

# VIH, comorbilidades y envejecimiento

**Eugènia Negredo**

Fundació de la Lluita contra la Sida

Hospital Germans Trias i Pujol

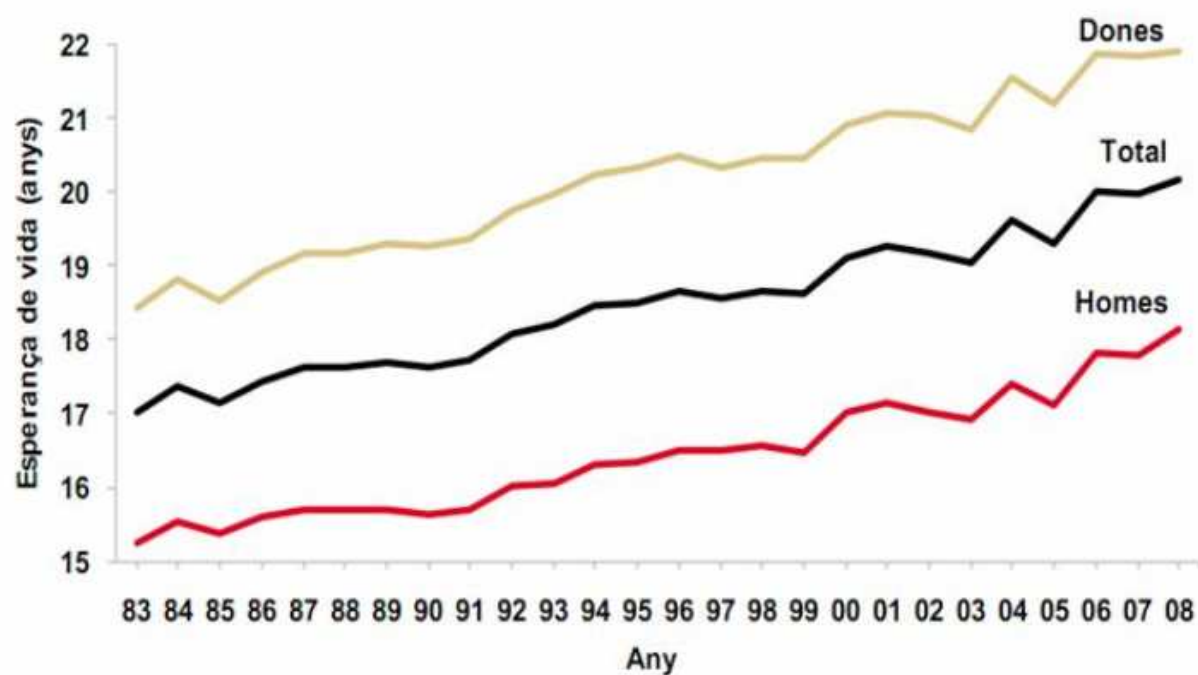
Badalona



Noviembre 2016

# ENVEJECIMIENTO

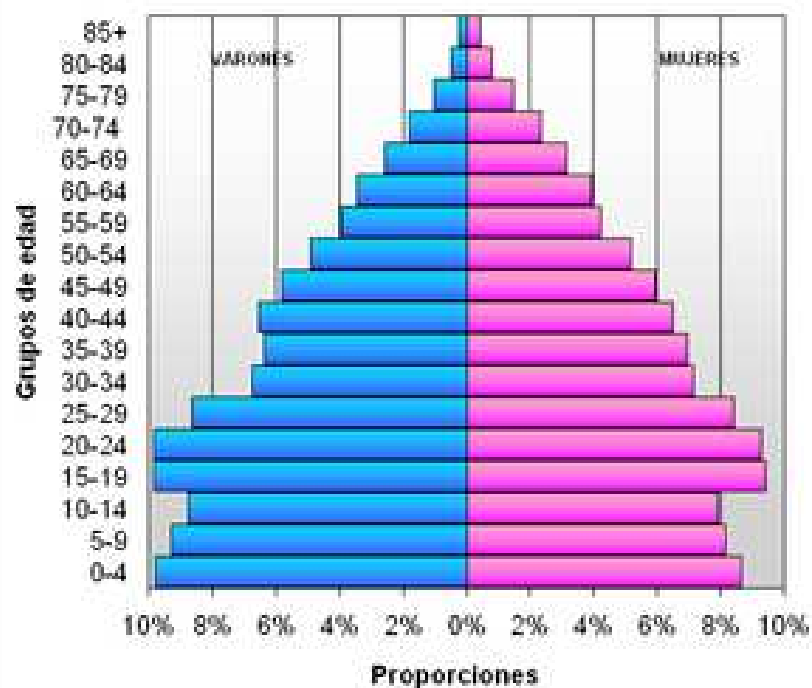
Taula 1. Evolució de l'esperança de vida als 65 anys d'edat per sexe. Catalunya, 1983-2008.



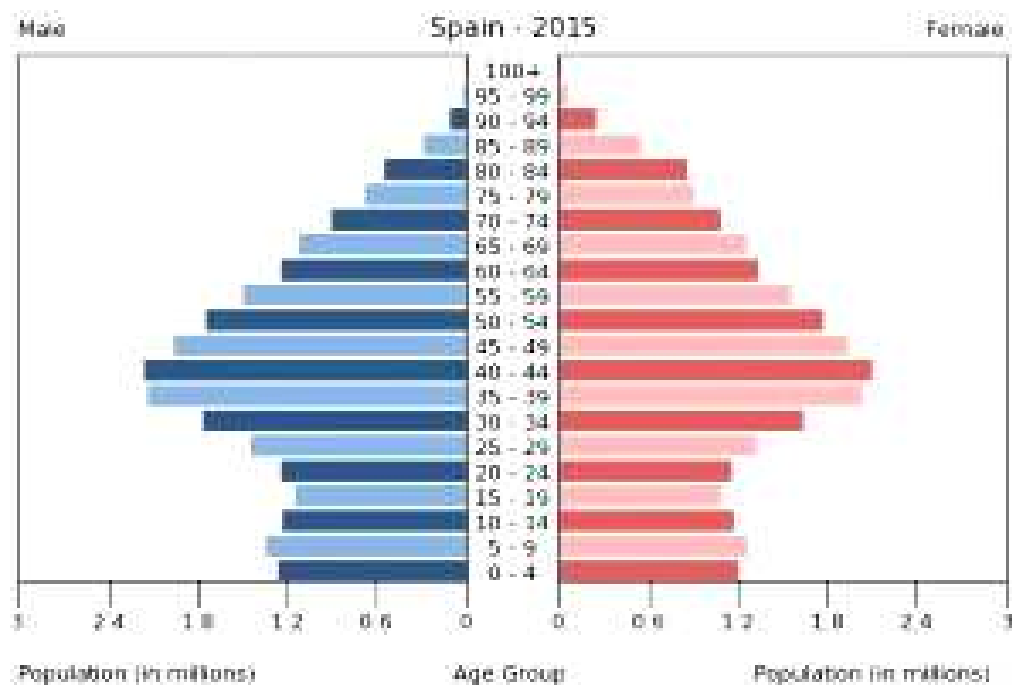
Font: Departament de Salut (2011): *Anàlisi de la mortalitat a Catalunya, 2008* [en línia].  
Versió actualitzada en data 17 de juny de 2011. Generalitat de Catalunya. 32 pàg.

# ENVEJECIMIENTO

Pirámide de población de España, año 1950



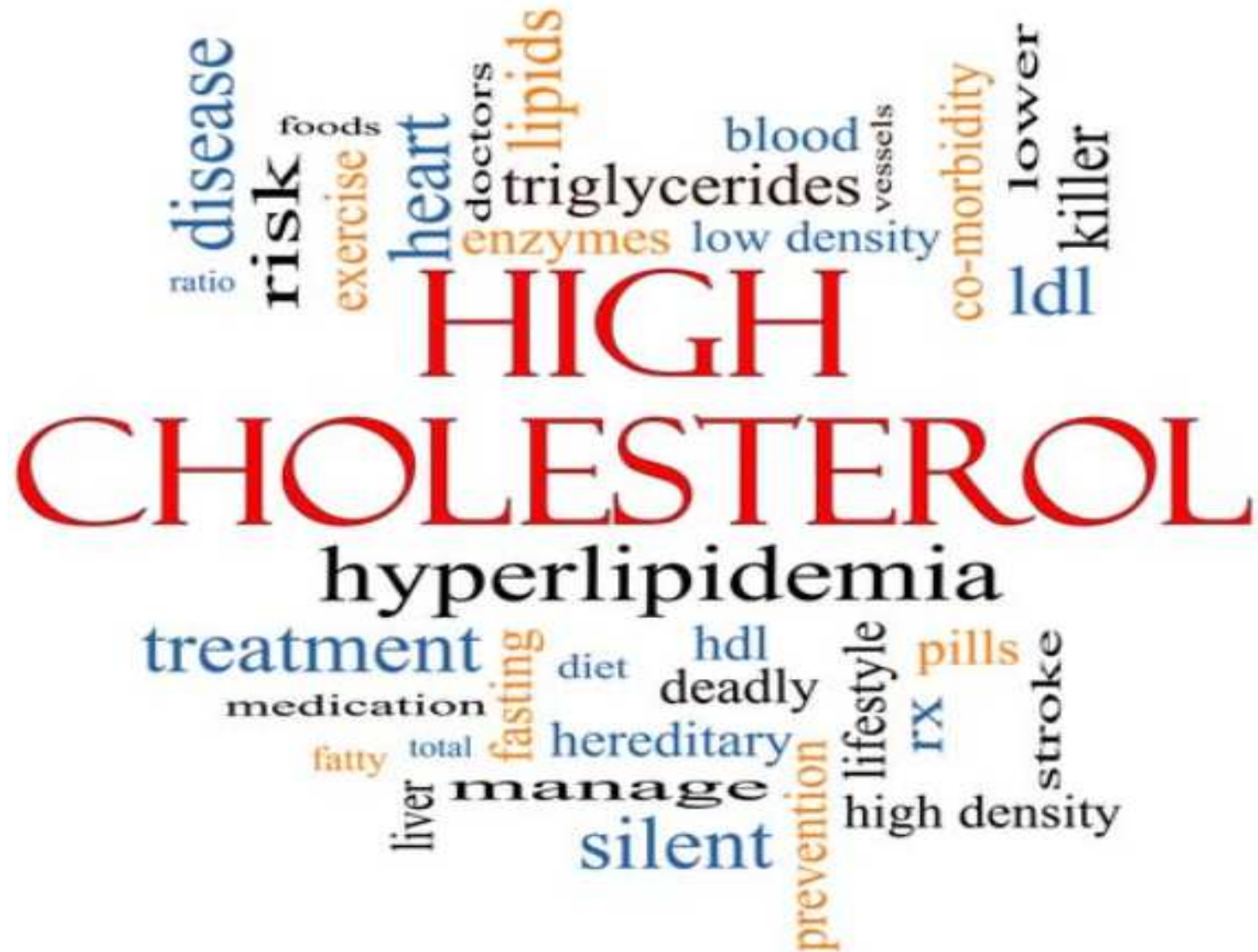
Fuente: Instituto Nacional de Estadística. Censo de 1950



