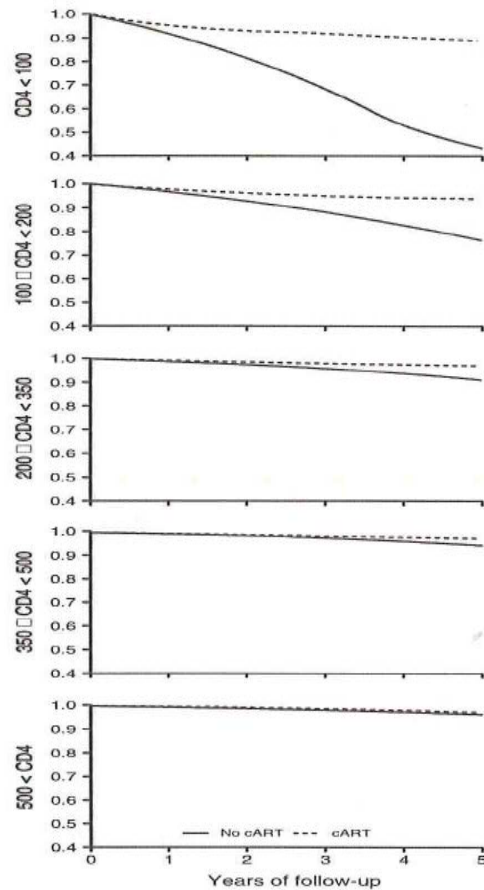


Fig. 2. Estimated survival curves under the regimes 'initiate cART at baseline' and 'never start cART' by CD4 cell count at baseline, HIV-CAUSAL Collaboration.

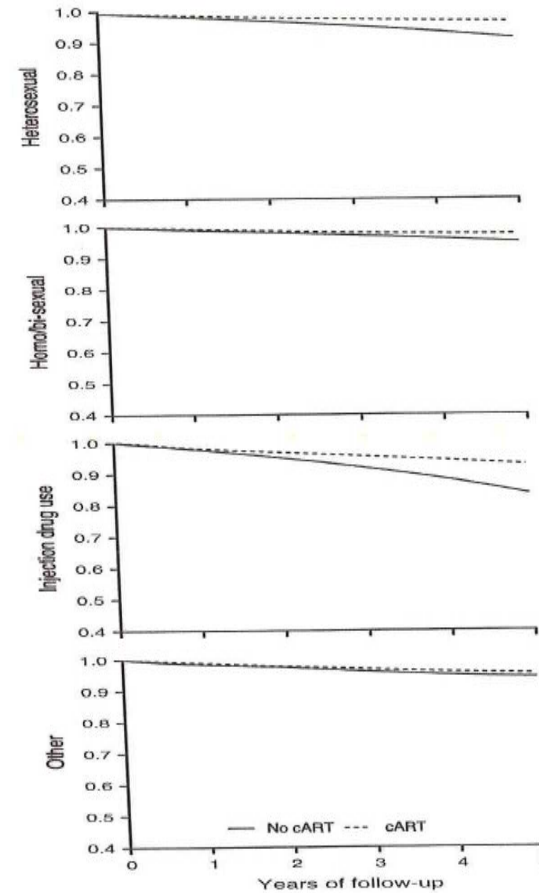


Fig. 3. Estimated survival curves under the regimes 'initiate cART at baseline' and 'never start cART' by transmission group, HIV-CAUSAL Collaboration.

Anon, 2010. The effect of combined antiretroviral therapy on the overall mortality of HIV-infected individuals. *AIDS (London, England)*, 24(1), pp.123-137.

3. - Cambios en la esperanza de vida - evidencia

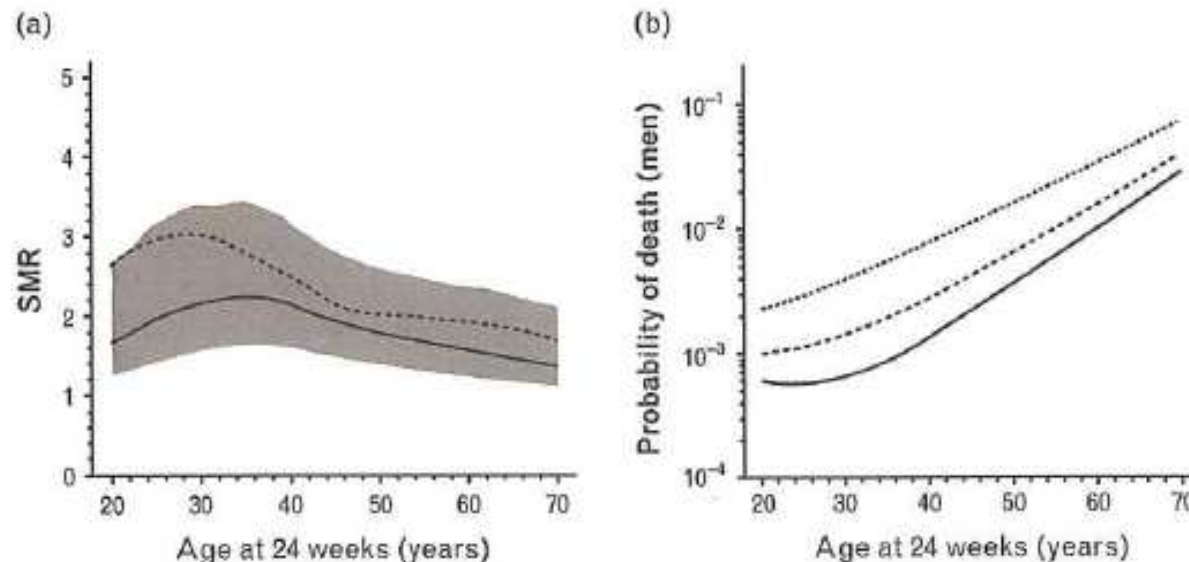


Fig. 1. Standardized mortality ratios (SMRs) and probability of death for men and women. (a) SMR in the first year after 24 weeks after diagnosis as a function of age at 24 weeks for men (solid line) and women (dashed line) without a history of drug use, without a CDC-B event, and born in Western countries or sub-Saharan Africa. Shaded areas represent 95% confidence intervals for men. (b) Probability of death within 1 year for uninfected men (solid line), HIV-infected men (dashes), and HIV-infected men with a CDC-B event at 24 weeks (dots).

van Sighem, A.I. et al., 2010. Life expectancy of recently diagnosed asymptomatic HIV-infected patients approaches that of uninfected individuals. *AIDS (London, England)*, 24(10), pp.1527-1535.

