

**RISC CARDIOVASCULAR,  
TOXICITAT RENAL i  
OSTEOPOROSIS  
en PACIENTS HIV**

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**Eugènia Negredo**

Fundació Lluita contra la SIDA

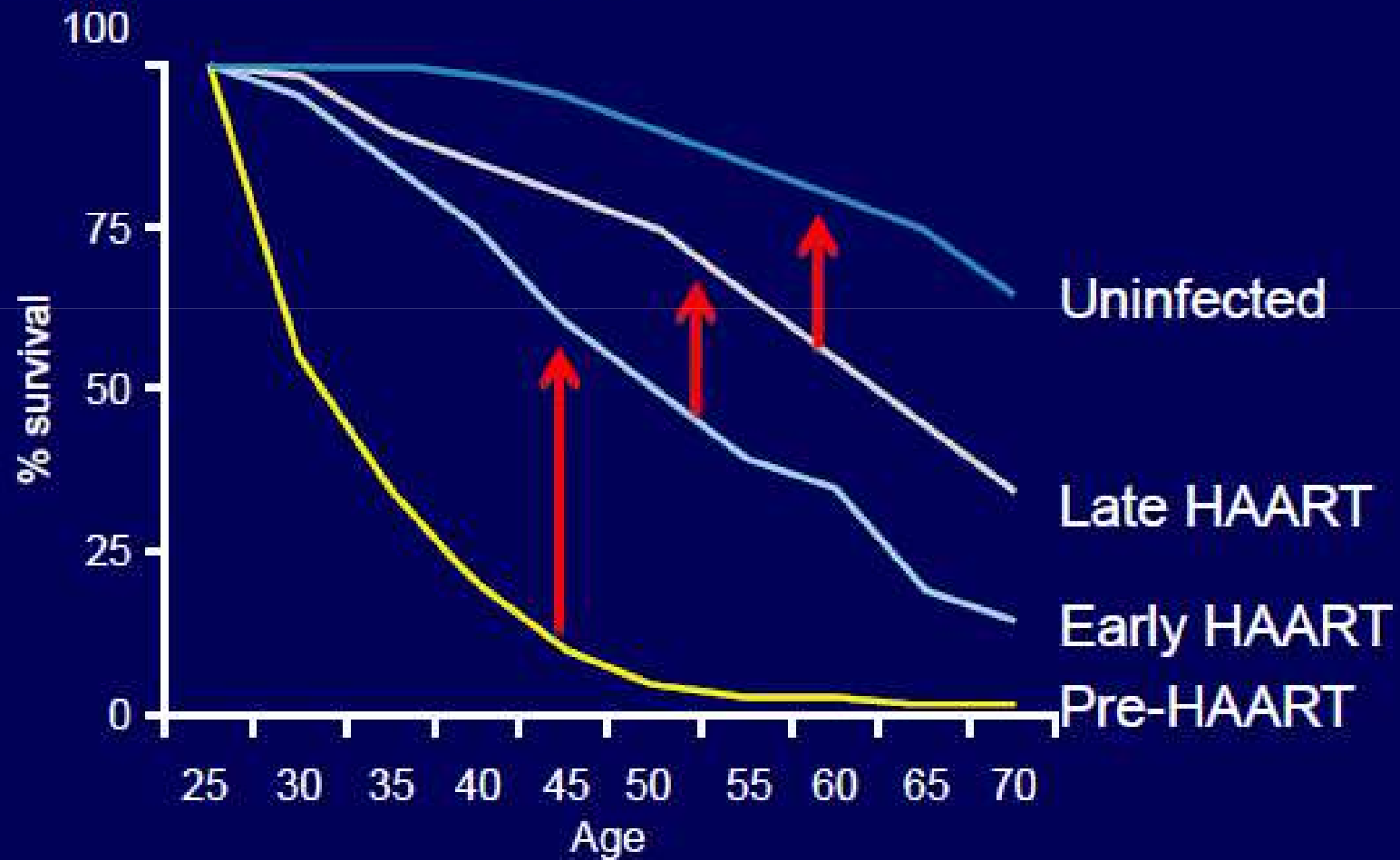
Hospital Universitari Germans Trias i Pujol