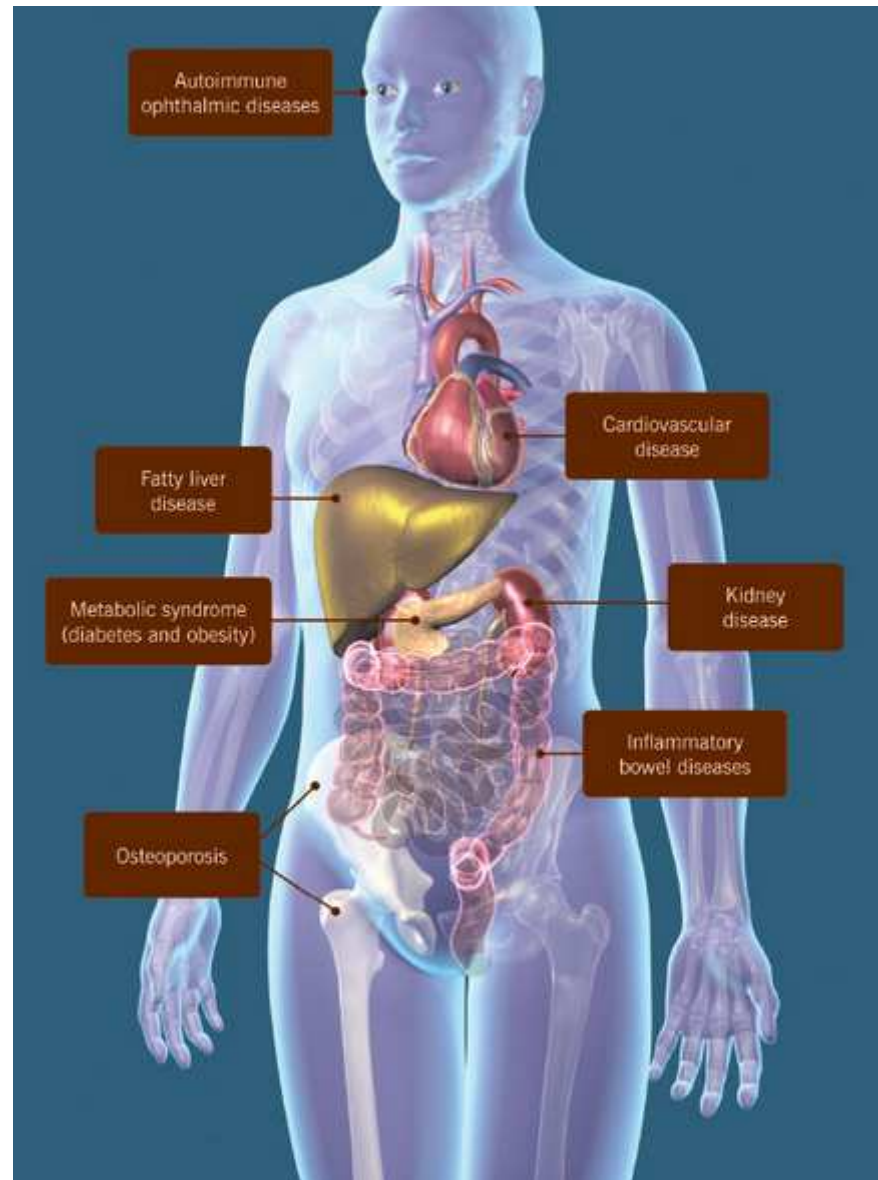
# CONSECUENCIAS



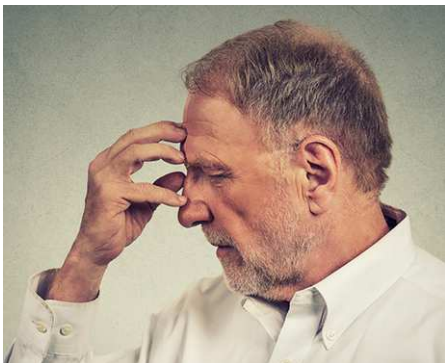
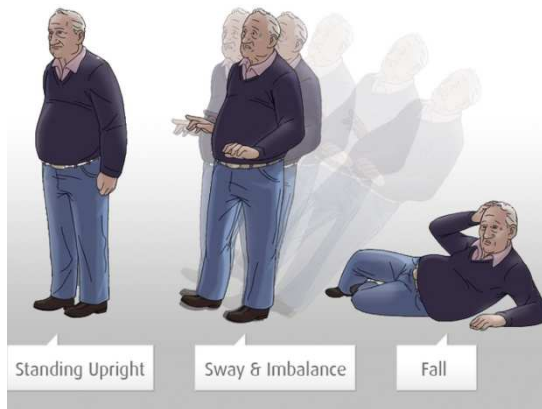
# COMORBILIDADES