3. - Cambios en la esperanza de vida - evidencia

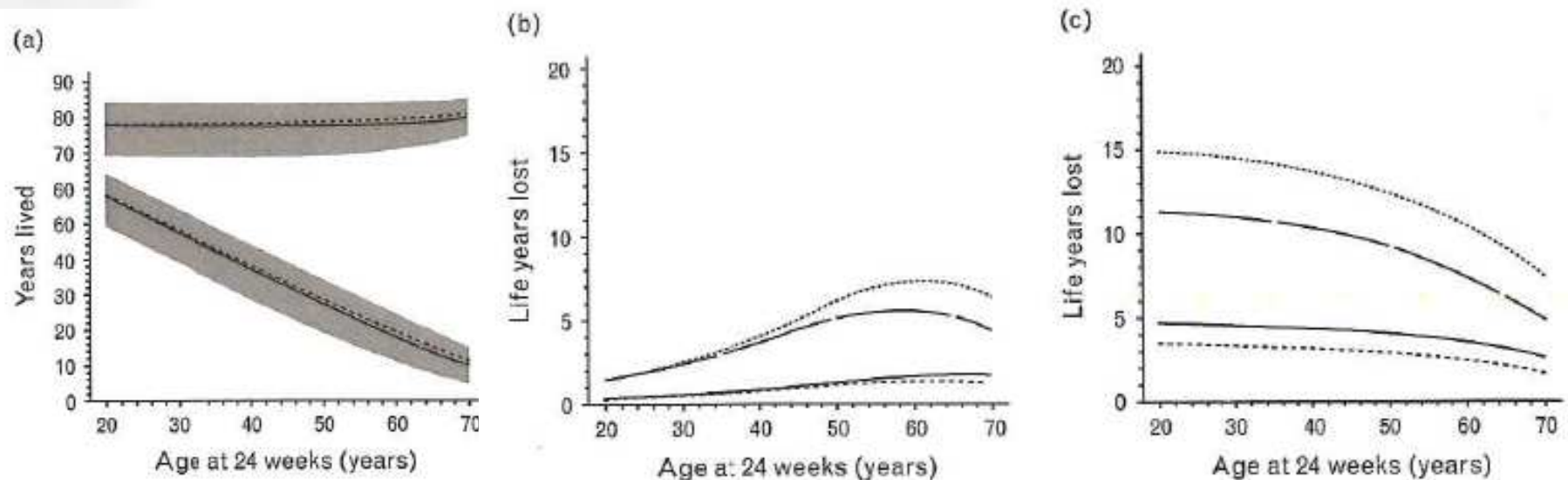


Fig. 2. The median age reached and number of life years lost for HIV-infected patients. (a) Median age reached (upper lines) and median number of years lived (lower lines) after 24 weeks after diagnosis for HIV-infected men without a CDC-B event. Shaded areas represent the interquartile range and dashed lines represent the general population. (b) Number of life years lost for HIV-infected men (short dashes) and women (solid line) without a CDC-B event and for HIV-infected men (long dashes) and women (dotted line) with a CDC-B event at 24 weeks compared to age and sex-matched non-infected individuals. (c) Number of life years lost in an alternative model including current age instead of age at 24 weeks. All patients were born in Western countries or sub-Saharan Africa.

van Sighem, A.I. et al., 2010. Life expectancy of recently diagnosed asymptomatic HIV-infected patients approaches that of uninfected individuals. *AIDS (London, England)*, 24(10), pp.1527-1535.

3. – Causas de muerte en PVVHS

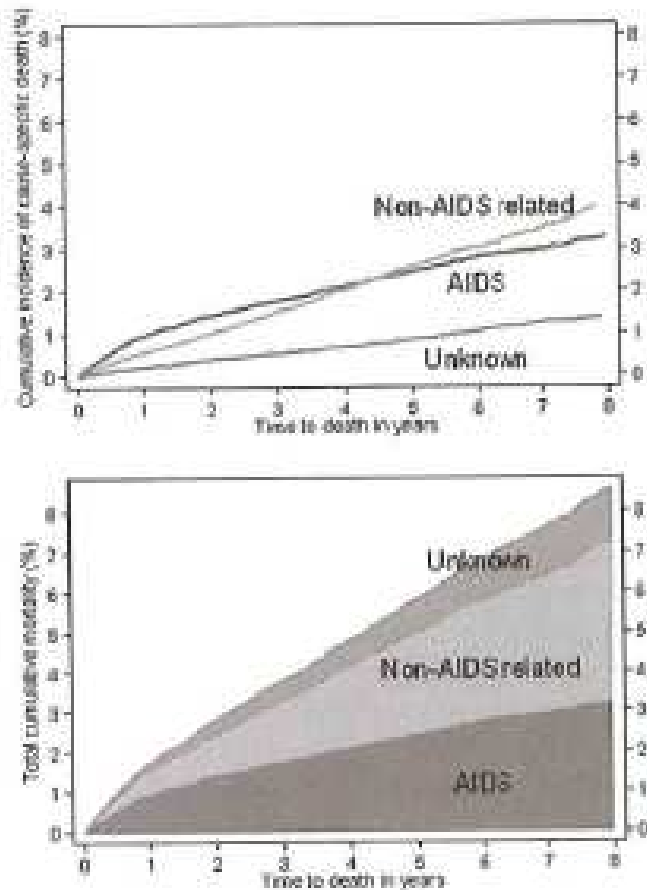
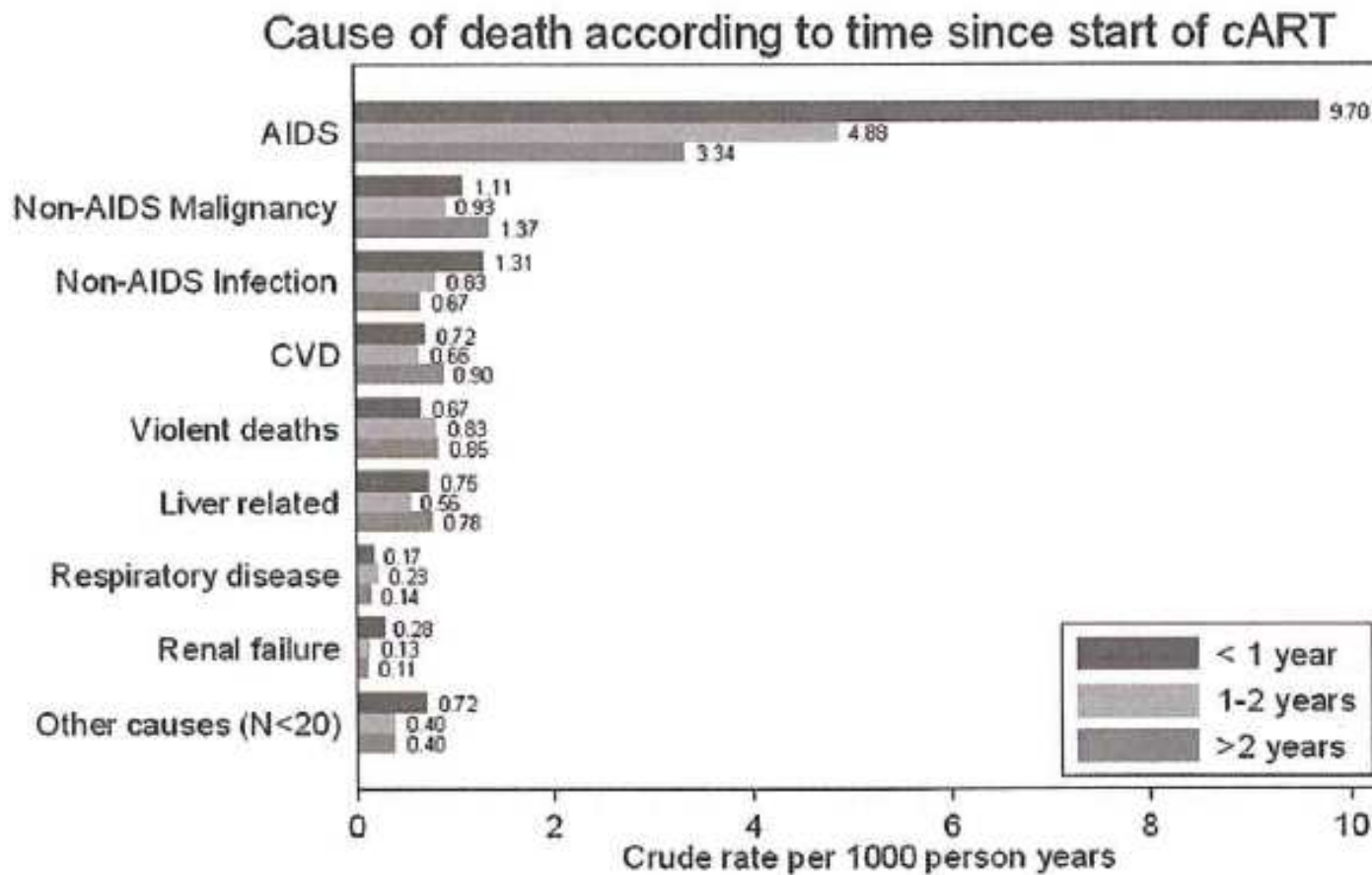