Barcelona

Barcelona, Octubre 2014

# CVD and HIV infection

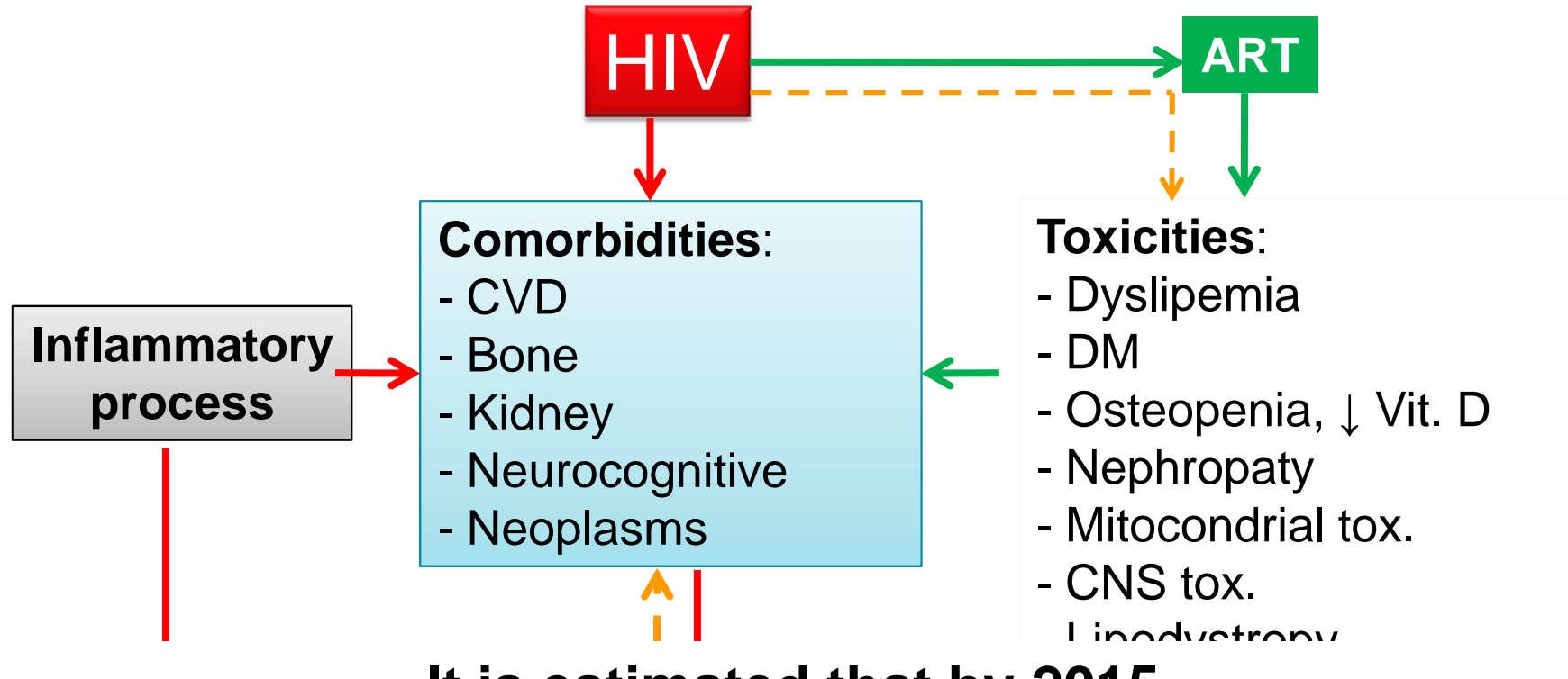
- Life expectancy in HIV population



Adapted from Lohse N. et al. Intern Med 2007;146:87

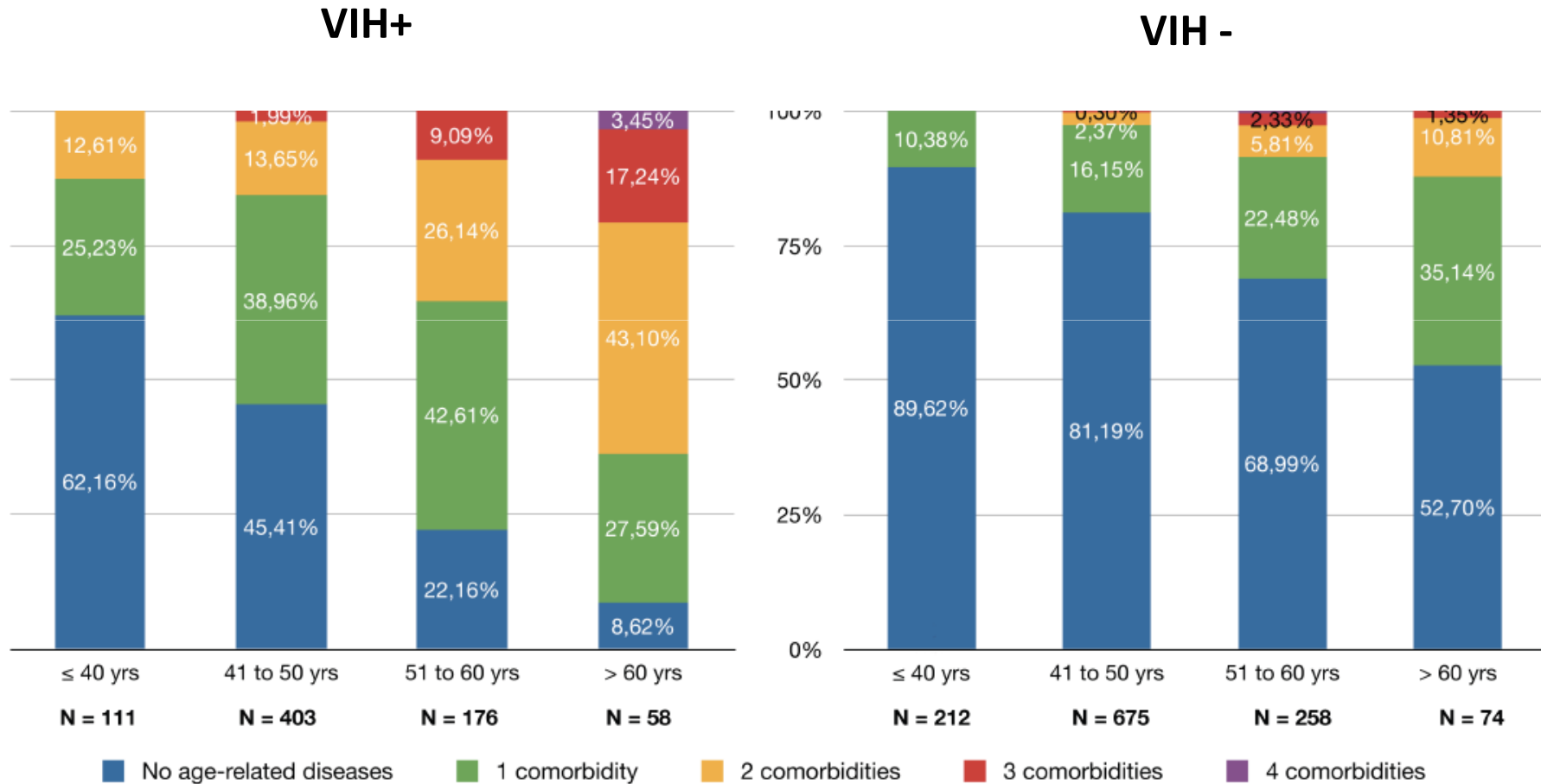


# Non-AIDS events

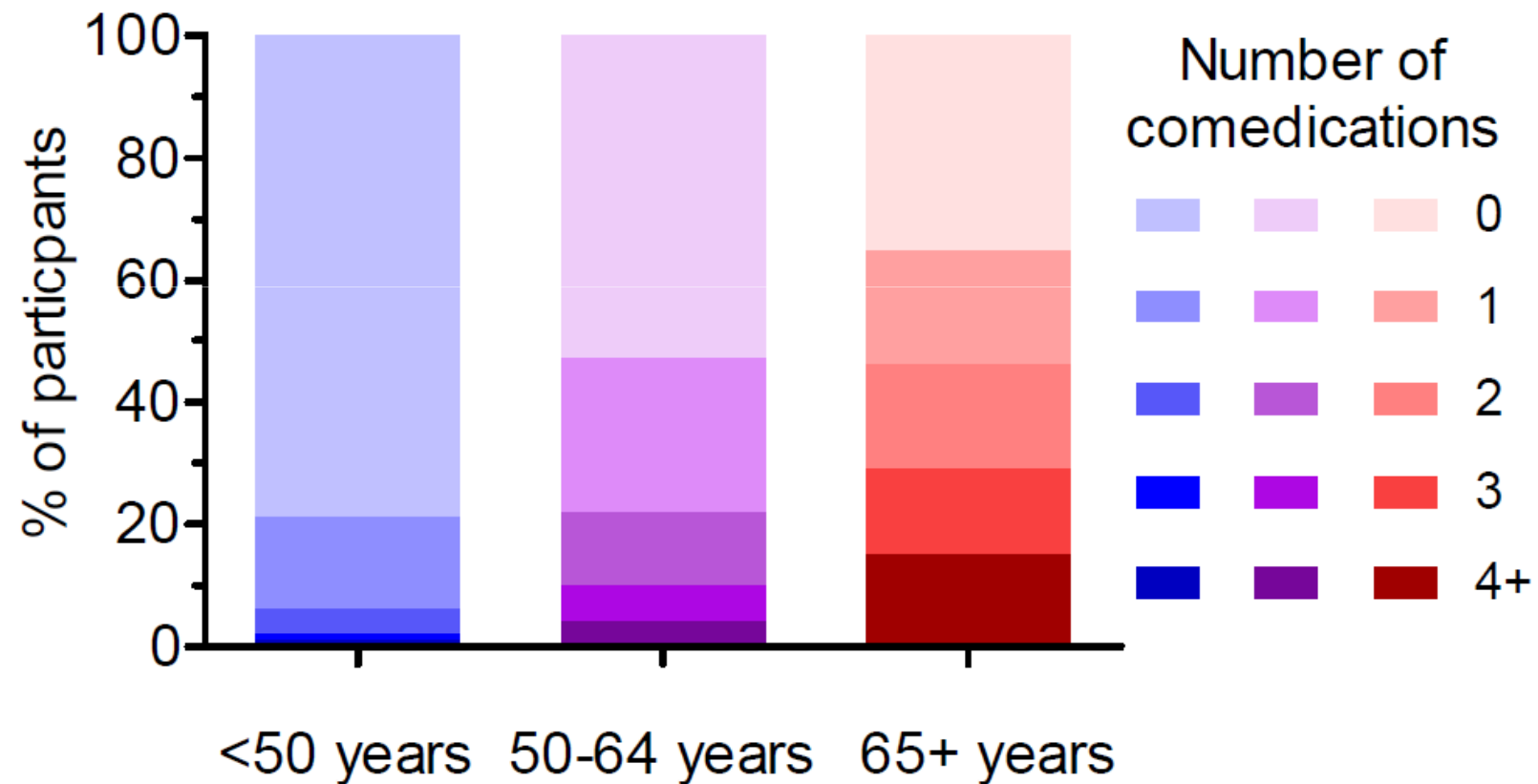


**It is estimated that by 2015  
more than 50% of HIV positive patients  
will be > 50 years**

# Prevalencia de comorbilidades en pacientes con y sin infección por VIH en función de la