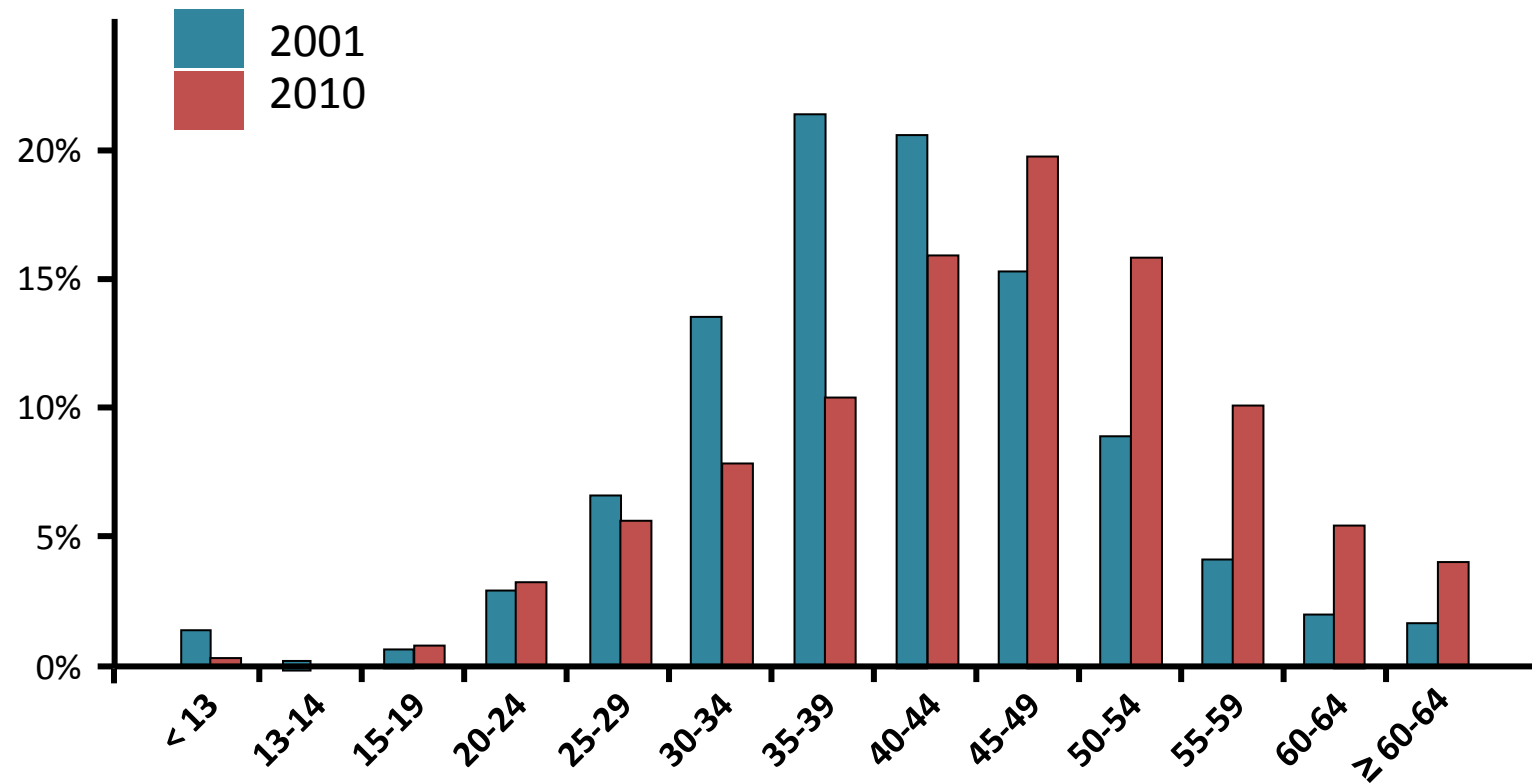
# COMORBILIDADES



# ENVEJECIMIENTO

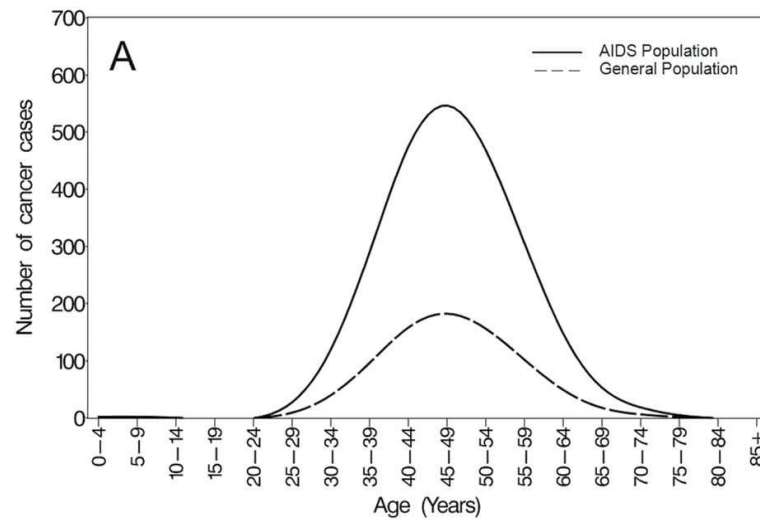


# ENVEJECIMIENTO y VIH



# AGING and HIV

## Accentuated



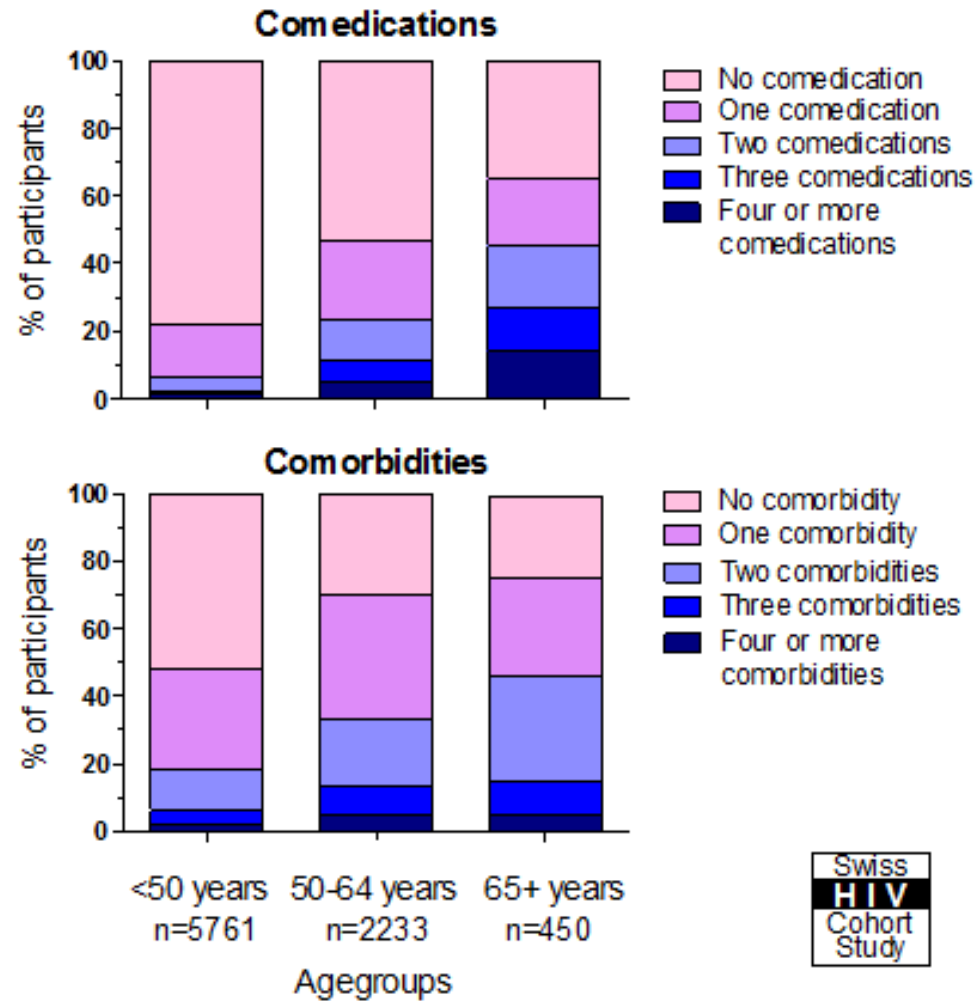
Is aging an accentuated process in HIV people?

## ACCENTUATED AGING

### Overall and age-specific incidence rates

Outcome	Adjusted Mean Difference in Age (years)	Risk aIRR (95% CI)
Myocardial infarction	-0.04 (-0.62 to 0.54)	<b>1.81 (1.49-2.20)</b>
End stage renal disease	-0.23 (-0.69 to 0.23)	<b>1.43 (1.22-1.66)</b>
HIV-associated cancers	-0.57 (-0.93 to -0.21)	<b>1.84 (1.62-2.09)</b>
Other cancers	-0.45 (-0.78 to -0.12)	0.95 (0.85-1.06)