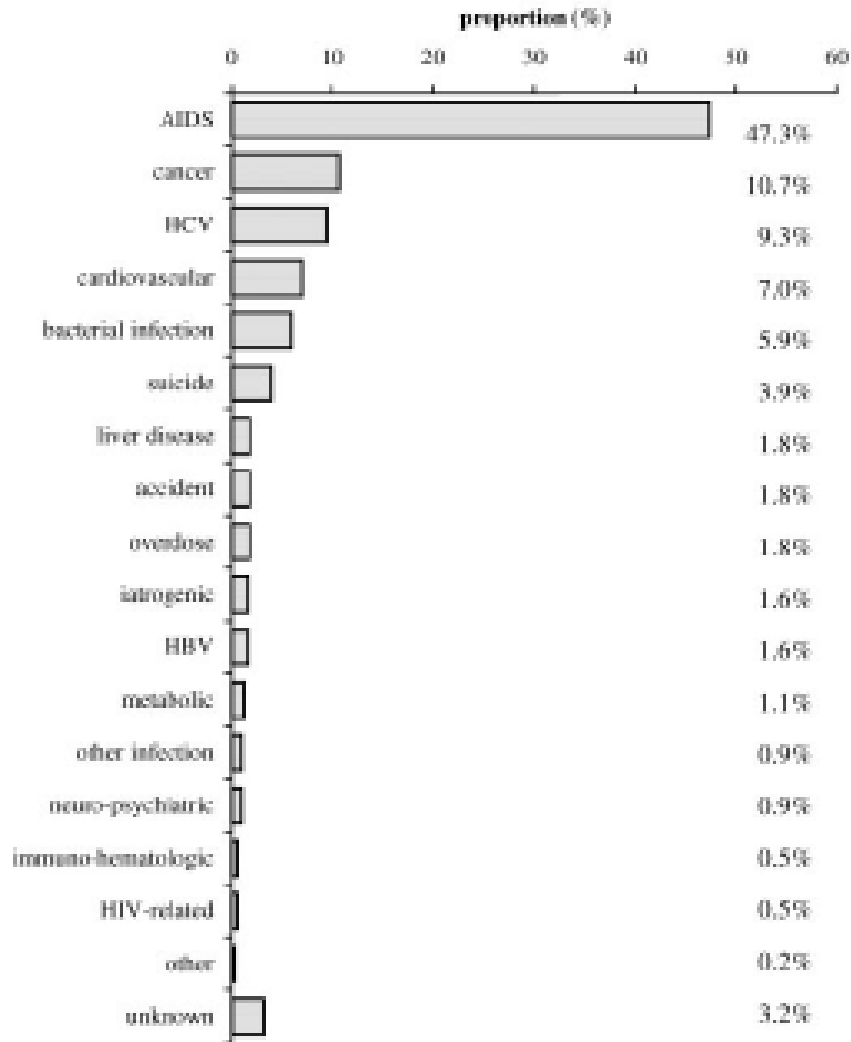
Figure 3. Cumulative incidence of AIDS-related, non-AIDS-related, and unknown deaths (upper panel) and total cumulative mortality partitioned by cause of death (lower panel).

Anon, 2010. Causes of death in HIV-1-infected patients treated with antiretroviral therapy, 1996-2006: collaborative analysis of 13 HIV cohort studies. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*, 50(10), pp.1387-1396.

3. – Causas de muerte en PVVHS



3. – Causas de mortalidad – Francia 2000



Lewden, C. et al., 2005. Causes of death among human immunodeficiency virus (HIV)-infected adults in the era of potent antiretroviral therapy: emerging role of hepatitis and cancers, persistent role of AIDS.

International Journal of Epidemiology, 34(1), pp.121-130.