edad



## Número de medicaciones no-antirretrovirales estratificadas en función de la edad



# **Cardiovascular risk and HIV Infection**

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# Etiology and pathogenesis

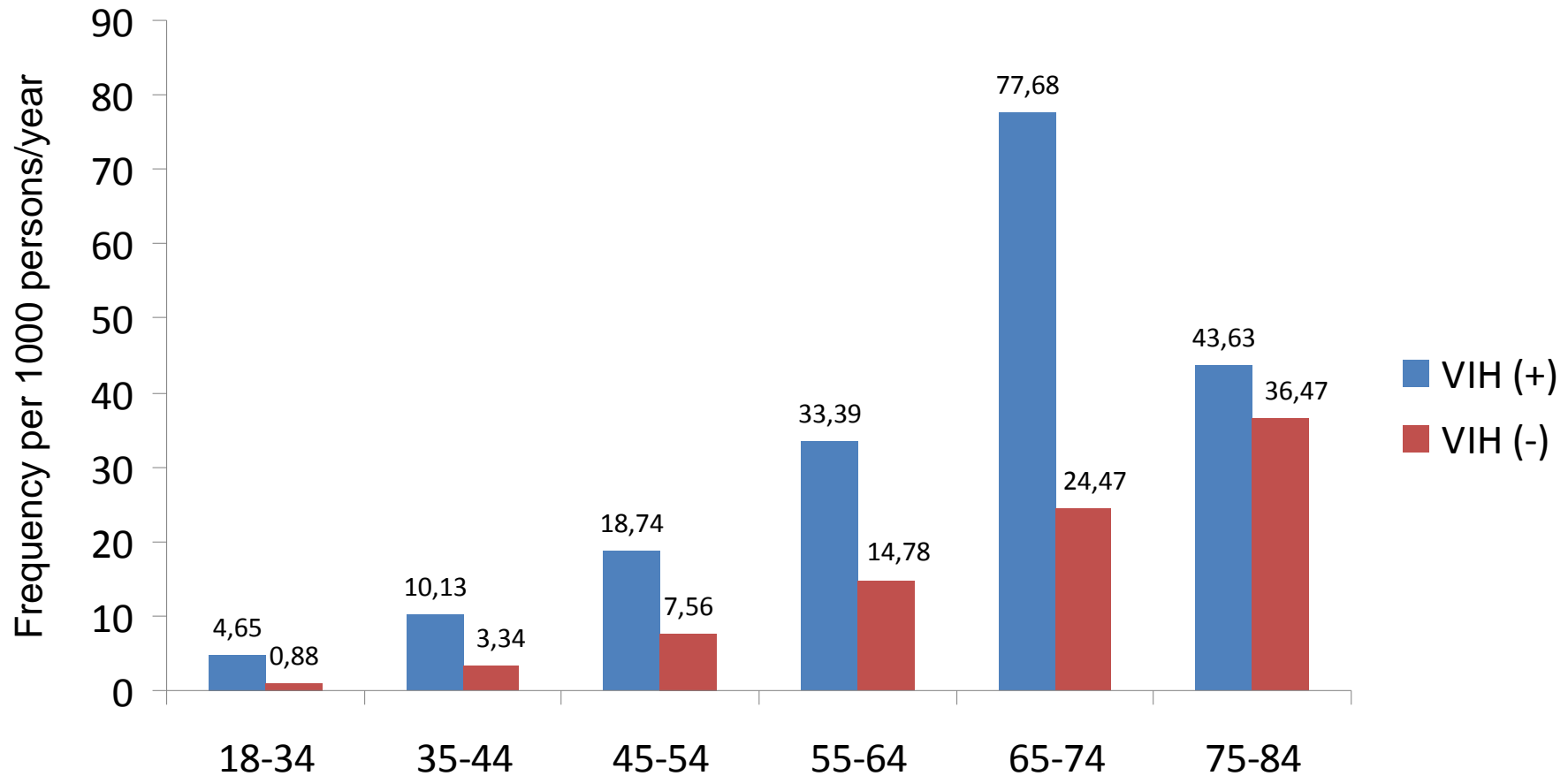
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# Myocardial infarction

Database Massachusetts Administration Hospital Database. 1996-2004

-HIV(n=3851)

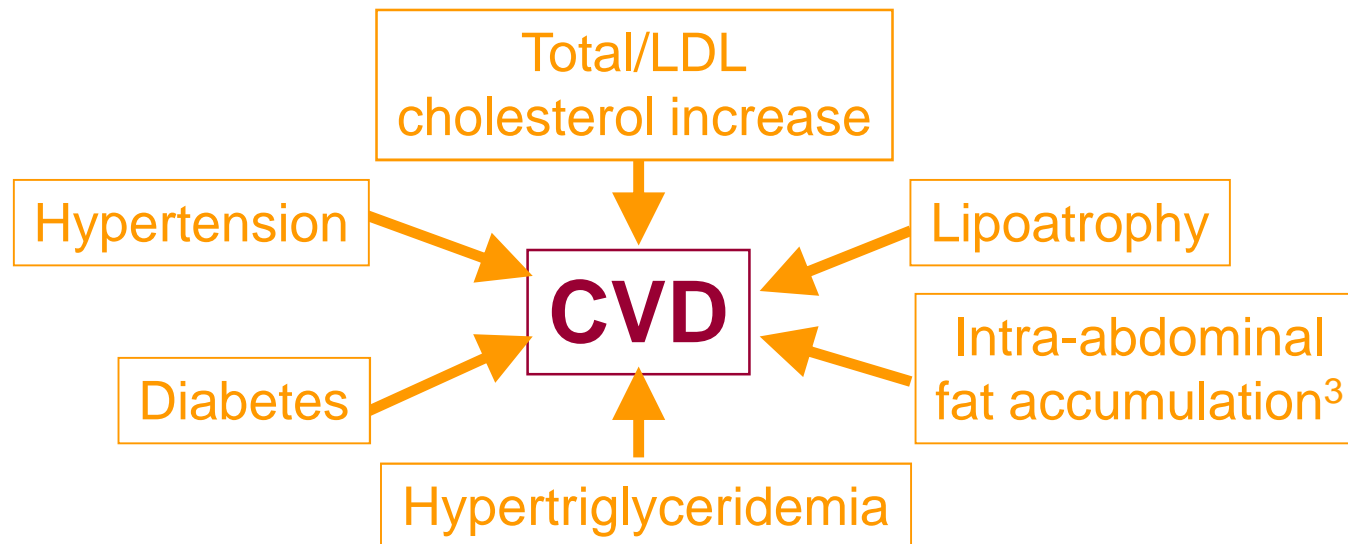
- No HIV (n=1.044.589)