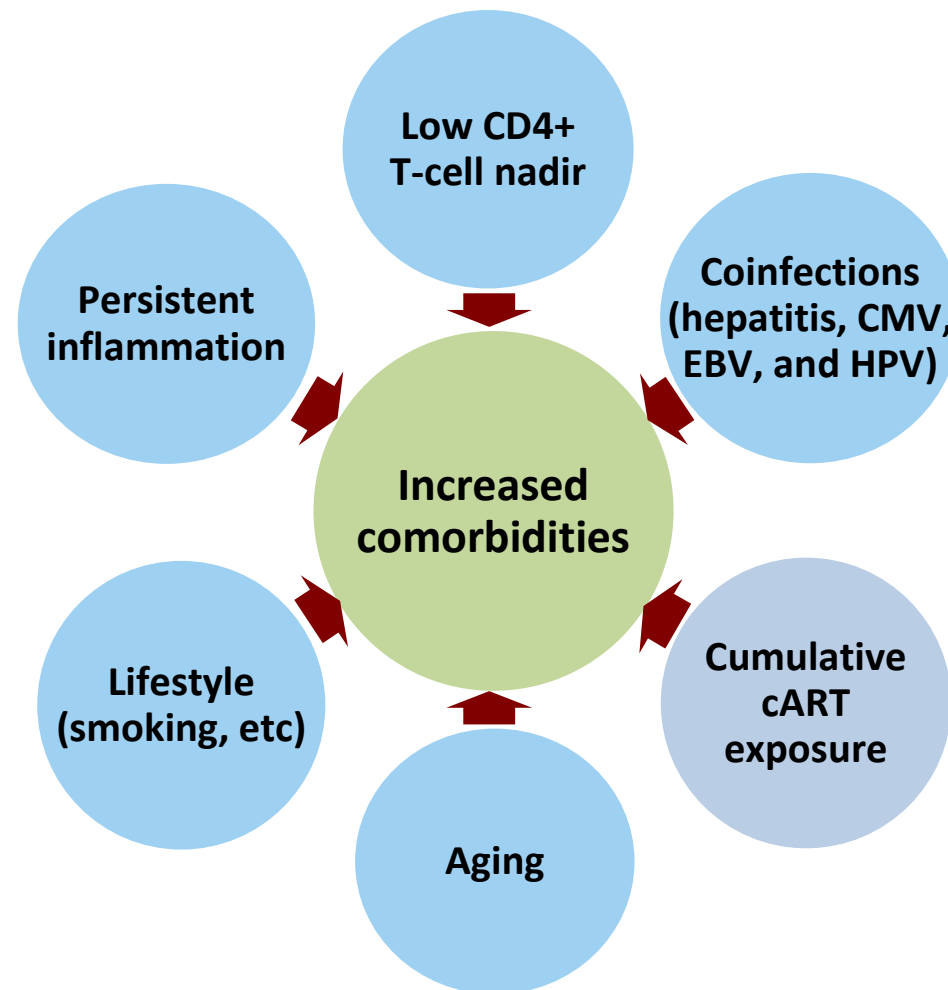
# ACCENTUATED AGING



## **SURVIVAL FOR HIV INFECTED PATIENTS**

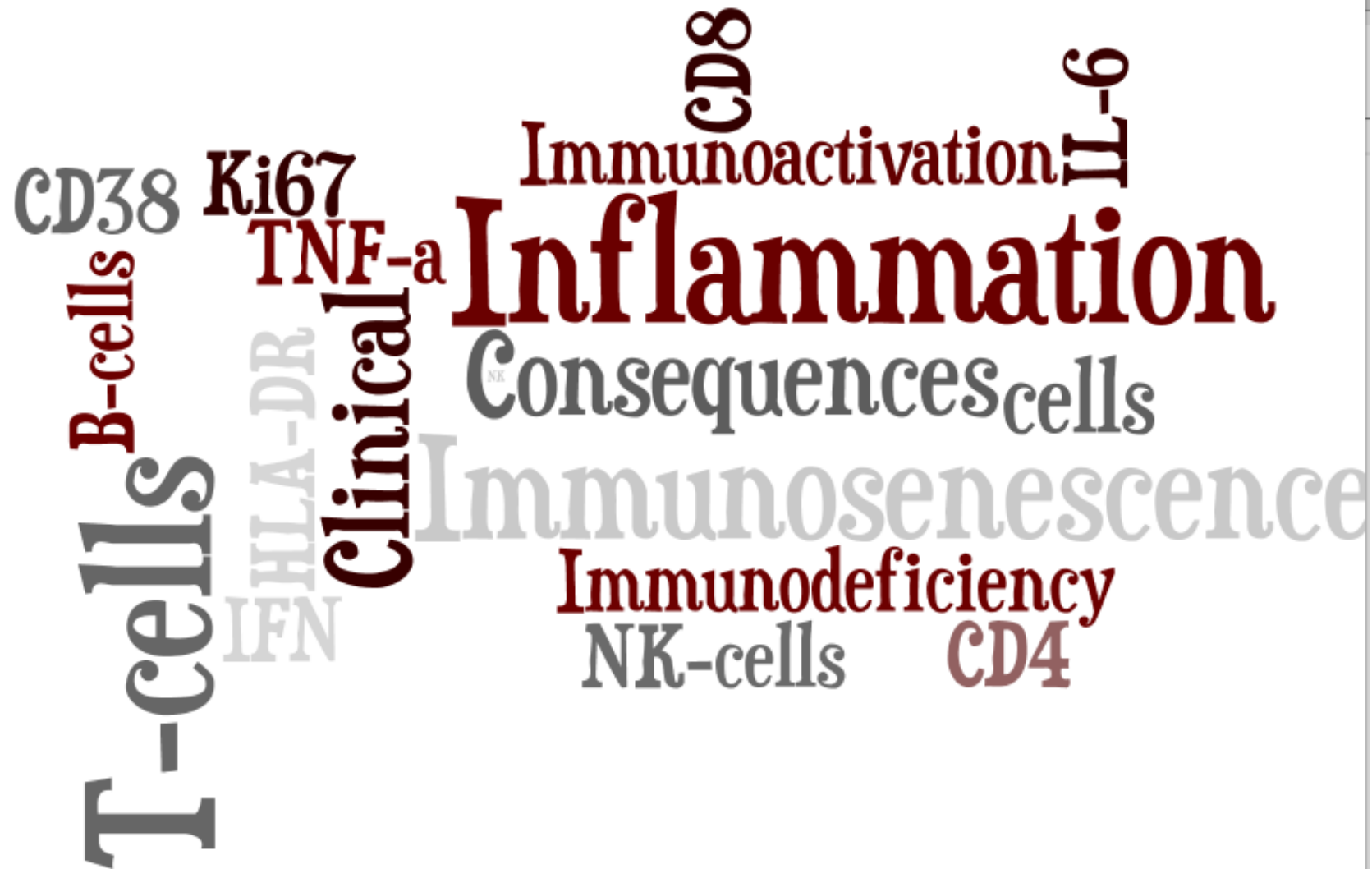


## CAUSES OF INCREASED COMORBIDITIES

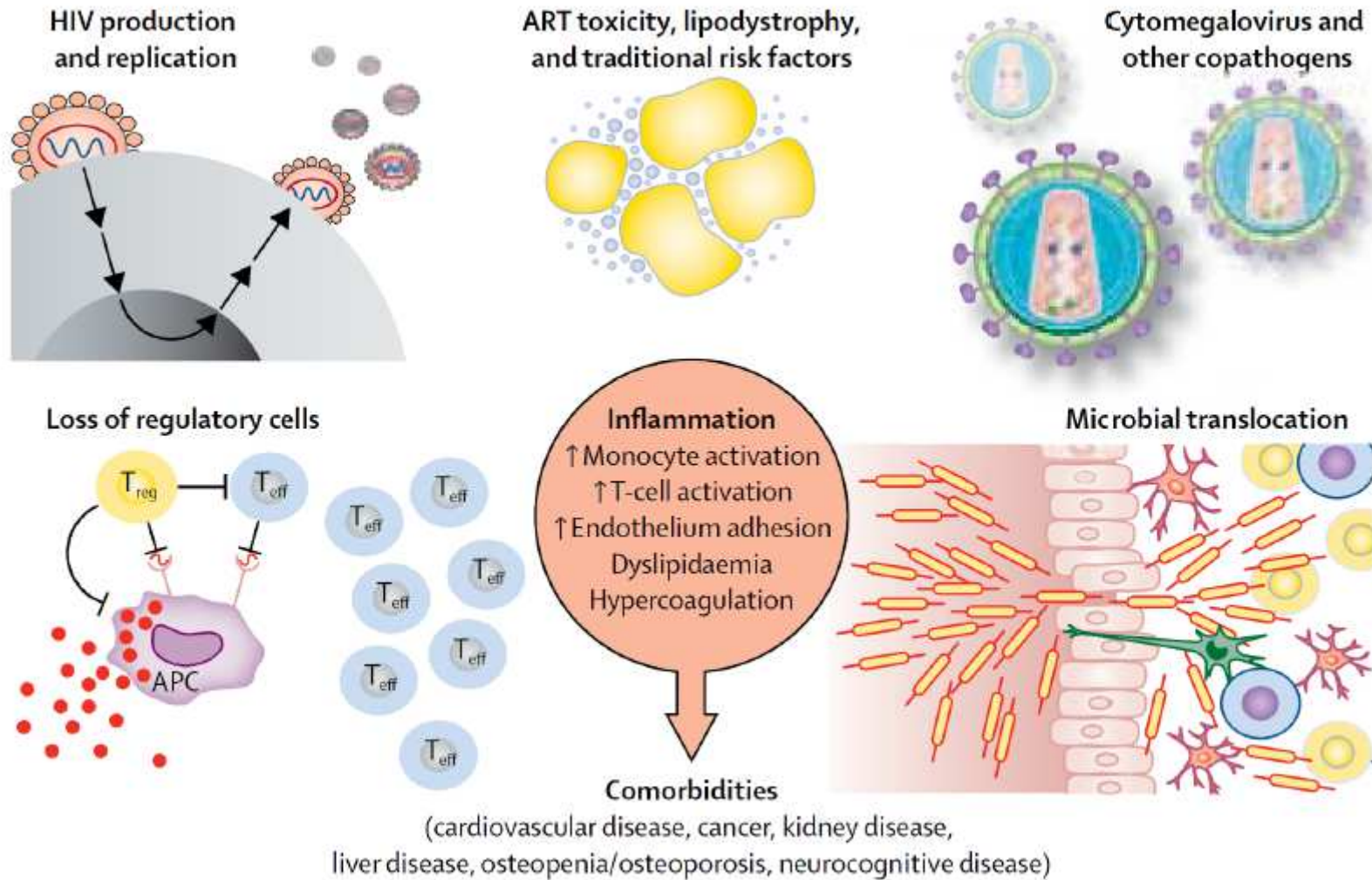


Adapted from Deeks SG, et al. BMJ. 2009;338:a3172. Operskalski EA. Curr HIV/AIDS Rep. 2011;8:12-22.

## CAUSES OF INCREASED COMORBIDITIES: 1. INFLAMMATION



# CAUSES OF INFLAMMATION



# CAUSES OF INFLAMMATION

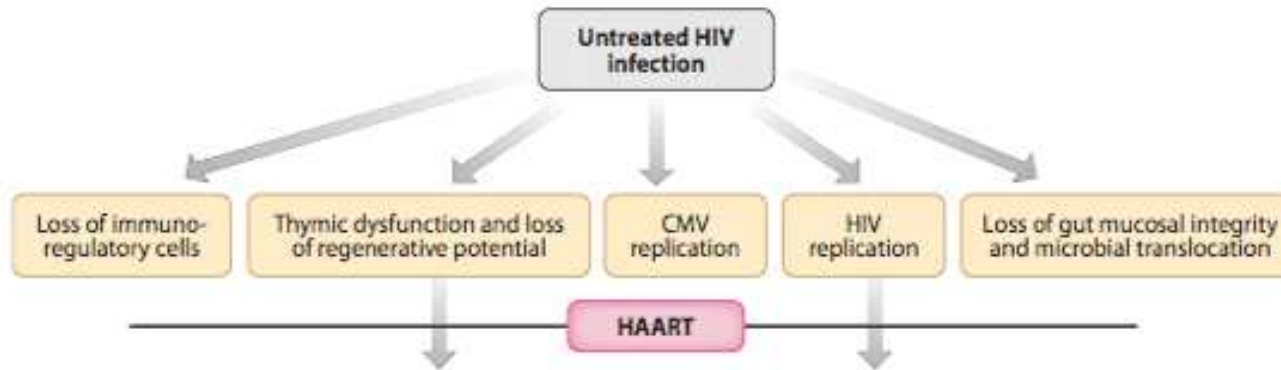


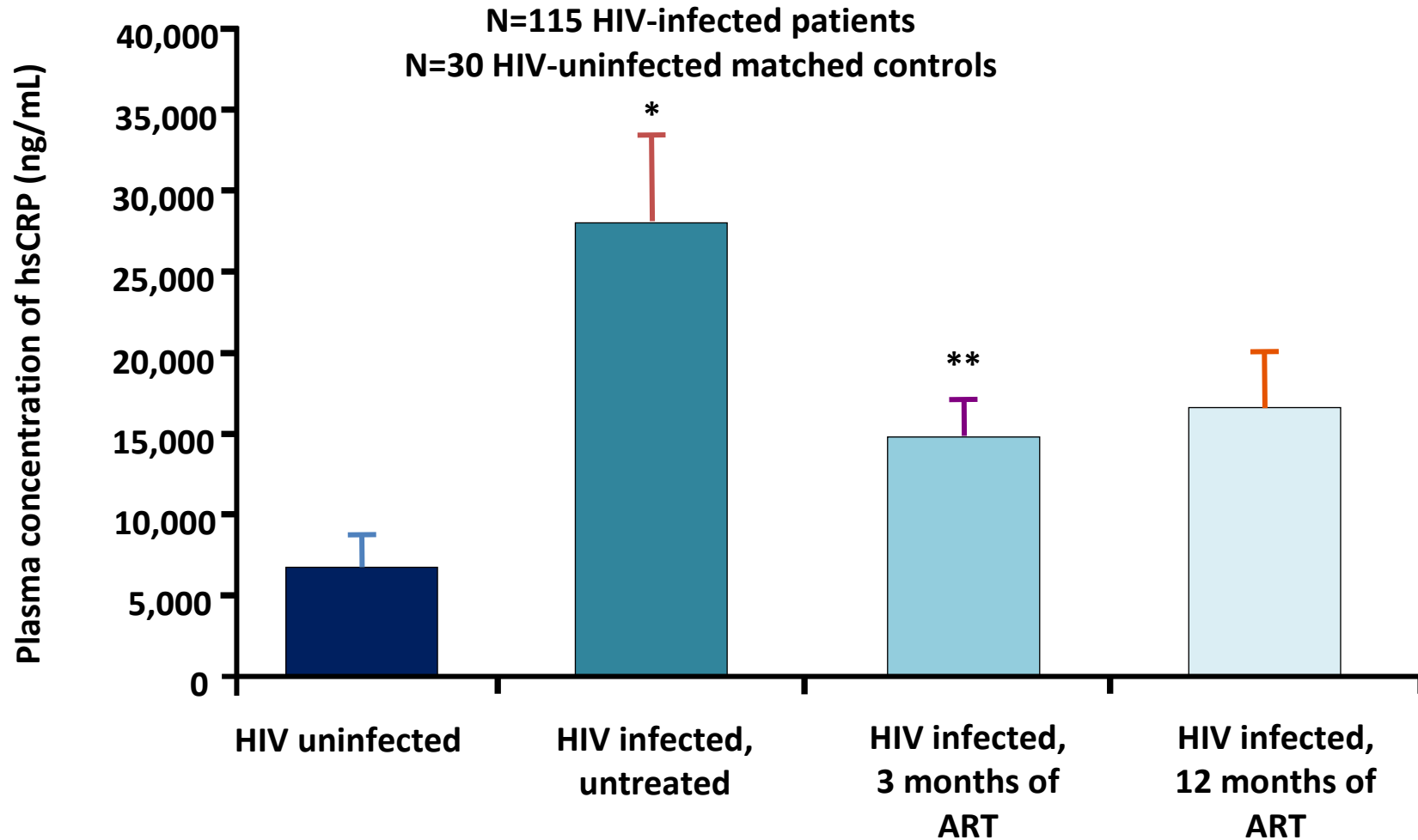
Figure 1

The effect of HIV infection and its treatment on inflammation and immunosenescence.

Deeks et al.  
Annual Review  
of Medicine 2011.

## CAUSES OF INCREASED COMORBIDITIES: 1. INFLAMMATION

Markers of inflammation may persist at elevated levels despite ART



\*  $P < 0.001$  vs HIV uninfected

\*\*  $P < 0.001$  vs HIV infected, untreated

Adapted from Kristoffersen US, et al. 15th CROI 2008; Poster 953.

# CAUSES OF INFLAMMATION

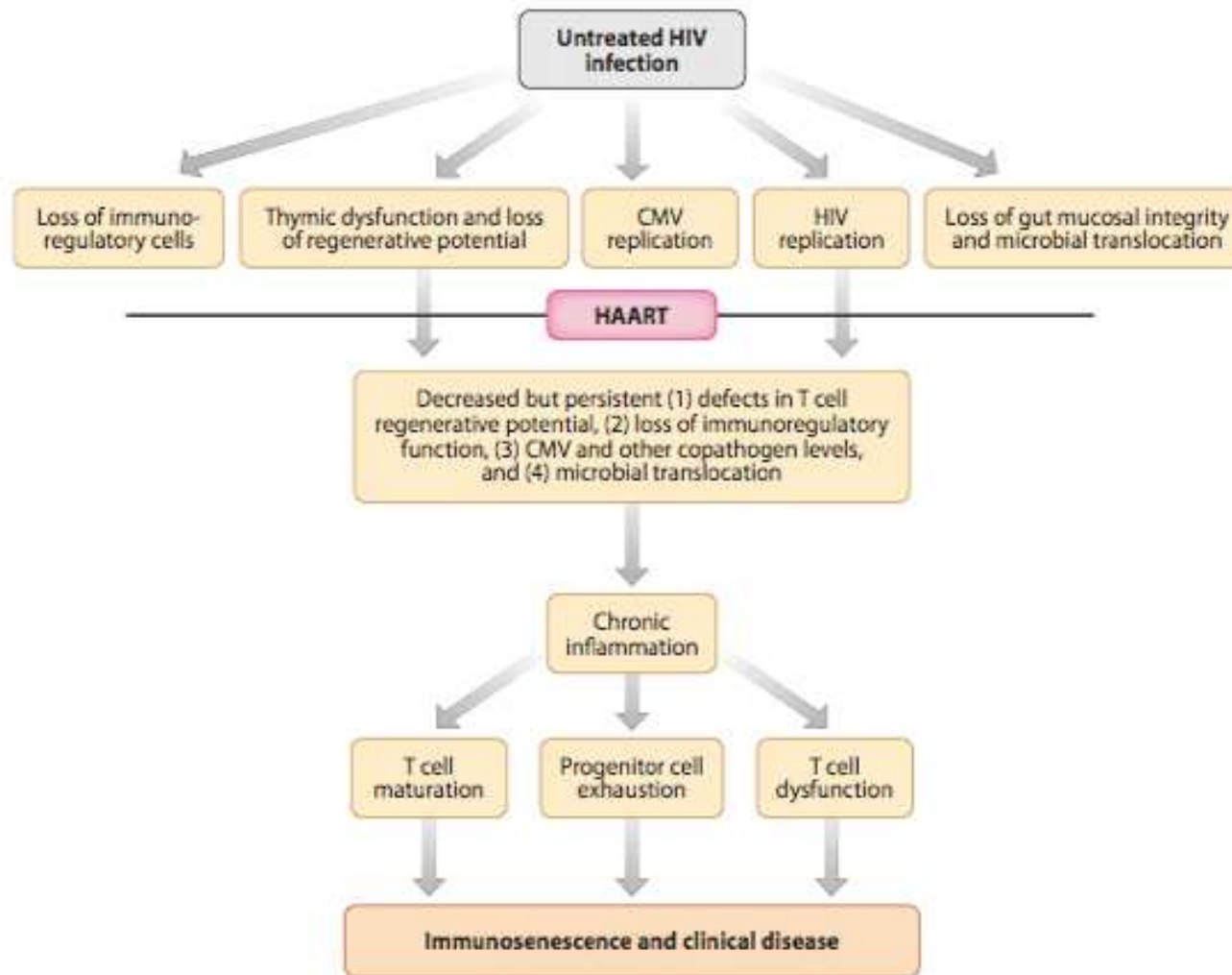


Figure 1

The effect of HIV infection and its treatment on inflammation and immunosenescence.