3. – Causas de mortalidad por edad – Francia 2000

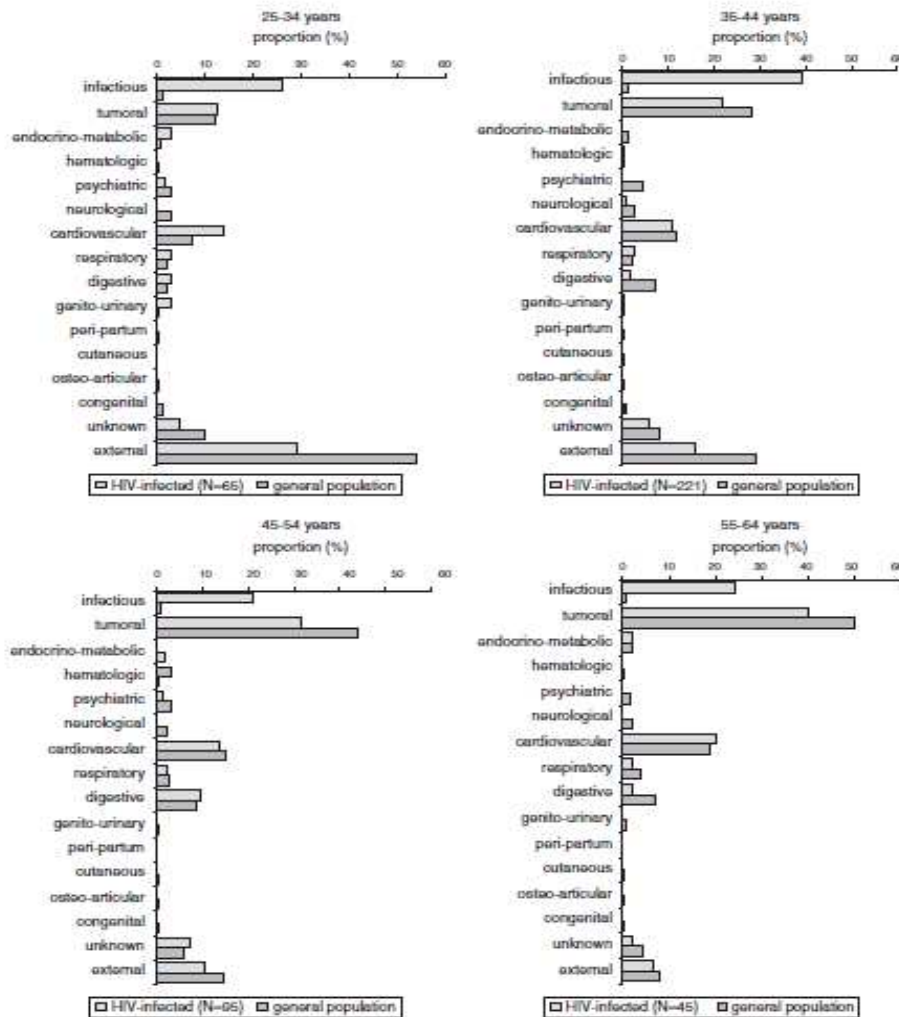


Figure 2 Distribution of the underlying causes of non-human immunodeficiency virus (HIV) related deaths in 426 HIV-infected adults aged 25-64 (France, 2000) compared with the distribution of the causes of death in the general population (France, 1999)

Lewden, C. et al., 2005. Causes of death among human immunodeficiency virus (HIV)-infected adults in the era of potent antiretroviral therapy: emerging role of hepatitis and cancers, persistent role of AIDS. *International Journal of Epidemiology*, 34(1), pp.121-130.

3. – Cambios en mortalidad – Canada

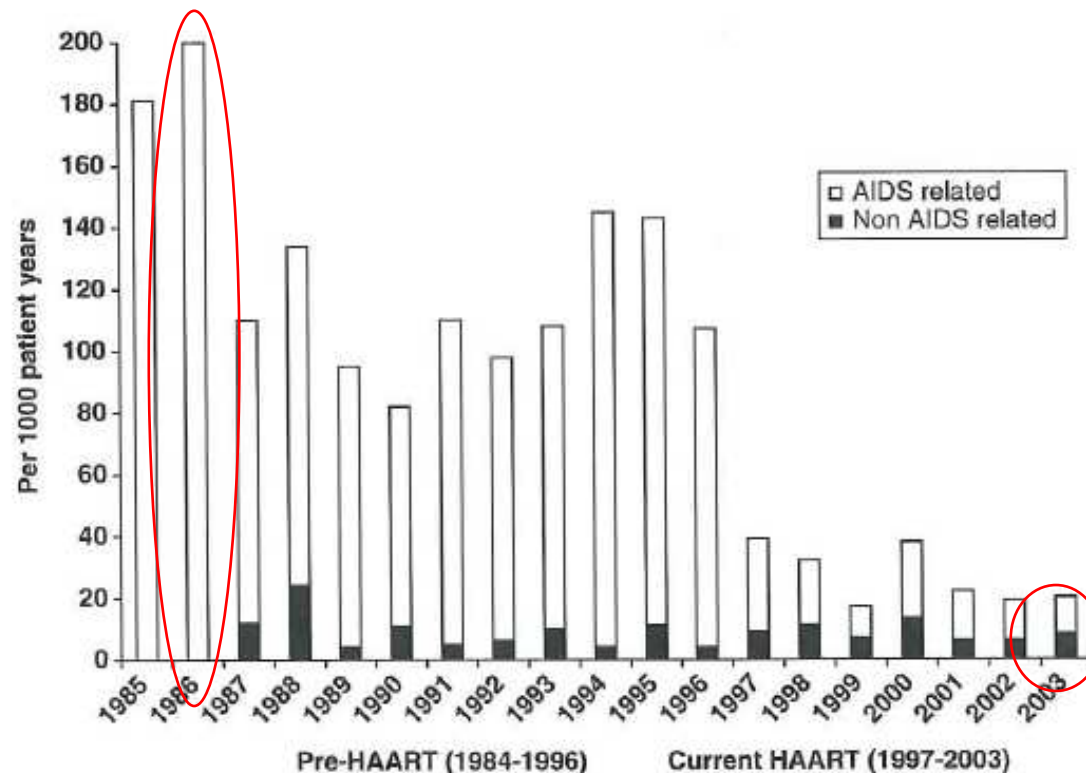
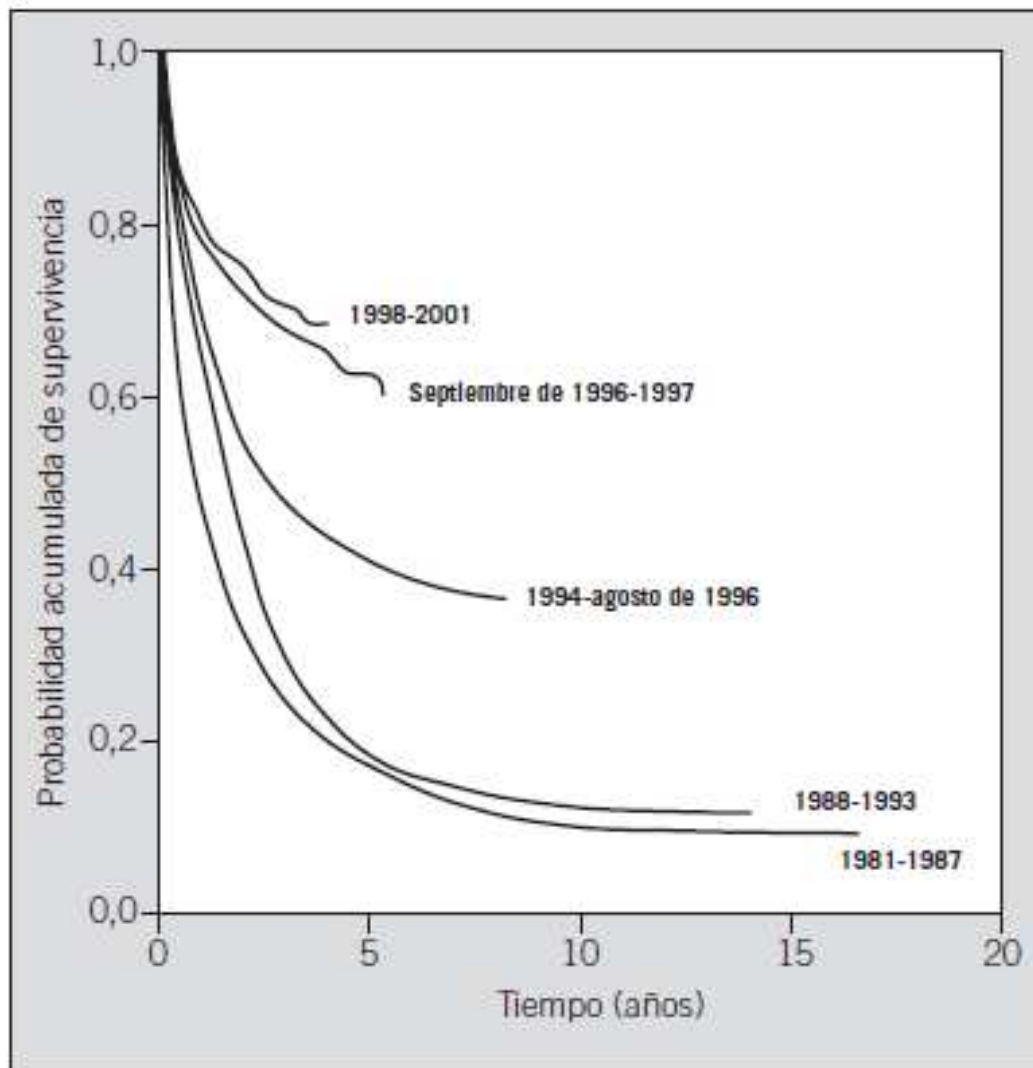