# CVD and HIV infection



# CVD and HIV infection



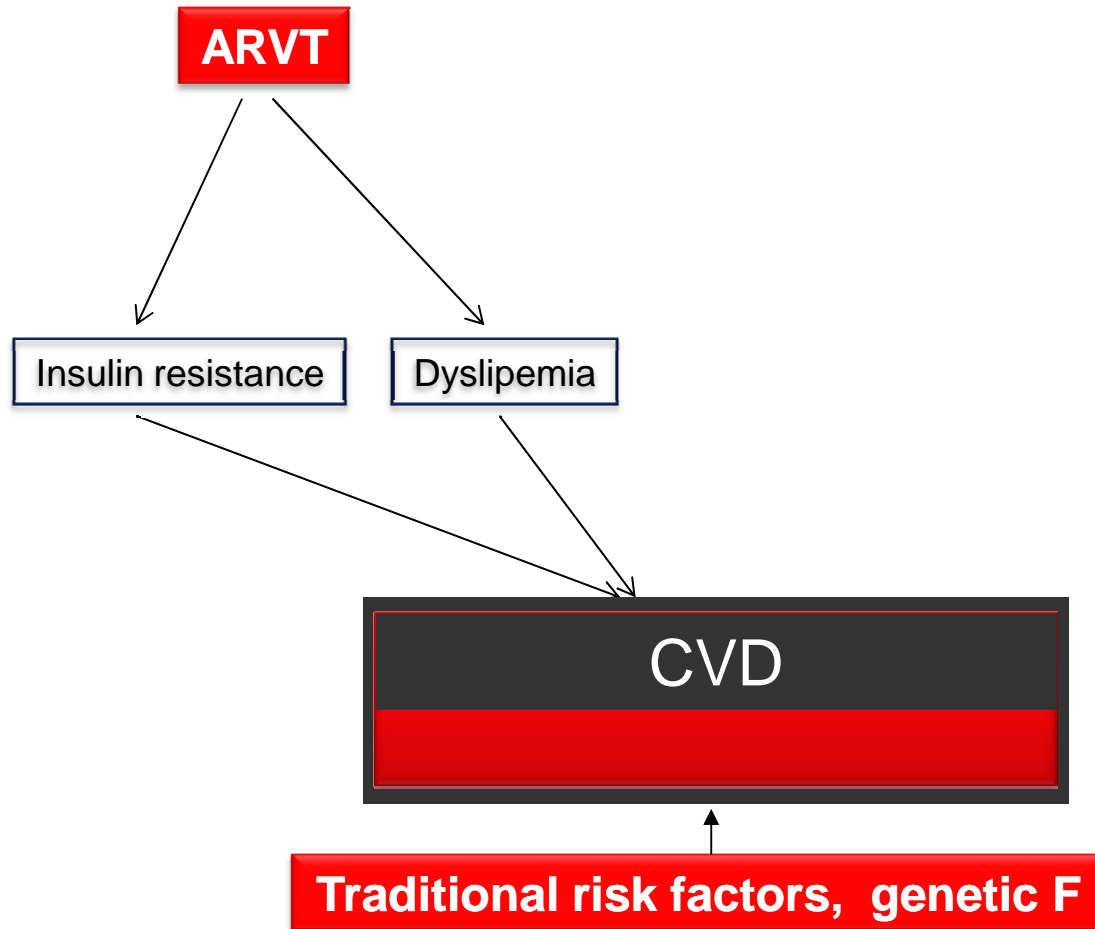
# Traditional Risk Factors in VIH

CV risk factors	Prevalence (%)	CV risk factors	Prevalence (%)
Age*	♂ ≥ 45a.: 37% ♀ ≥ 55a.: 25%	Dyslipidemia**	22-46
Gender	Men > women	Hypertriglyceridemia**	34
Smoke**	37-72	Erectil dysfunction **	61-74
High blood presure	8-28	Overweight	3,90
Diabetes mellitus**	17	Sedentary	-
Insulin resistance**	14-51	Microalbuminuria**	8,7
Metabolic syndrome	14-25	Hypogonadism	17-25