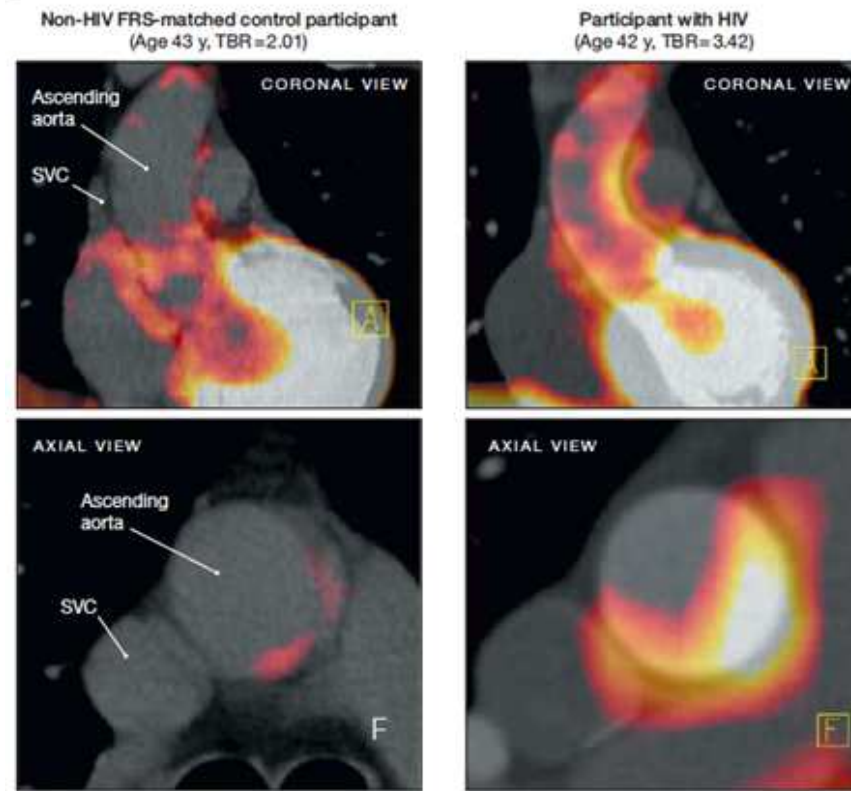
Deeks et al.  
Annual Review  
of Medicine 2011.

## CONSEQUENCES OF INFLAMMATION

### Arterial inflammation as measured by PET-scan:

Increased in HIV-infected patients as compared to VIH negative subjects with the same FRS

**Figure 2.** Representative  $^{18}\text{F}$ -FDG-PET/CT Imaging of the Aorta

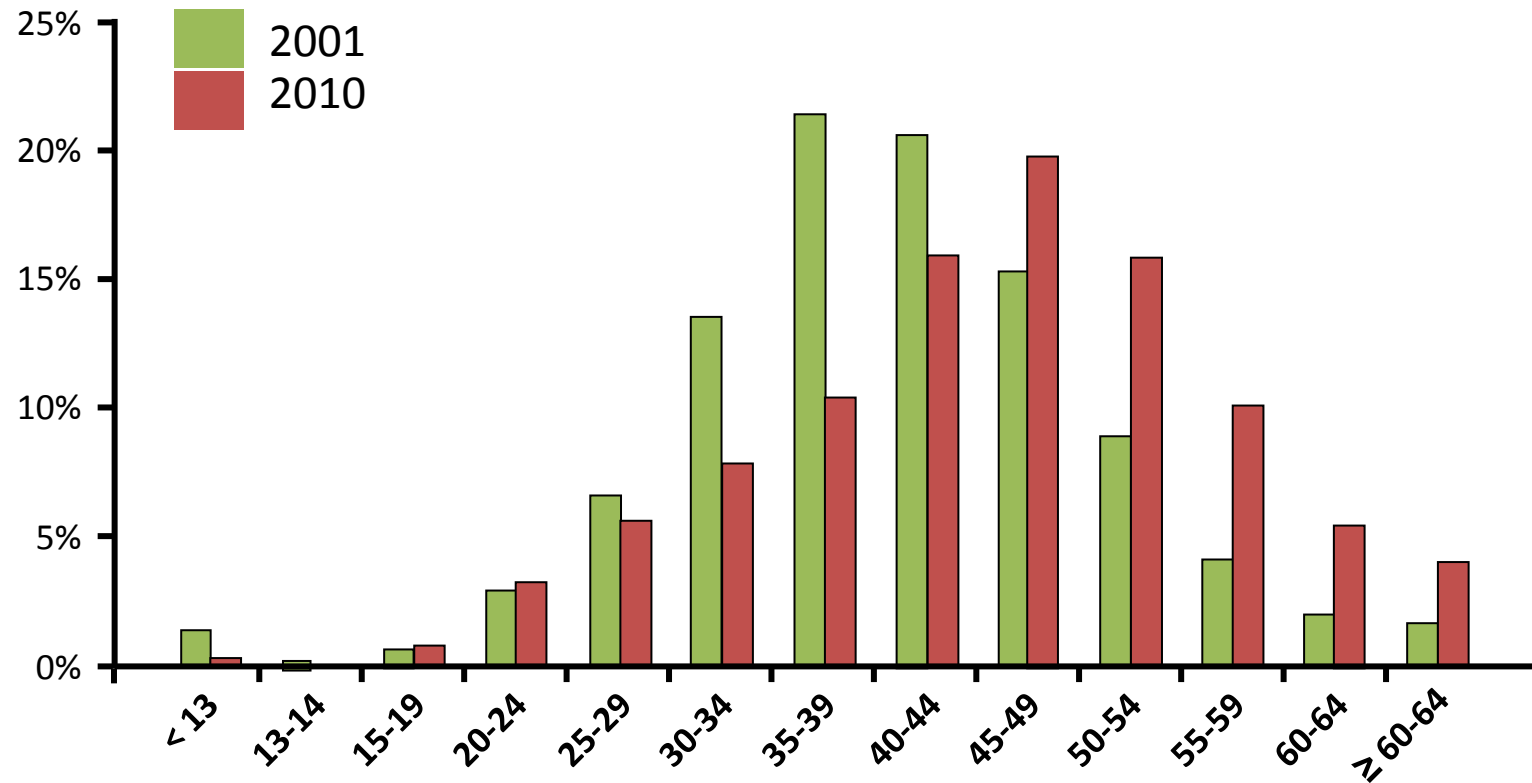


## CONSEQUENCES OF INFLAMMATION

### Inflammation Predicts Disease in Treated HIV Infection

- **Cardiovascular Disease** (Duprez, Atherosclerosis 2009)
- **Cancer** (Breen, Cancer Epi Bio Prev 2010; Borges, AIDS 2013)
- **Venous Thromboembolism** (Musselwhite, AIDS 2011)
- **Type II Diabetes** (Brown, Diabetes Care 2010)
- **Cognitive Dysfunction** (Burdo, AIDS 2013; Letendre CROI 2012, Abs#82)
- **Frailty** (Erlandson, JID 2013)
- **Mortality** (Kuller, PLoS Med 2008; Tien, JAIDS, 2010; Justice, CID 2012)

## CAUSES OF INCREASED COMORBIDITIES: 2. AGING



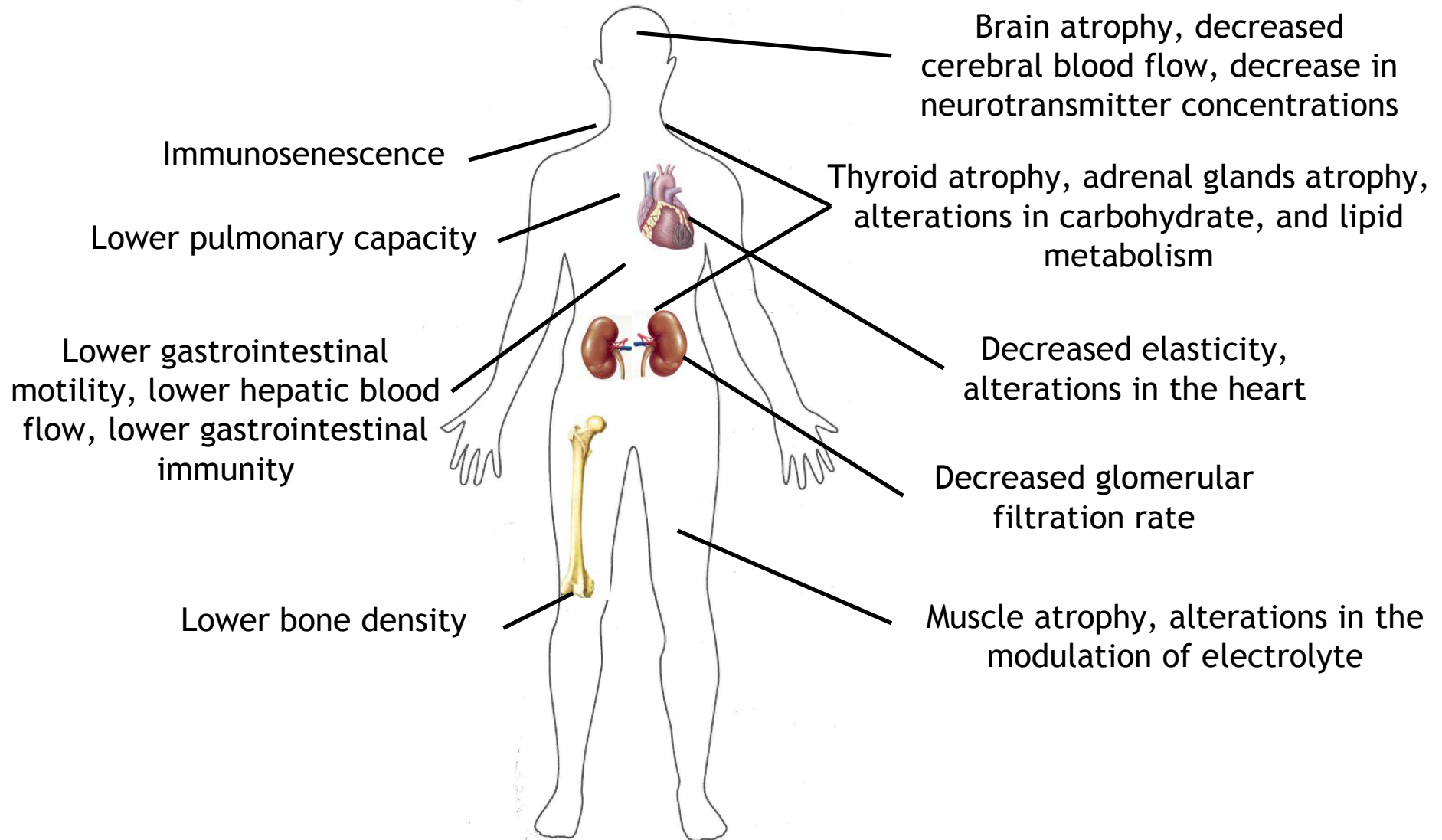
# AGING

From Wikipedia

**Ageing** (British English) or **aging** (American English) is the process of becoming older.

In humans, ageing represents the accumulation of changes in a human being over time, encompassing physical, psychological, and social change.