Fig. 1 Crude mortality rate (1984 to 2003) = 66 per 1000 patient years. Pre-highly active antiretroviral therapy (HAART) (1984-1996) = 117.0. Current HAART (1997-2003) = 24.0.

Krentz, H.B., Kliwer, G. & Gill, M.J., 2005. Changing mortality rates and causes of death for HIV-infected individuals living in Southern Alberta, Canada from 1984 to 2003. *HIV Medicine*, 6(2), pp.99-106.

3. - Cambios en la esperanza de vida - Cataluña



Rius, C. et al., 2006.
[Survival changes
among AIDS cases
in Catalonia, Spain
(1981-2001)].
Medicina Clínica,
127(5), pp.167-171.

Fig. 1. Estimación de Kaplan-Meier de la función de supervivencia según el período diagnóstico. Cataluña, 1981-2001 ($n = 13.485$).

3. - Cambios en la esperanza de vida – Taiwan

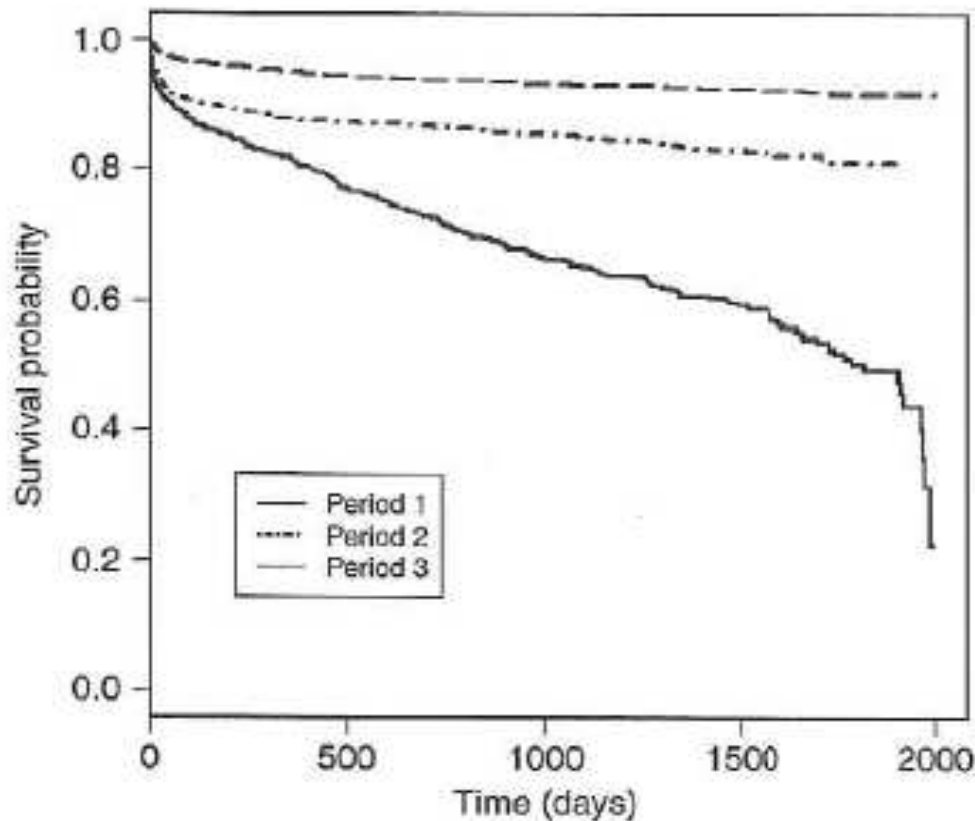


Fig. 1 Kaplan-Meier survival plot for patients enrolled in three different study periods: period 1 (before 31 March 1997), period 2 (1 April 1997 to 31 December 2001), and period 3 (1 January 2002 to 31 December 2005) (log-rank test: $P < 0.0001$ for comparisons between periods 1 and 2, and periods 1 and 3).

Yang, C.-H. et al., 2008. Trends of mortality and causes of death among HIV-infected patients in Taiwan, 1984-2005. *HIV Medicine*, 9(7), pp.535-543.