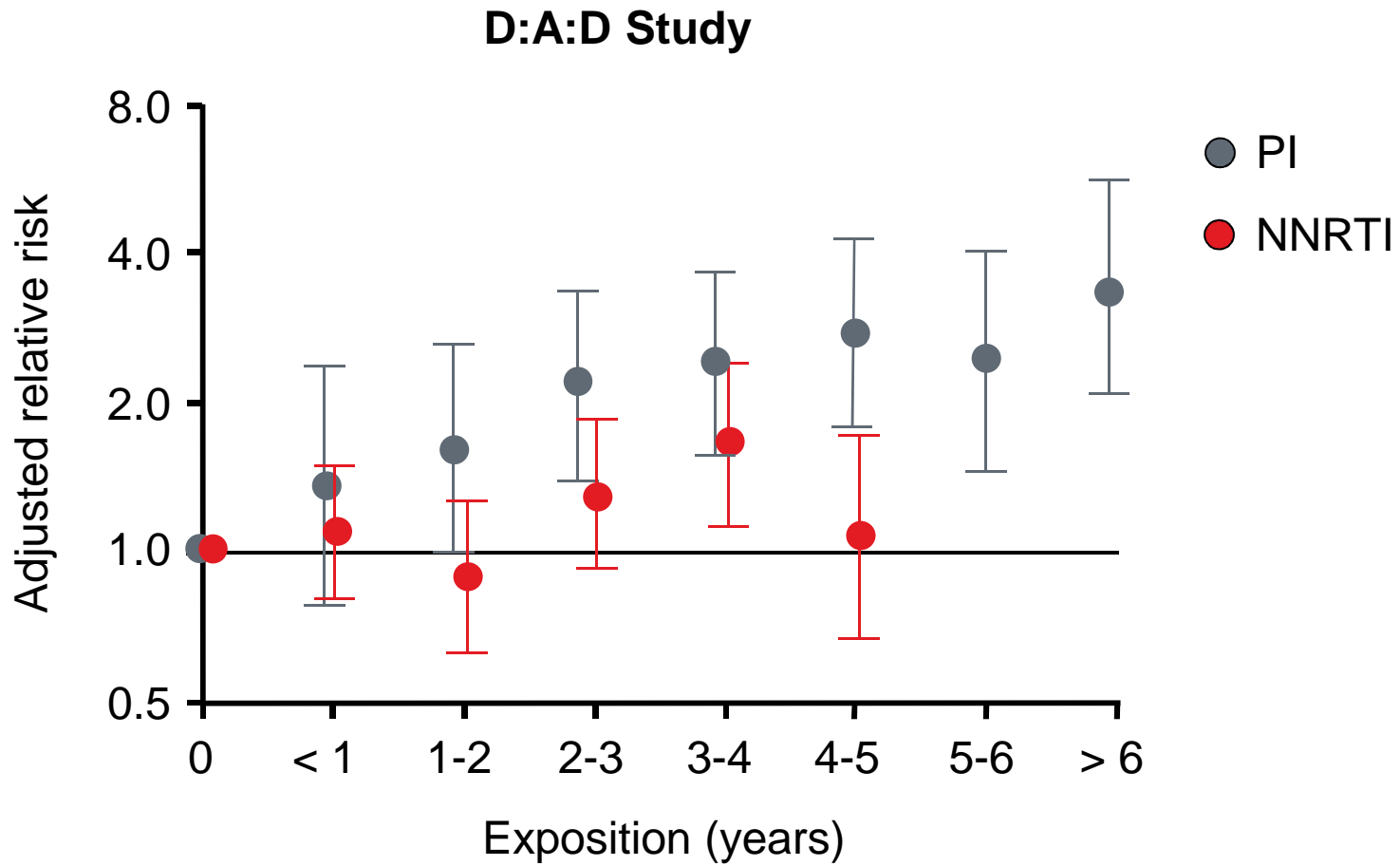
\*: D:A:D Cohoort 2006

\*\* : Higher prevalence in HIV than in general population

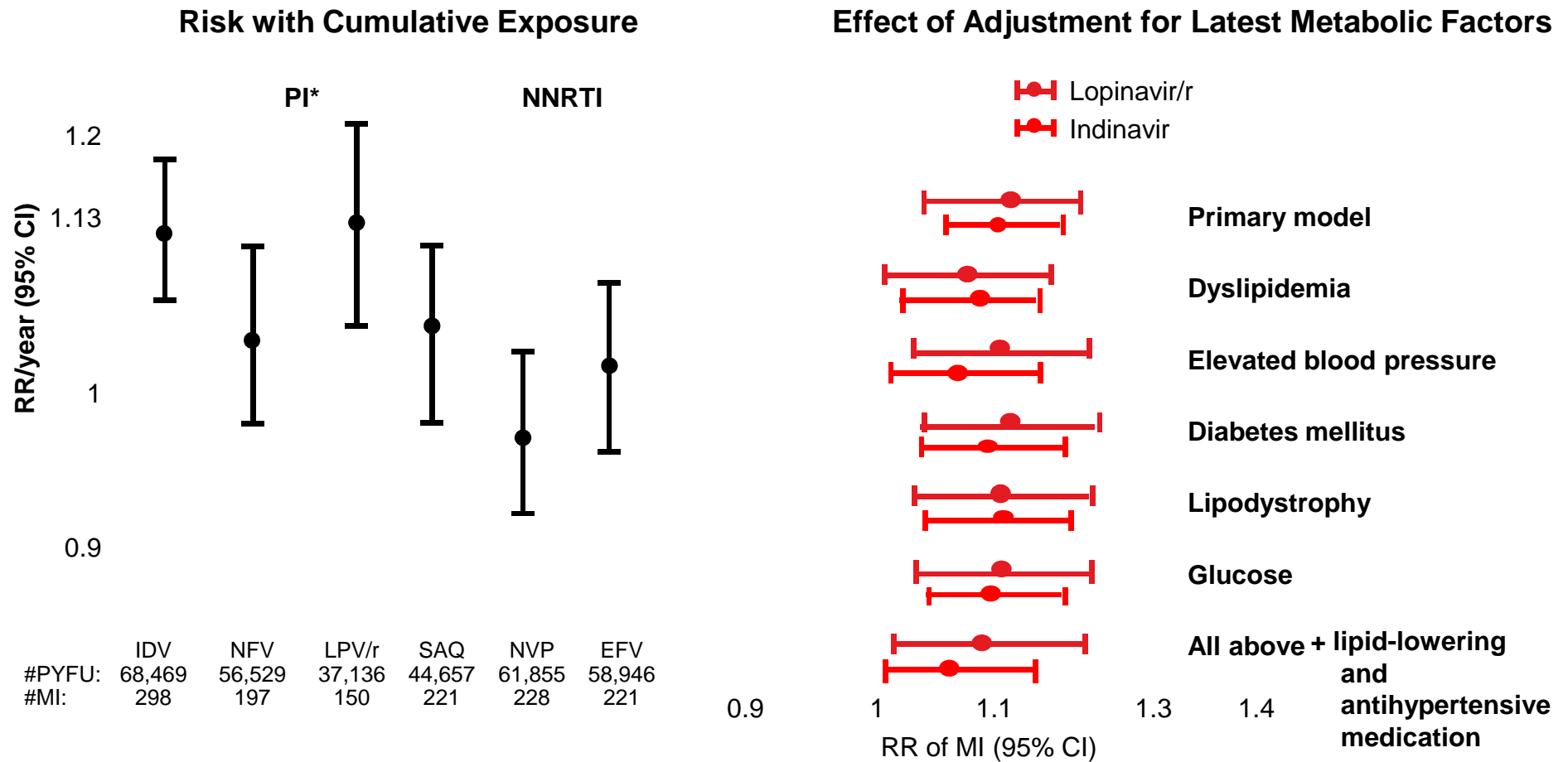
# RCV en pacientes VIH



# Myocardial infarction



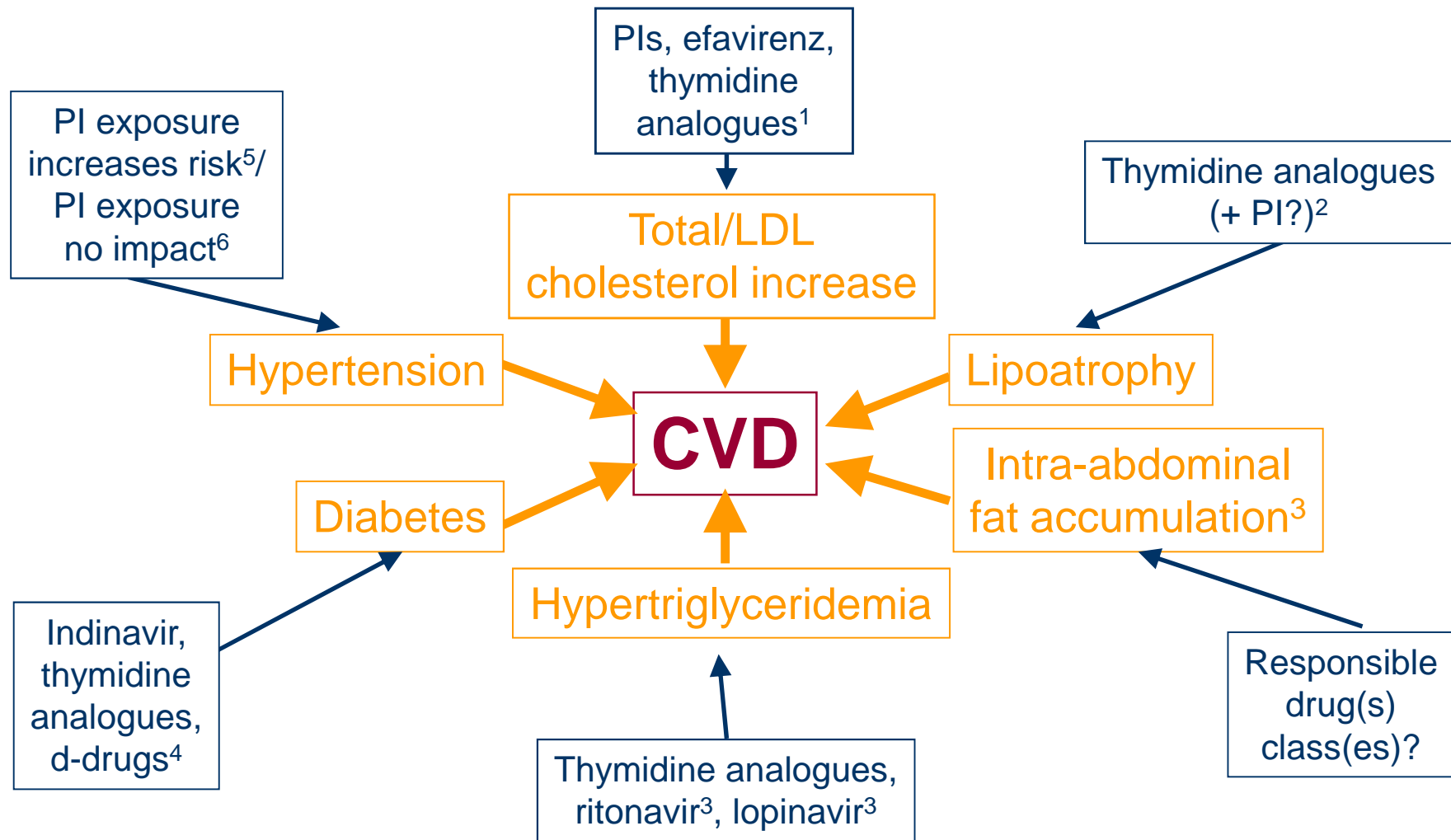