# PHYSIOLOGICAL PROCESS OF AGING



# IMMUNESENESCENCE

## Immunosenescence

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From Wikipedia, the free encyclopedia

**Immunosenescence** refers to the gradual deterioration of the [immune system](#) brought on by [natural age advancement](#).



Thymic atrophy  
Decreased bone marrow production



Decreased B and T cell activation and maturation resulting in decreased humoral and cell-mediated immunity (naïve and memory cells).



**Increased frequency and severity of diseases such as chronic inflammation disorders (neurodegenerative, cardiovascular...) and autoimmunity**  
**And major susceptibility to cancers and infections**

# INFLAMMAGING

The **aging immune system** is characterized by a low level chronic systemic inflammatory state, termed “**InflammAging**”.

This inflammatory phenotype is marked by elevated circulating levels of markers of:

- Inflammation (e.g., C-reactive protein (CRP))
- Pro-inflammatory cytokines (interleukin-6 (IL-6) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ))

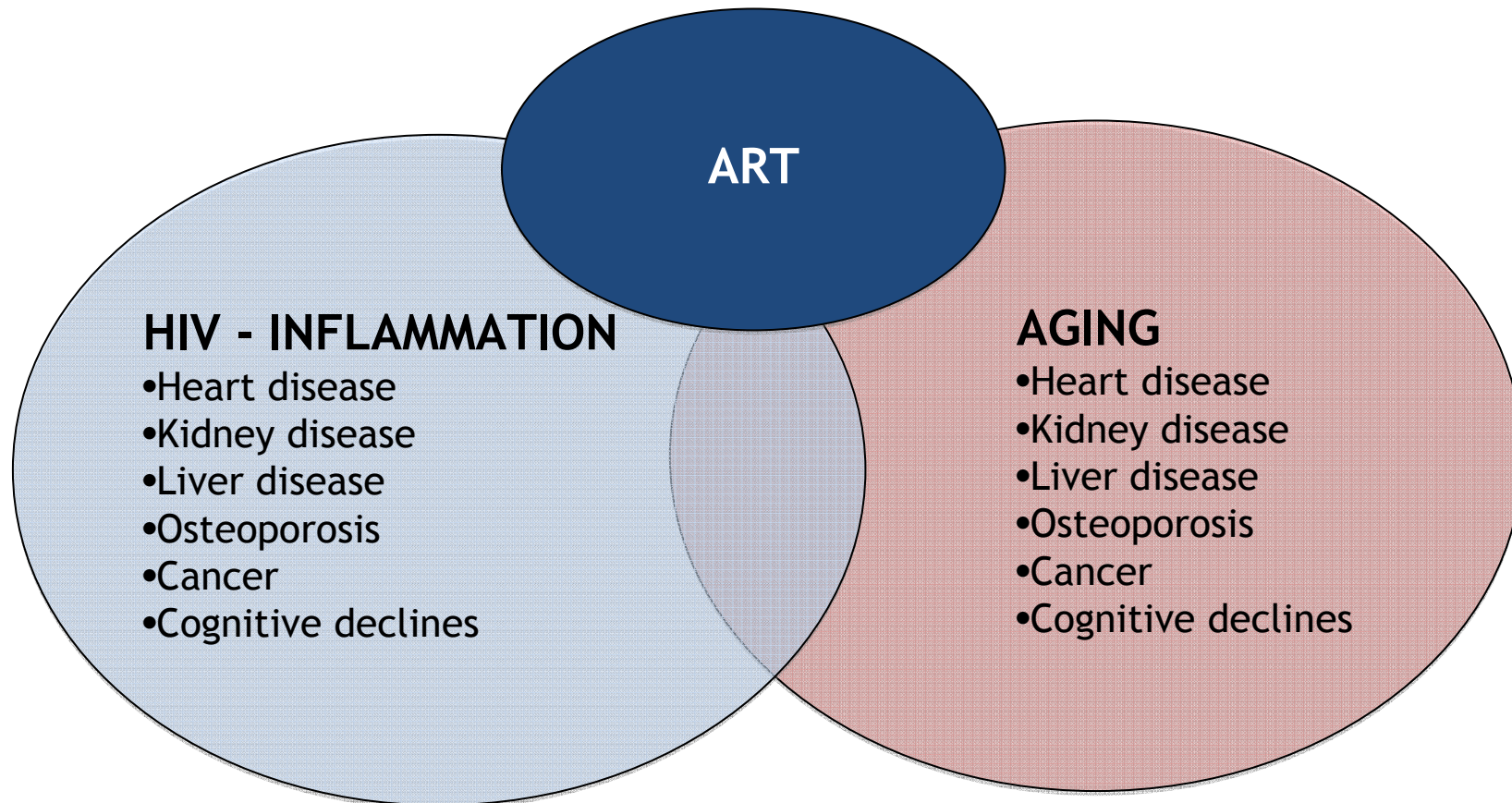
It is associated with increased **morbidity and mortality** in older adults

-Franceschi C, et al. Inflamm-aging. An evolutionary perspective on immunosenescence. *Ann N Y Acad Sci.* 2000;908:244–54.

-De Martinis Met al. Inflammation markers predicting frailty and mortality in the elderly. *Exp Mol Pathol.* 2006;80(3):219–27.

-Roubenoff R, et al. Cytokines, insulin-like growth factor 1, sarcopenia, and mortality in very old community-dwelling men and women: the Framingham Heart Study. *Am J Med.* 2003;115(6):429–35.

## CONSEQUENCES OF VIH/INFLAMMATION and AGING



Adapted from Vance DE. Am J Nurs 2010

# FRAILTY SYNDROME

Frailty is a distinct clinical entity, **differing from:**

- Comorbidity as defined by the presence of  $\geq 2$  diseases.
- Disability as measured by impairment in activities of daily living (ADL)

The **frailty phenotype** in older adults consists of three or more of the following:

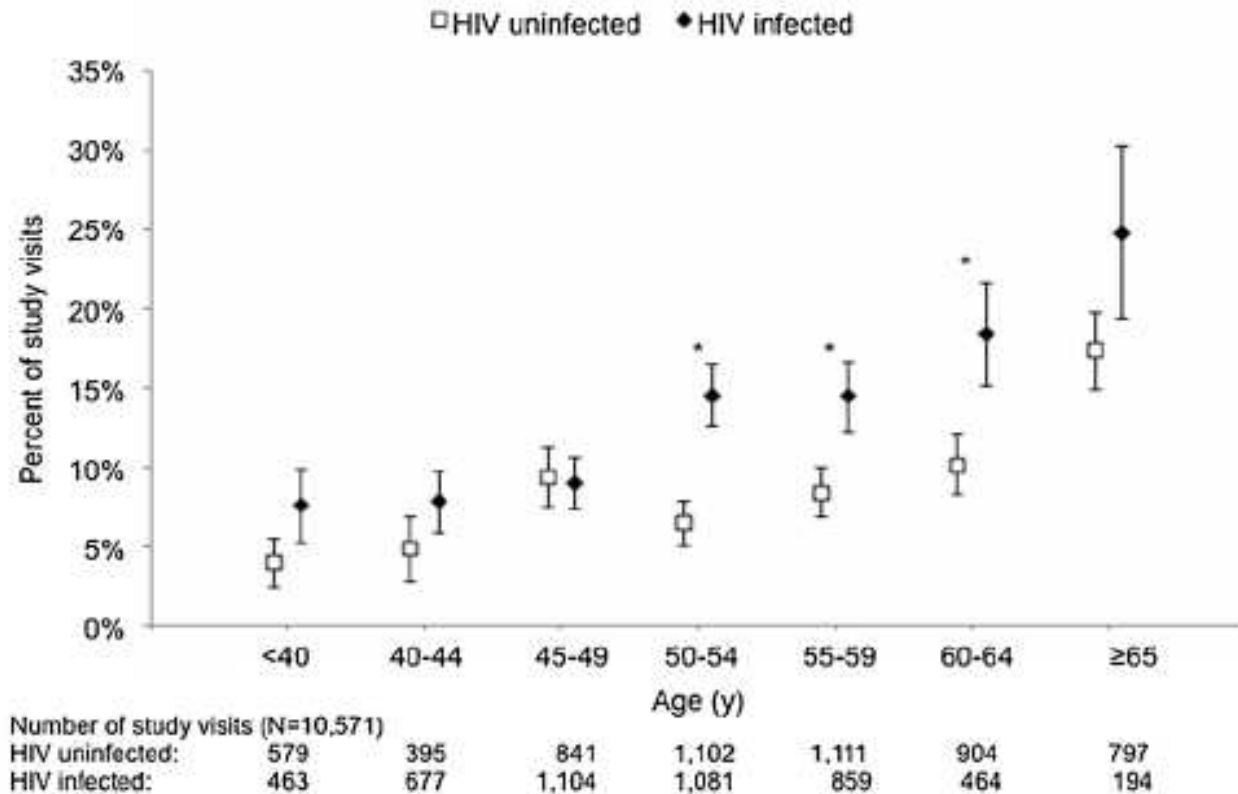
- Weakness (measured by grip strength),
- Low physical activity,
- Slowed motor performance (measured by walking speed),
- Exhaustion, and
- Unintentional weight loss.

# FRAILTY PHENOTYPE

**Predicts** a number of serious adverse health outcomes in community-dwelling older adults, including:

- acute illness,
- falls,
- cognitive decline,
- hospitalization,
- disability,
- dependency, and
- mortality, adjusting for comorbidities.