3. - Cambios en la esperanza de vida - evidencia

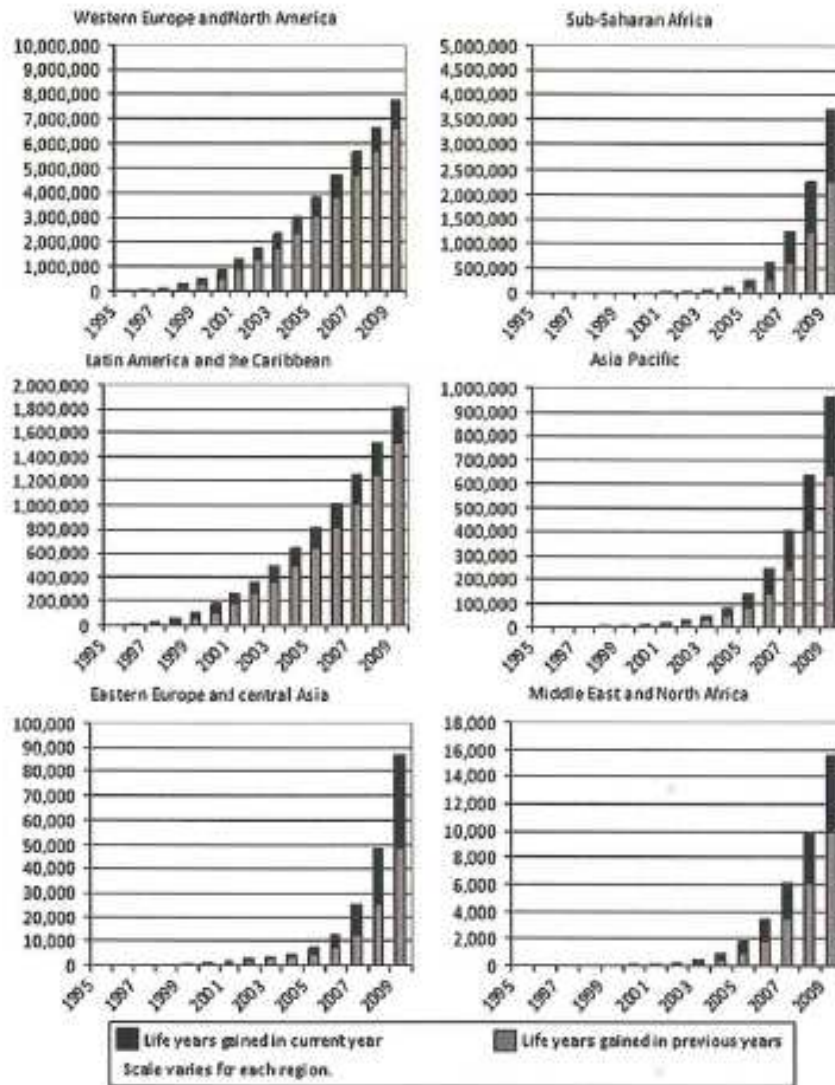


Figure 3 Life-years gained in current year and in previous years among adults due to antiretroviral therapy, by region, 1995–2009.

Mahy, M. et al., 2010. Estimating the impact of antiretroviral therapy: regional and global estimates of life-years gained among adults. *Sexually Transmitted Infections*, 86 Suppl 2, pp.ii67-71.

3. - Cambios en la esperanza de vida con fallo virológico

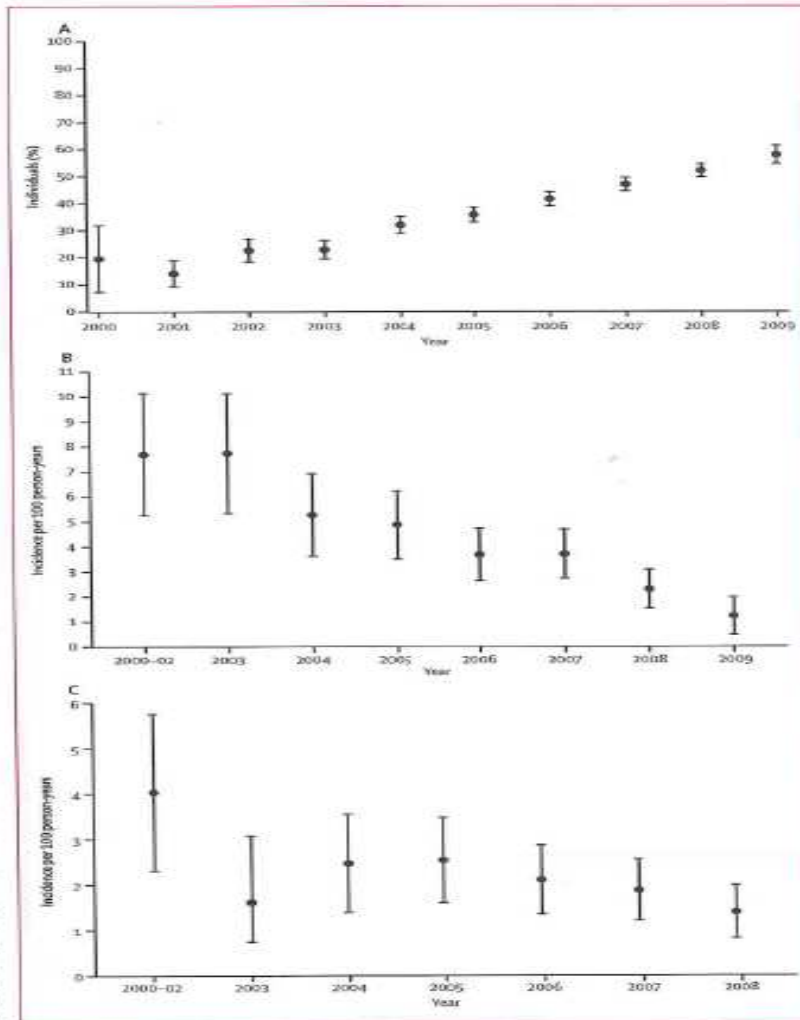


Figure: 2000-09 trends in virological and clinical outcomes in people with triple-class virological failure (A) Individuals with plasma HIV-1 RNA <50 copies per mL. (B) Incidence of new AIDS event. (C) Death rate.

Anon, 2011. Trends in virological and clinical outcomes in individuals with HIV-1 infection and virological failure of drugs from three antiretroviral drug classes: a cohort study. *The Lancet Infectious Diseases*. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21988895> [Accessed November 3, 2011].

The Pursuing Later Option II (PLATO II) project team for the Collaboration of Observational HIV Epidemiological Research Europe (COHERE) Group

3. - Cambios en la esperanza de vida – Tablas de vida

Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies

The Antiretroviral Therapy Cohort Collaboration*

- Period of study: 1996-2005 (10 years)
- n=43,355 patients included in the analysis
 - 2,050 deaths (4.7%)
- 170,990 person-years of follow-up
 - Mean follow-up: 3.9 years

Anon, 2008. Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies. *The Lancet*, 372, pp.293-299.

Objectivos del estudio

- To compare changes in mortality rates and life expectancy among HIV-positive individuals on combination therapy in high-income countries over three separate periods:
 - 1996–99
 - 2000–02
 - 2003–05
- and in subgroups defined by patient characteristics at initiation of such treatment:
 - Sex
 - Risk factor for transmission
 - CD4+ cell count

The abridged life tables

- **Central idea:**
 - The abridged life tables will describe the mortality experience that *hypothetical cohorts* of HIV-positive individuals would have had if they were subjected to the mortality rates in the observed calendar periods

The life table

- **Life tables** describe the extent to which a generation of people (i.e. life table cohort) dies off with age
- Widely used for descriptive and analytical purposes in many areas of interest
- A number of statistics can be derived:
 - the probability of surviving any particular year of age
 - remaining life expectancy for people at different ages
 - the proportion of the original birth cohort still alive

3. - Cambios en la esperanza de vida – Tablas de vida

	Men	Women	Injecting drug users	Non-Injecting drug users
Mortality rates (per 1000 person-years)				
Overall	12.9 (12.3-13.6)	9.1 (8.2- 10.1)	20.7 (19.0-22.5)	10.5 (10.0-11.0)
Between the ages 20 and 44years	10.3 (9.7 -11.0)	7.9 (7- 8.9)	18.6 (16.9-20.6)	7.8 (7.2-8.3)
Potential years of life lost before age 65 years (per 1000 person-years)				
20-64 years	257.8	214.4	505.5	202.5
Life expectancy (years; adjusted)				
Exact age 20years	42.8 (SE 0.45)	44.2 (SE 0.55)	32.6 (SE 1.06)	44.7 (SE 0.34)
Exact age 35 years	31.7 (SE 0.24)	32.5 (SE 0.44)	23.4 (SE 0.60)	33.0 (SE 0.22)
Percent surviving from 20 to 44 years	80.2%	83.1%	66.5%	84.1%
Mortality rates are deaths per 1000 person-years (95% CI). [A:correct?]				
Table 4: Health indicators stratified by sex and injecting drug use				

Anon, 2008. Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies. *The Lancet*, 372, pp.293-299.