# D:A:D Study: PIs/NNRTIs and Risk of MI



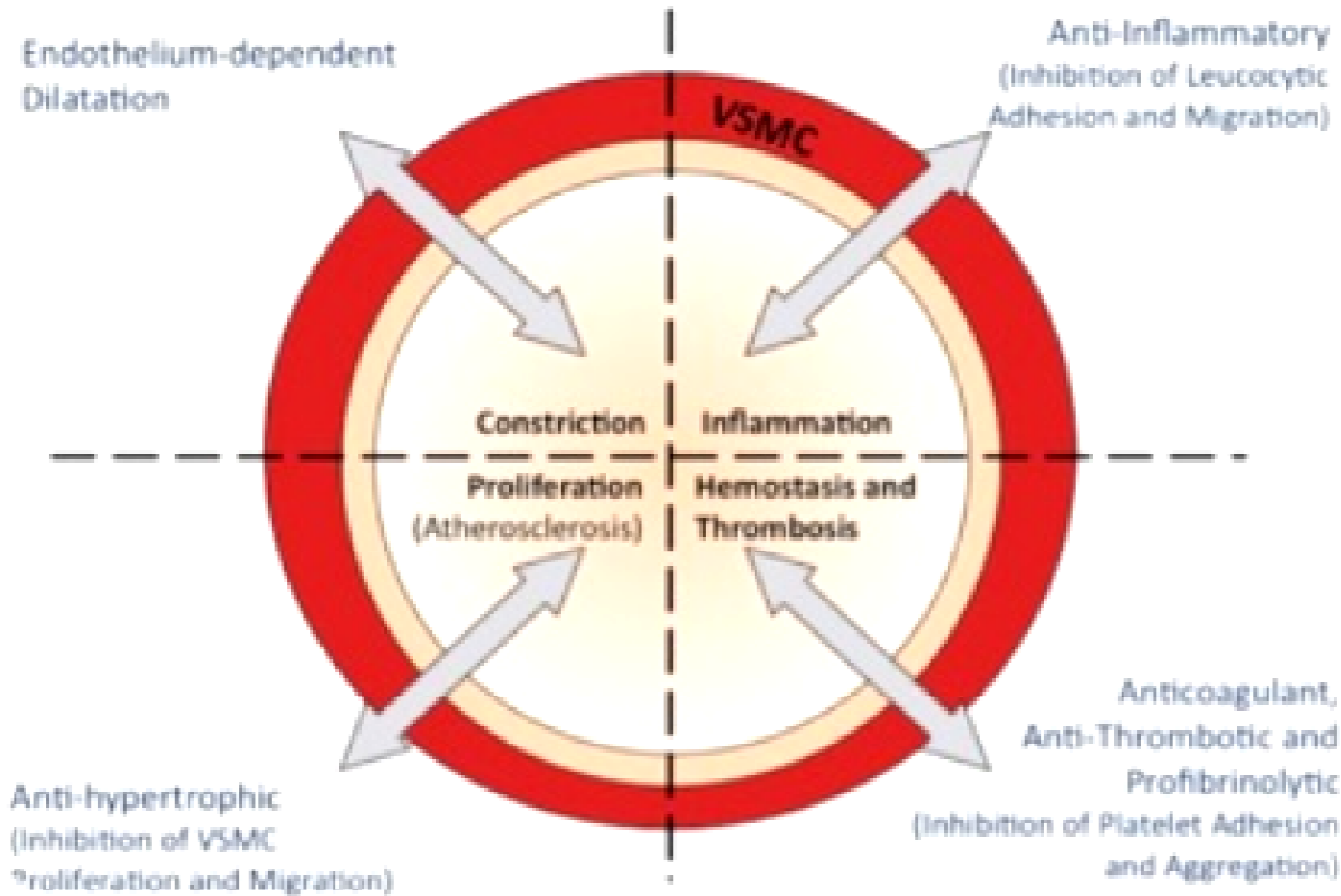
\* Approximate test for heterogeneity:  $P=0.02$

Lundgren JD, et al. 16th CROI; Montreal, Canada; February 8-11, 2009. Abst. 42LB.