# FRAILTY PHENOTYPE in HIV



**Fig. 1** The percent of study visits (and 95 % confidence intervals) at which the criteria for the frailty phenotype were met, stratified by age and HIV status. October 1, 2007, to September 30, 2011, the Multicenter AIDS Cohort Study. \* $p < 0.05$ . Intraclass correlation coefficient 0.491 for HIV-infected men; 0.579 for HIV-uninfected men (reprinted with permission from Althoff K N et al. J Gerontol A Biol Sci Med Sci 2014;69A:189–198)

## FRAILITY PHENOTYPE in HIV

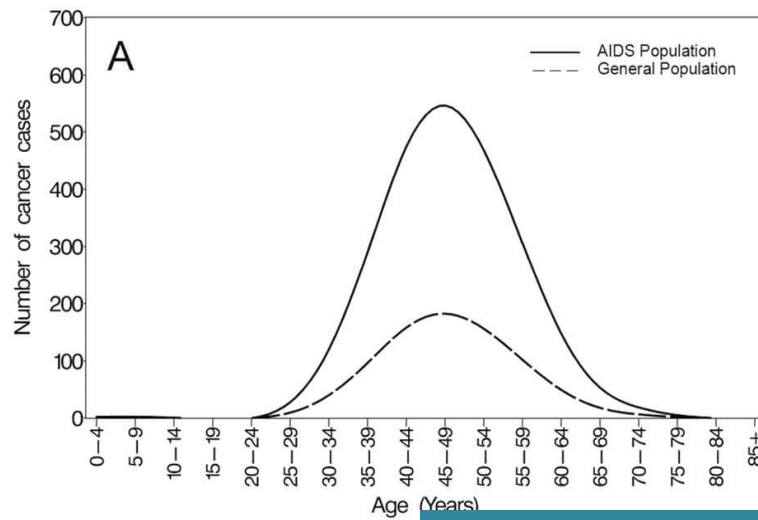
**Factors that have been associated with frailty in HIV+ populations include:**

- age,
- lower current or nadir CD4 T cell counts and
- other HIV-infection-related inflammation,
- hepatitis C co-infection,
- other comorbidities,
- depressive symptoms, and
- certain social factors (e.g., lower education, unemployment)

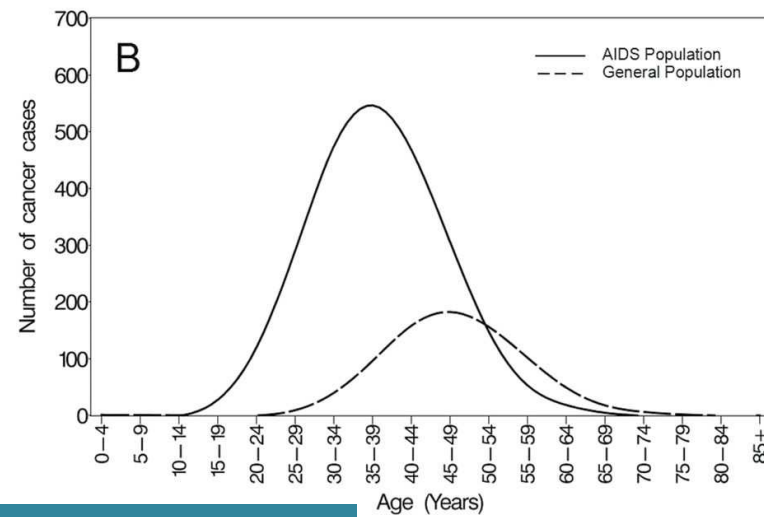
Desquilbet L, et al. HIV-1 infection is associated with an earlier occurrence of a phenotype related to frailty. *J Gerontol A Biol Sci Med Sci.* 2007;62:1279–86. Piggott DA, et al. Frailty, HIVinfection, and mortality in an aging cohort of injection drug users. *PLoS ONE.* 2013;8(1):e54910. Terzian AS, et al. Factors associated with preclinical disability and frailty among HIV-infected and HIV-uninfected women in the era of cART. *J Womens Health (Larchmt).* 2009;18(12):1965–74.

# AGING

## Accentuated



## Accelerated ???



Is aging an accelerated process in HIV people?

## ACCELERATED AGING

### A prospective comparative cohort study



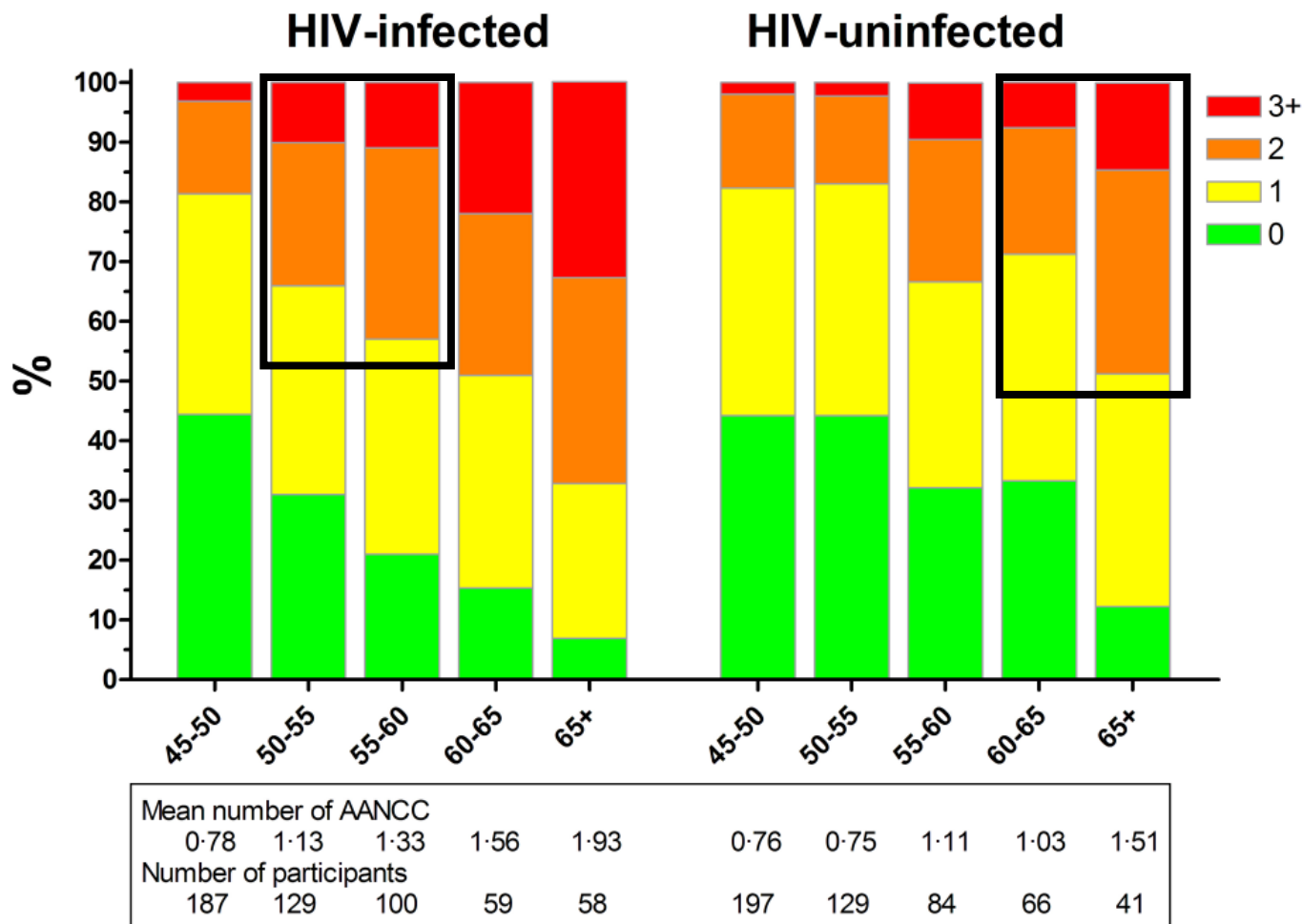
- Prevalence and incidence of age-associated non-communicable comorbidities (AANCC) and their risk factors in **persons  $\geq 45$  yrs**
- Started October **2010**
- Participants:
  - ✓ **HIV-1-infected**: from the HIV outpatient clinic at the Academic Medical Center (Amsterdam)
  - ✓ **HIV-1-uninfected**: from the Amsterdam Public Health Service sexual health clinic, and the ongoing Amsterdam Cohort Studies on HIV/AIDS

## Demographic and HIV characteristics

	HIV neg (n=524)	HIV pos (n=540)	p-value
Age (years)	52.1 (47.9-58.3)	52.9 (48.3-59.6)	0.20
Male gender	85.1%	88.1%	0.15
Dutch	81.3%	72.2%	<0.001
MSM	69.7%	73.9%	0.125
Time since HIV-1 diagnosis (yrs)		12.1 (6.2-17.1)	
Mean CD4 count at enrollment (cells/mm <sup>3</sup> )		565 (435-745)	
Nadir CD4 count (cells/mm <sup>3</sup> )		180 (78-260)	
Viral load > 200 at or within 4 mos prior to enrolment among cART-treated participants		1.5%	
Prior clinical AIDS		31.3%	
On cART		95.7% • 79.1% started R <sub>x</sub> -naive • 20.9% started ART-exp.	
Years since ART was first initiated (yrs)		10.4 (4.4-14.5)	
Duration of viral load < 200 (since last > 200) (yrs)		5.8 (2.4 – 10.2)	
Known cumulative duration CD4 < 200(mos)		0.8 (0.0 – 9.6)	

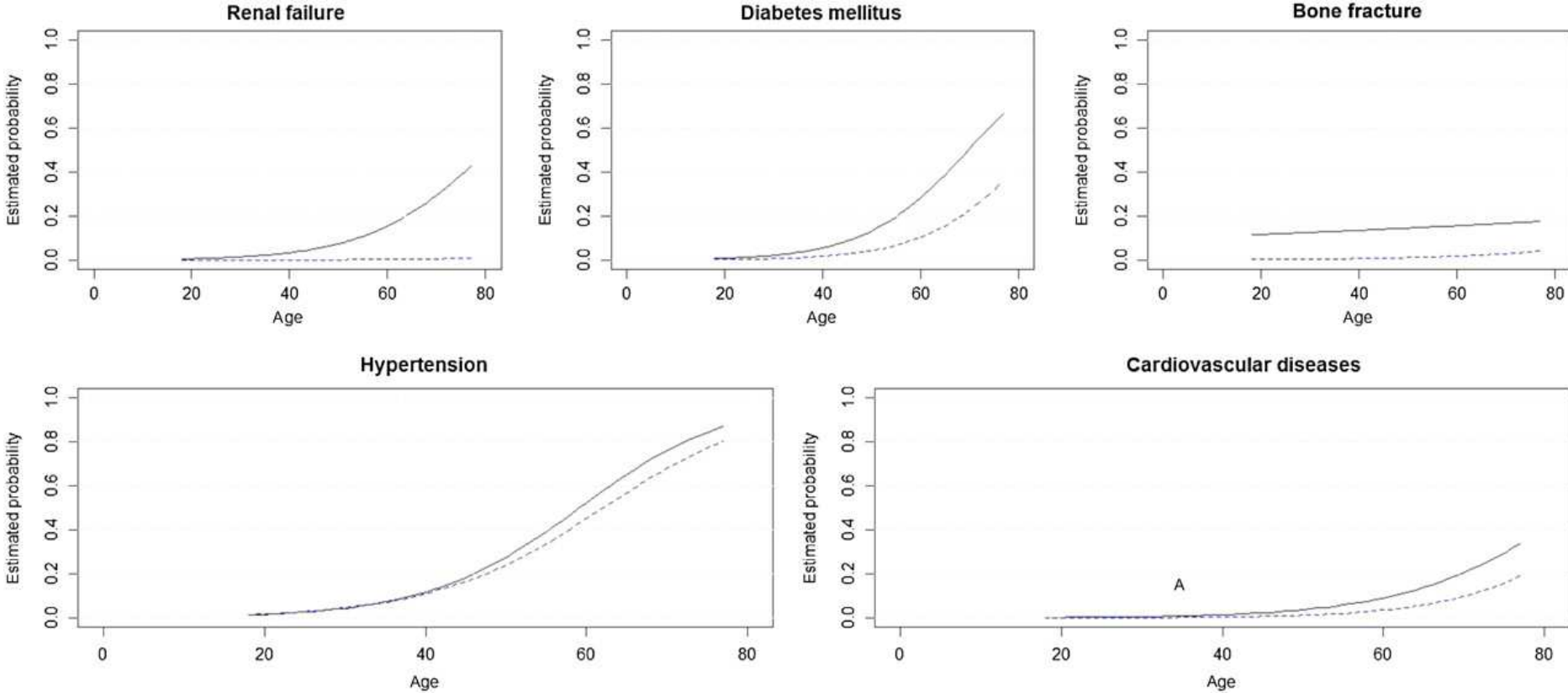
Data presented as median (IQR) or percentage as appropriate.  
P-value represents Wilcoxon Rank Sum or Chi2 as appropriate