3. - Cambios en la esperanza de vida – Tablas de vida

	1996-99	2000-02	2003-05	1996-2005
Mortality rates (per 1000 person-years)				
Overall	16.3 (14.9-17.8)	12.4 (11.5-13.2)	10.0 (9.3-10.8)	12.0 (11.5-12.5)
Between the ages 20 and 44 years	13.1 (11.7-14.7)	10.3 (9.4-11.2)	7.5 (6.8-8.3)	9.7 (9.1-10.2)
Potential years of life lost before age 65 years (per 1000 person-years)				
20-64 years	365.9	260.4	189.4	247.0
Life expectancy (years; adjusted)				
At exact age 20 years	36.1 (SE 0.60)	41.2 (SE 0.52)	49.4 (SE 0.54)	43.1 (SE 0.33)
At exact age 35 years	25.0 (SE 0.42)	30.1 (SE 0.31)	37.3 (SE 0.37)	31.7 (SE 0.21)
Percent surviving from 20 to 44 years	75.5%	79.5%	85.7%	81.1%
Mortality rates are deaths per 1000 person-years (95% CI). [A:correct?]				
Table 2: Health indicators for overall (20 years or older) population by period of follow-up				

Anon, 2008. Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies. *The Lancet*, 372, pp.293-299.

**Life expectancy of individuals on combination of
antiretroviral therapy.
PISCIS Cohort Study, 1998-2006.
(Anna Esteve Gómez, CEEISCAT)**

Resultados

- Periodo de estudio: 1998-2006 (9 años)
- n=3,902 pacientes incluidos en el analisis
 - 338 muertes (8.6%)
- 14,419 persona-años de seguimiento
 - Seguimiento medio: 3.7 años

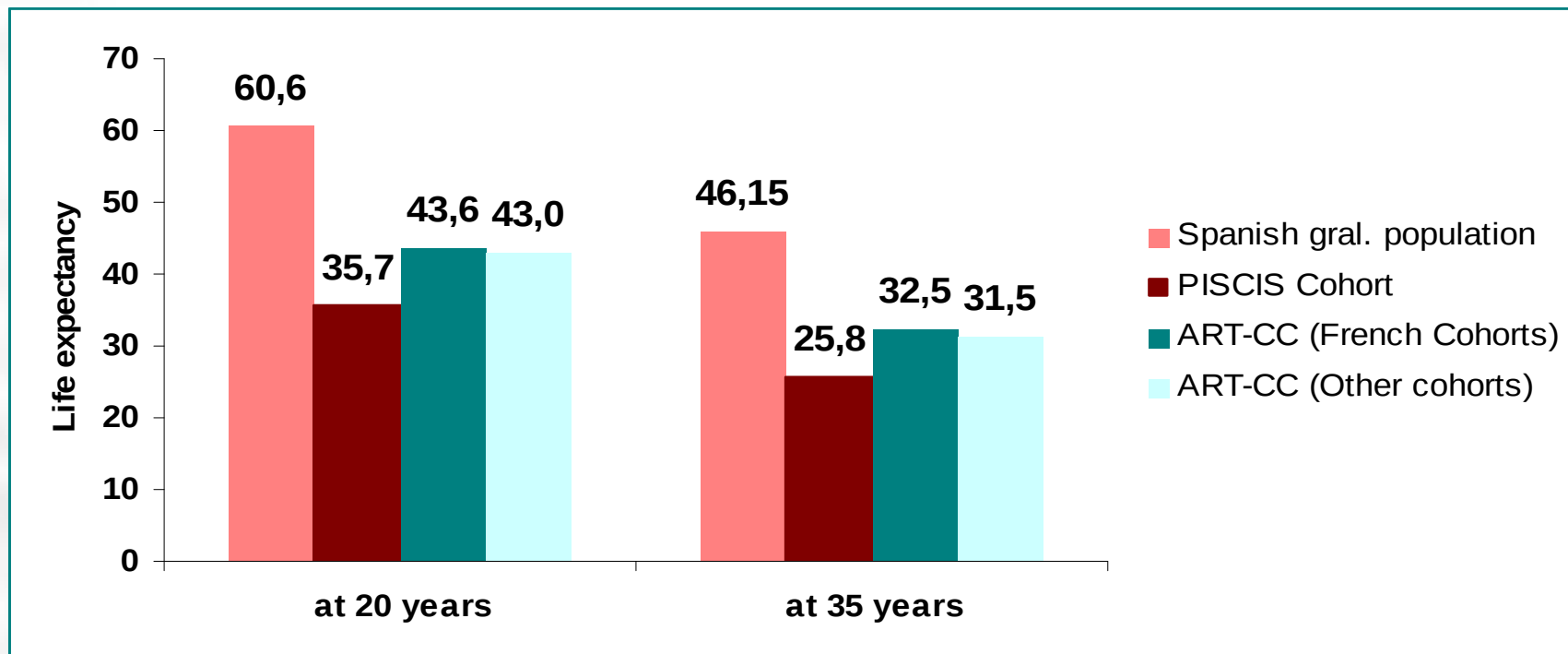
Resultados

	1998-99	2000-02	2003-06	1998-06
Mortality rates (per 1000 person-years)				
Overall	25.1 (14.8-35.3)	22.5 (18.1-27.0)	22.8 (19.7-25.8)	23.4 (20.9-25.9)
Between the ages 20 and 44 years	18.7 (8.9-28.4)	21.1 (16.2-25.9)	18.2 (14.9-21.4)	19.3 (16.6-21.9)
Potential Years of Life Lost before age 65 years (per 1000 person-years)				
20-64 years	542.8	522.6	440.6	483.6
Life expectancy				
At exact age 20 years	33.1 (SE 2.9)	35.7 (SE 2.29)	36.8 (SE 1.73)	35.7 (SE 1.47)
At exact age 35 years	21.1 (SE 2.9)	27.0 (SE 1.54)	25.8 (SE 0.97)	25.8 (SE 0.80)

Tabla 2. Health indicators by period of follow-up. PISCIS cohort 1998-2006

Discussion

- La esperanza de vida en los patients naïve que inician tratamiento es ~40% menor respecto la población general española*



* Fuente: HIV mortality Project (2000-2006)

3. – Conclusiones - i

- El tratamiento con antiretrovires drugs de personas infectadas con VIH-1 ha mejorado desde la introducción de TARGA en 1996
- Ensayos clínicos y observacionales han demostrado enormes cambios en la mortalidad y morbilidad en pacientes infectados por VIH como consecuencia de TARGA
- Esperanza de vida y mortalidad son indicadores importantes de la salud de poblaciones.