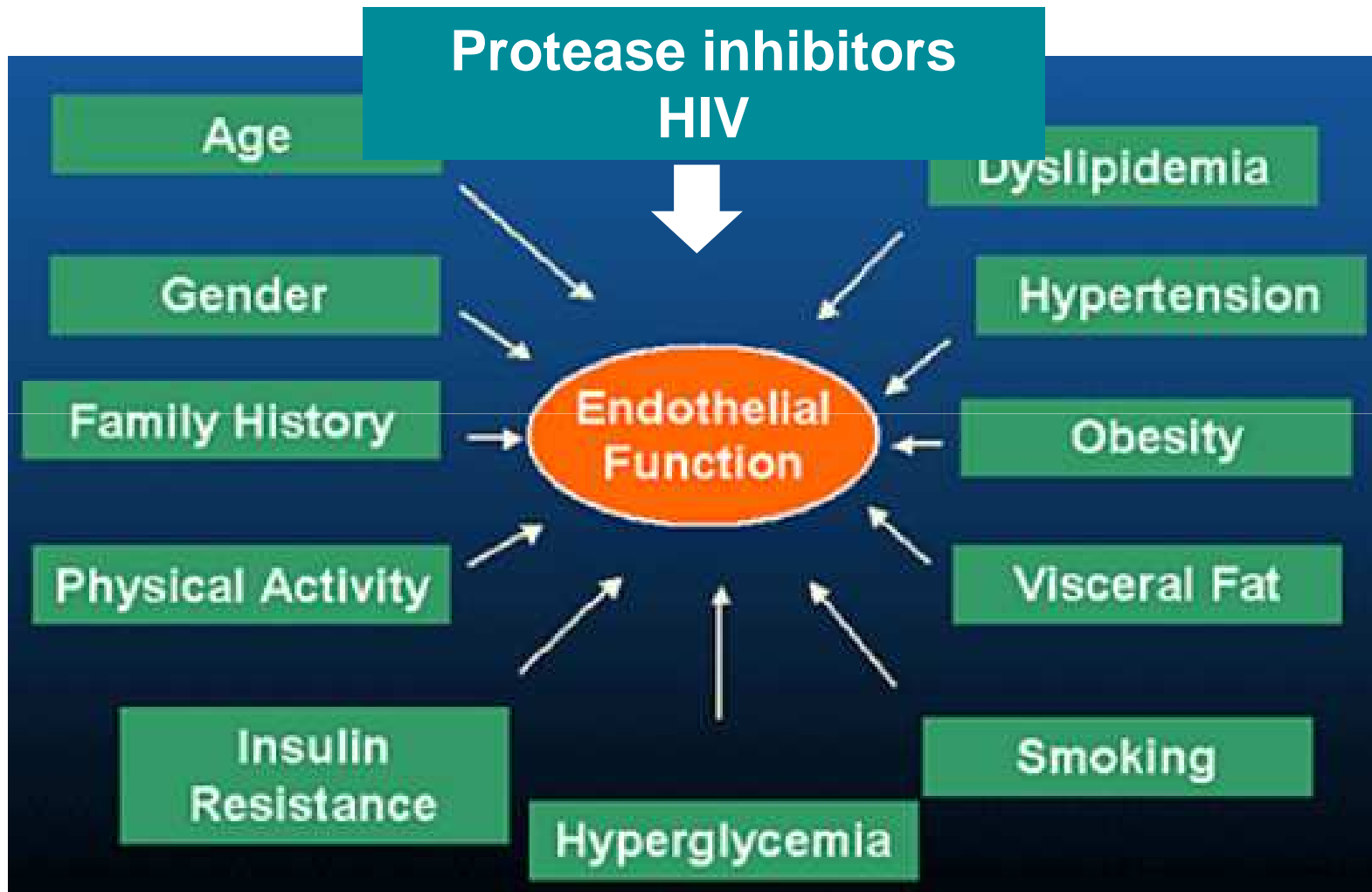
# CVD and HIV infection



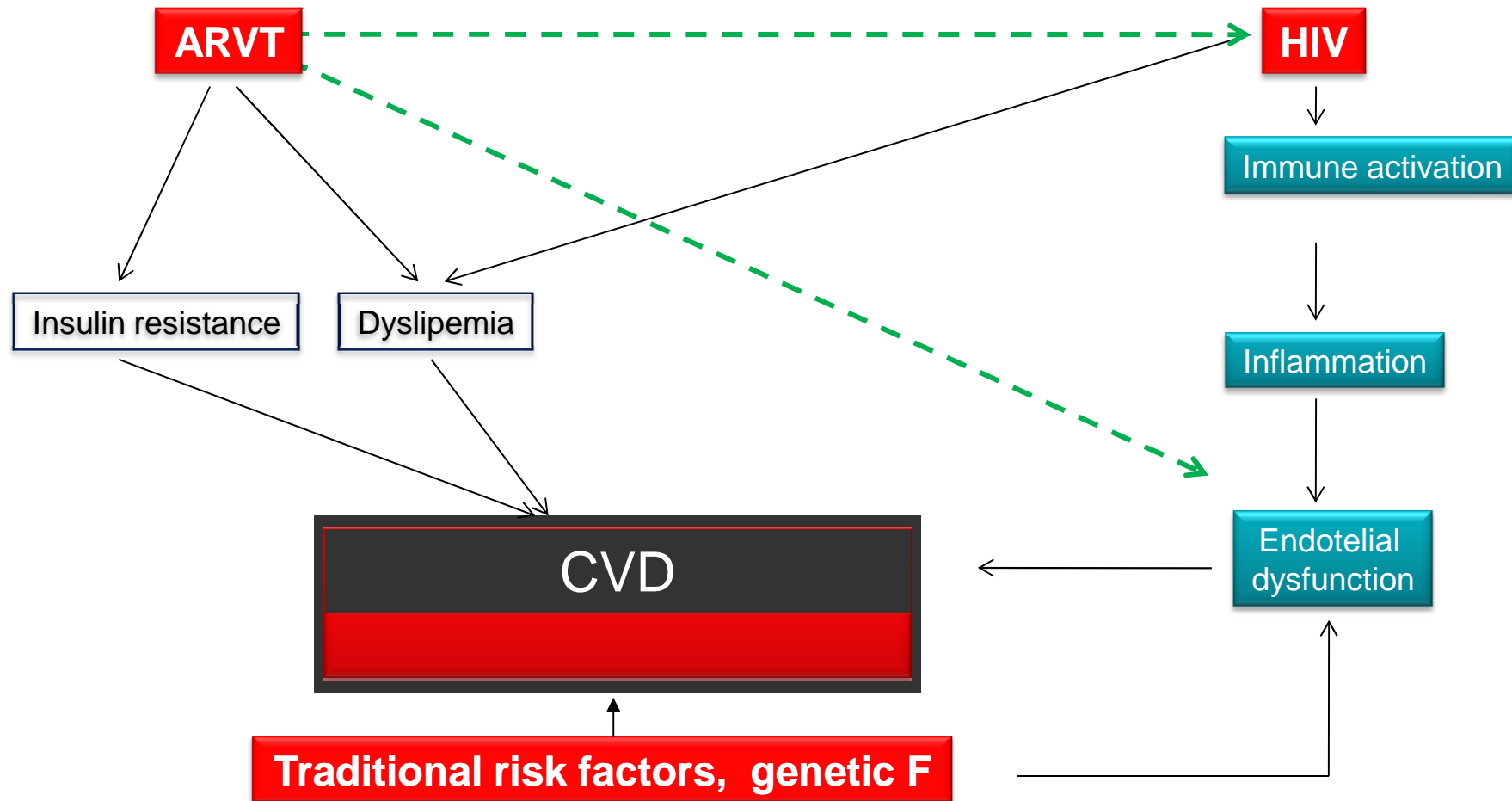
# Endothelial functions



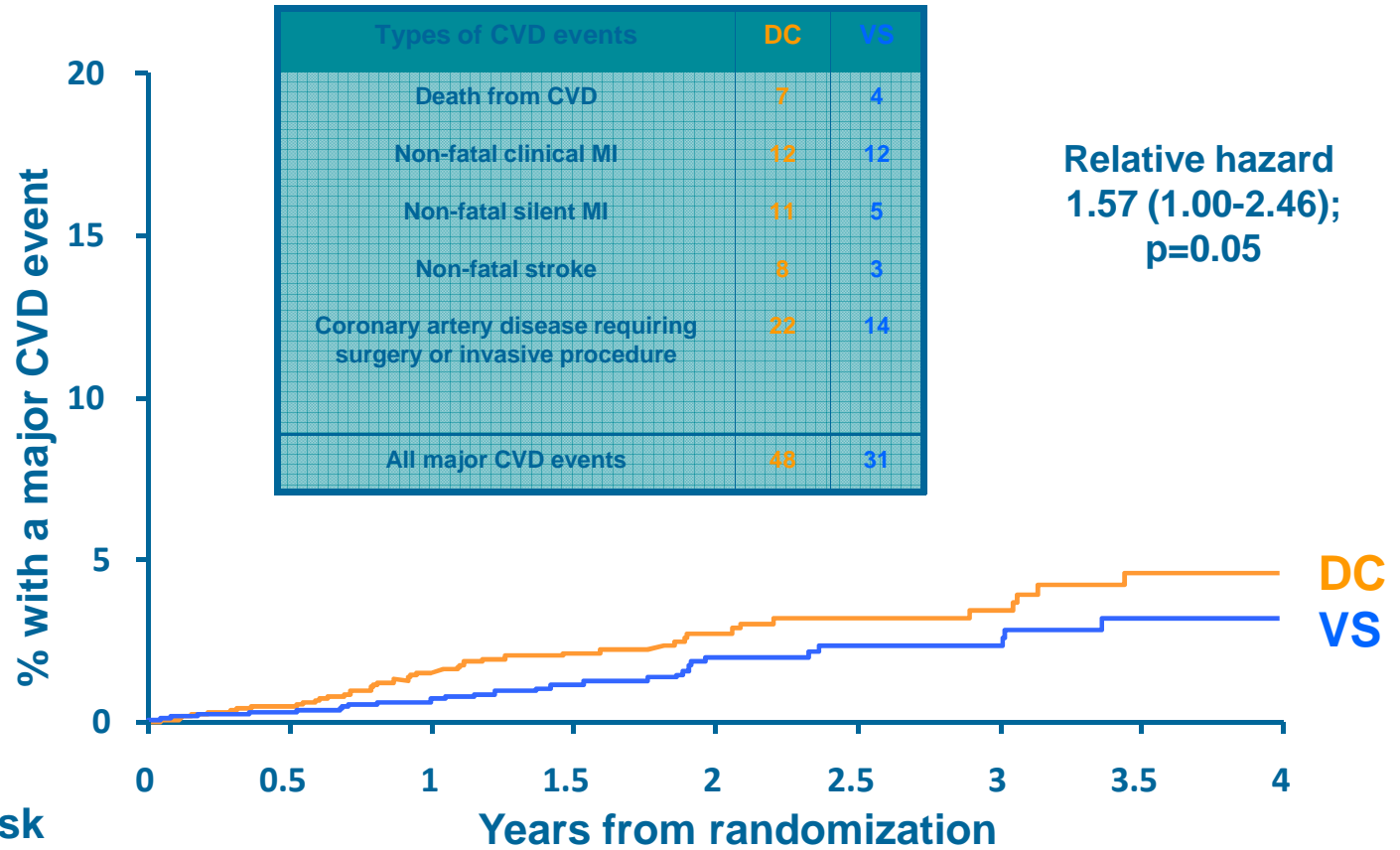
# Endothelial DYSFUNCTION



# RCV en pacientes