# ACCELERATED AGING

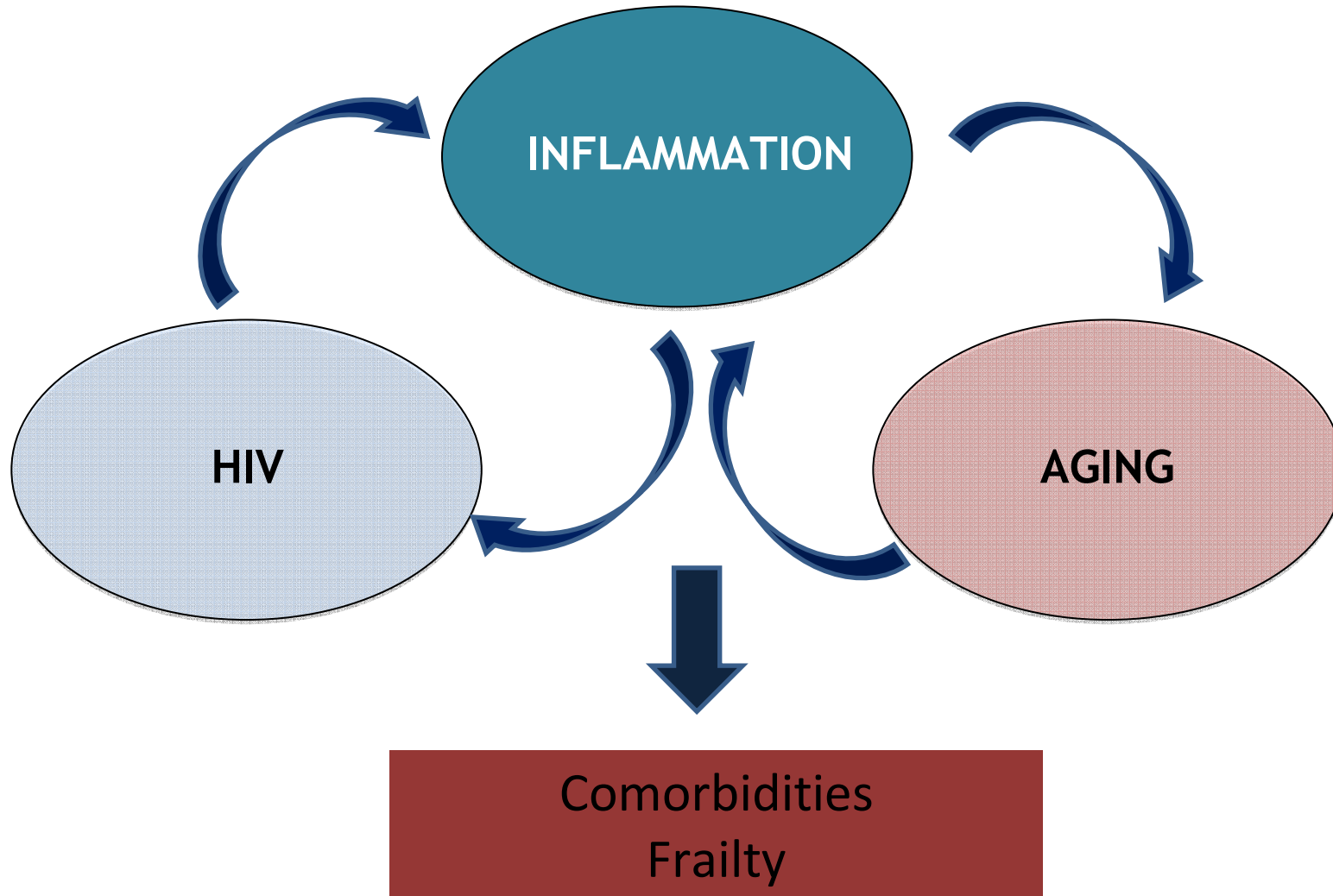


# ACCELERATED AGING

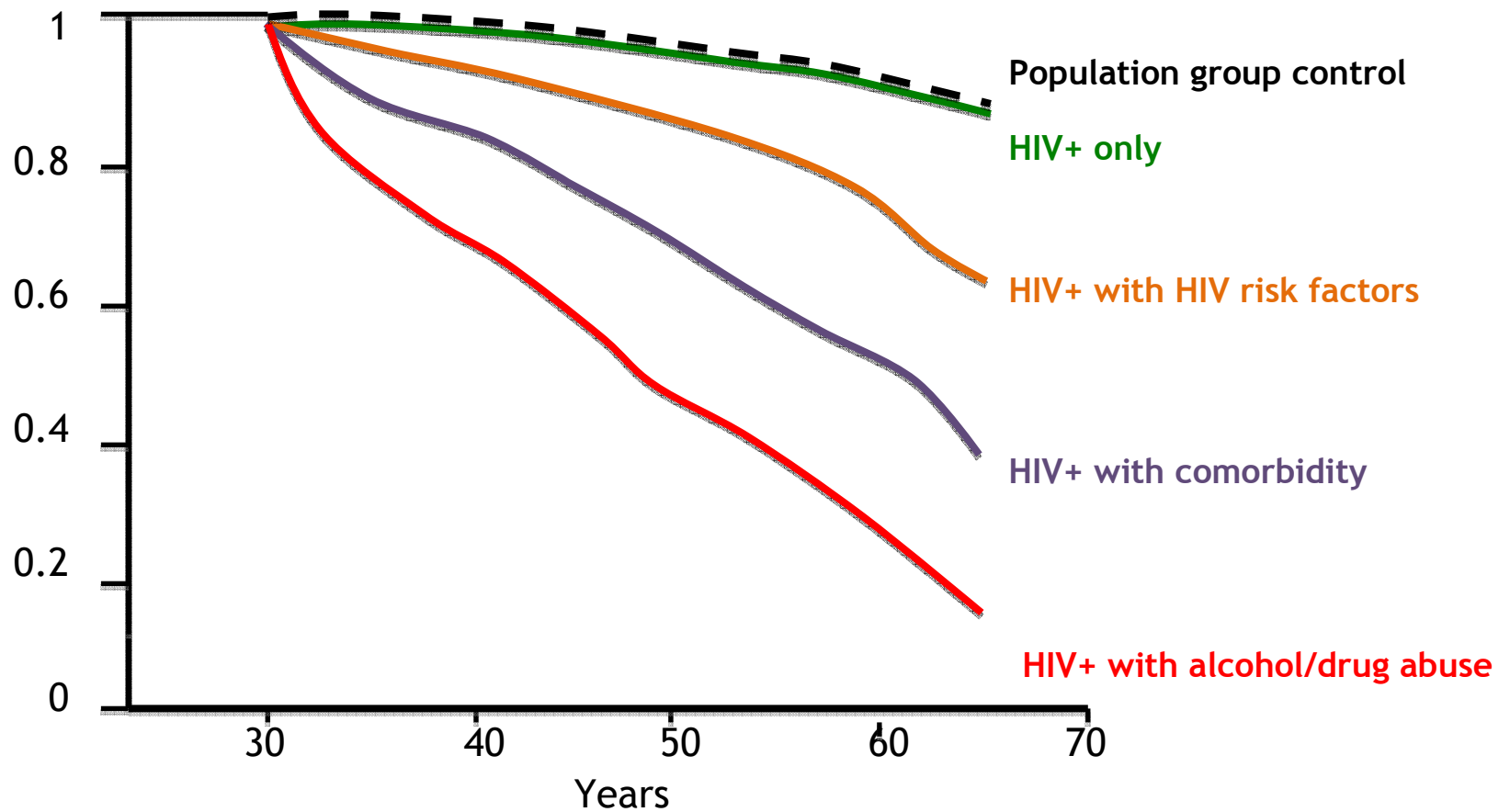
Comparative risk of hypertension, diabetes mellitus, renal failure, cardiovascular disease, and fracture, by age, among patients versus control subjects.



## VIH, INFLAMMATION and AGING



# SURVIVAL FOR HIV INFECTED PATIENTS



Based on Obel N et al. Plos One 2011

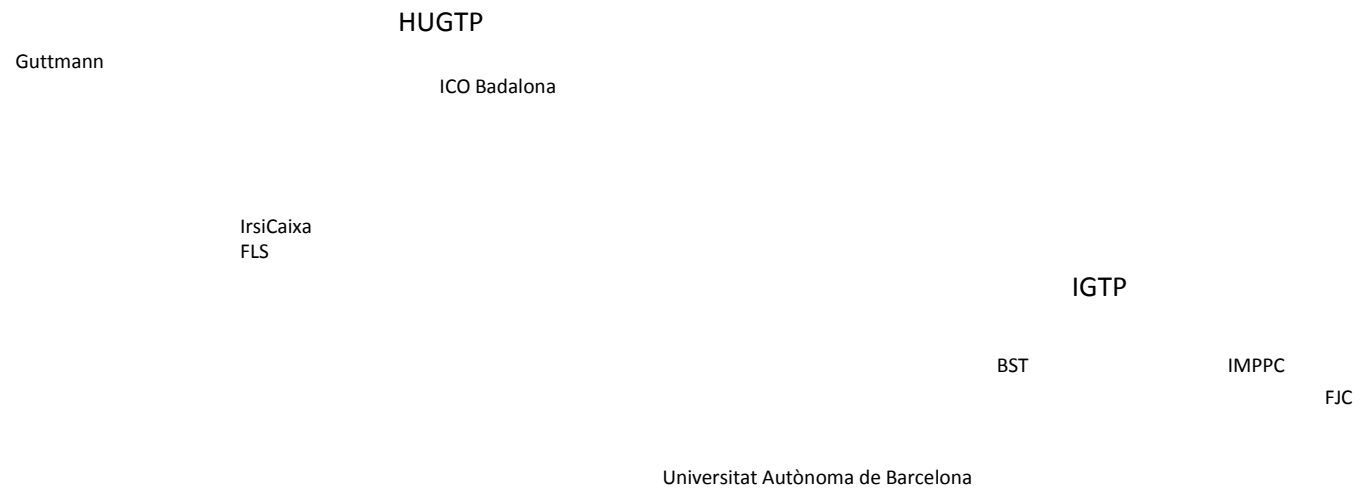
MUCHAS  
GRACIAS



Vive tu vida y olvida tu edad



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