4. – Perspectivas para el futuro

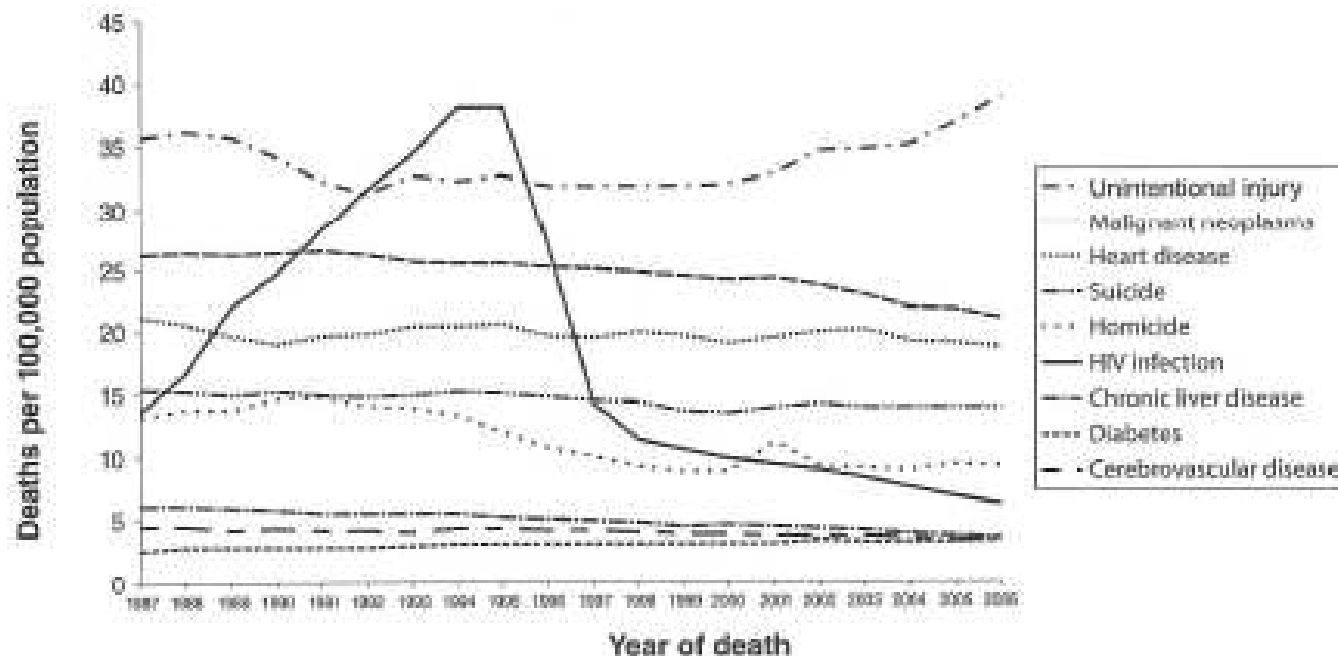
-

5. - Conclusiones

-

3. – Conclusiones - ii

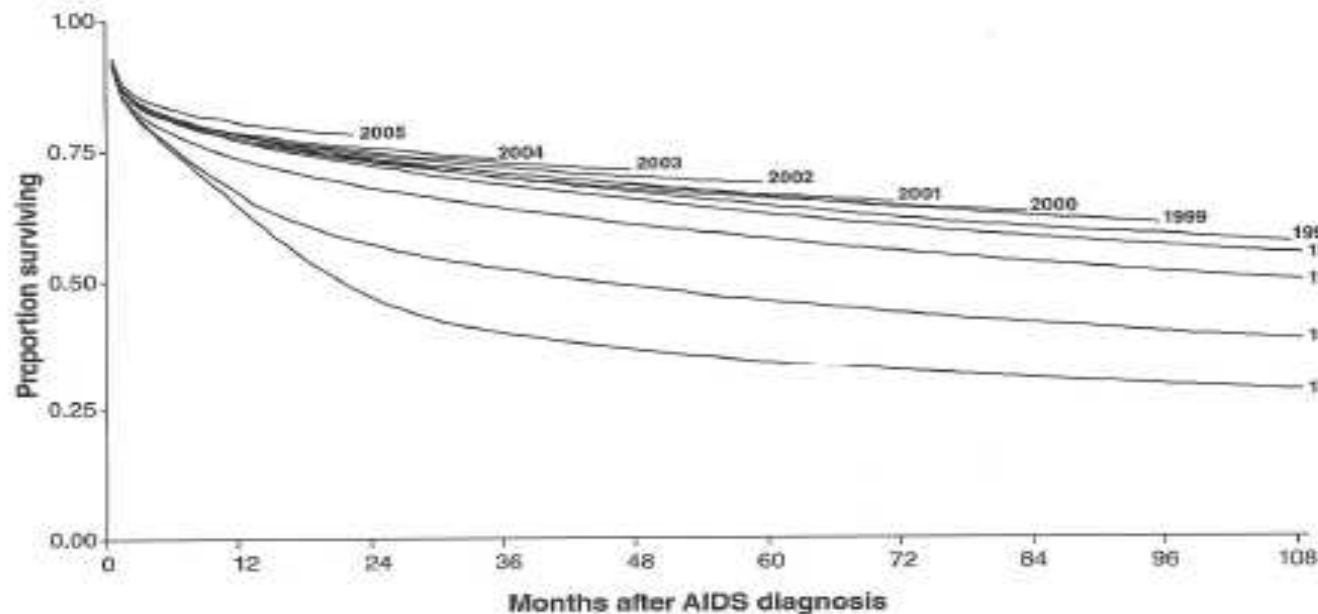
Figure 10. Trends in annual rates of death from leading causes of death among persons 25-44 years old, 1987-2006, 50 states and the District of Columbia



Centers for Disease Control and Prevention. Deaths among persons with AIDS through December 2006, *HIV/AIDS Surveillance Supplemental Report*, 2009. Vol. 14(No. 3): [inclusive page numbers]. <http://www.cdc.gov/hiv/topics/surveillance/resources/reports/>.

3. – Conclusiones - iii

Figure 1a. Proportion of persons surviving, by months after AIDS diagnosis by AIDS-defining opportunistic illness (OI) at the time of AIDS diagnosis, 1994-2005, United States and dependent areas



Centers for Disease Control and Prevention. Deaths among persons with AIDS through December 2006, *HIV/AIDS Surveillance Supplemental Report*, 2009. Vol. 14(No. 3): [inclusive page numbers]. <http://www.cdc.gov/hiv/topics/surveillance/resources/reports/>.

Moltes Gràcies

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