VIH



# Discontinuar TAR incrementa el riesgo de Enf CV SMART Study



## Number at risk

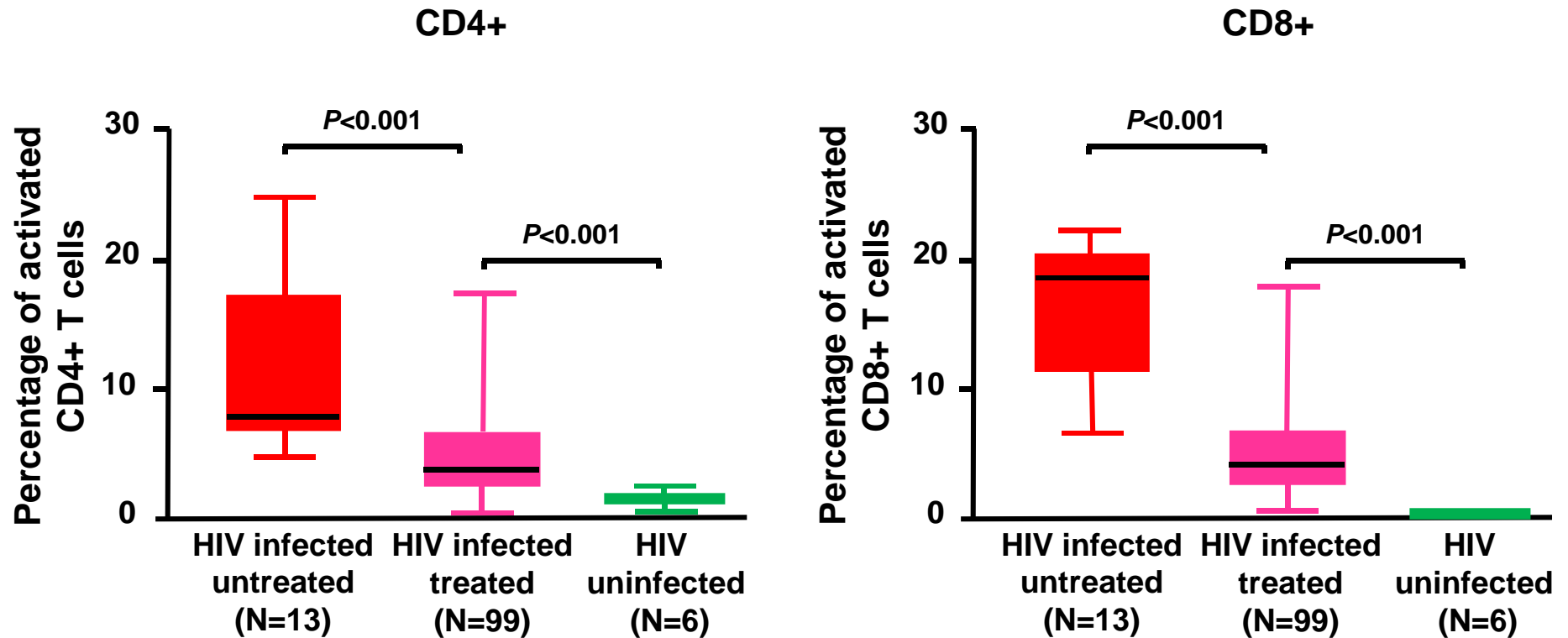
### Drug conservation

(DC) 2752 1306 713 379 10

### Viral suppression

(VS) 2720 1292 696 377 10

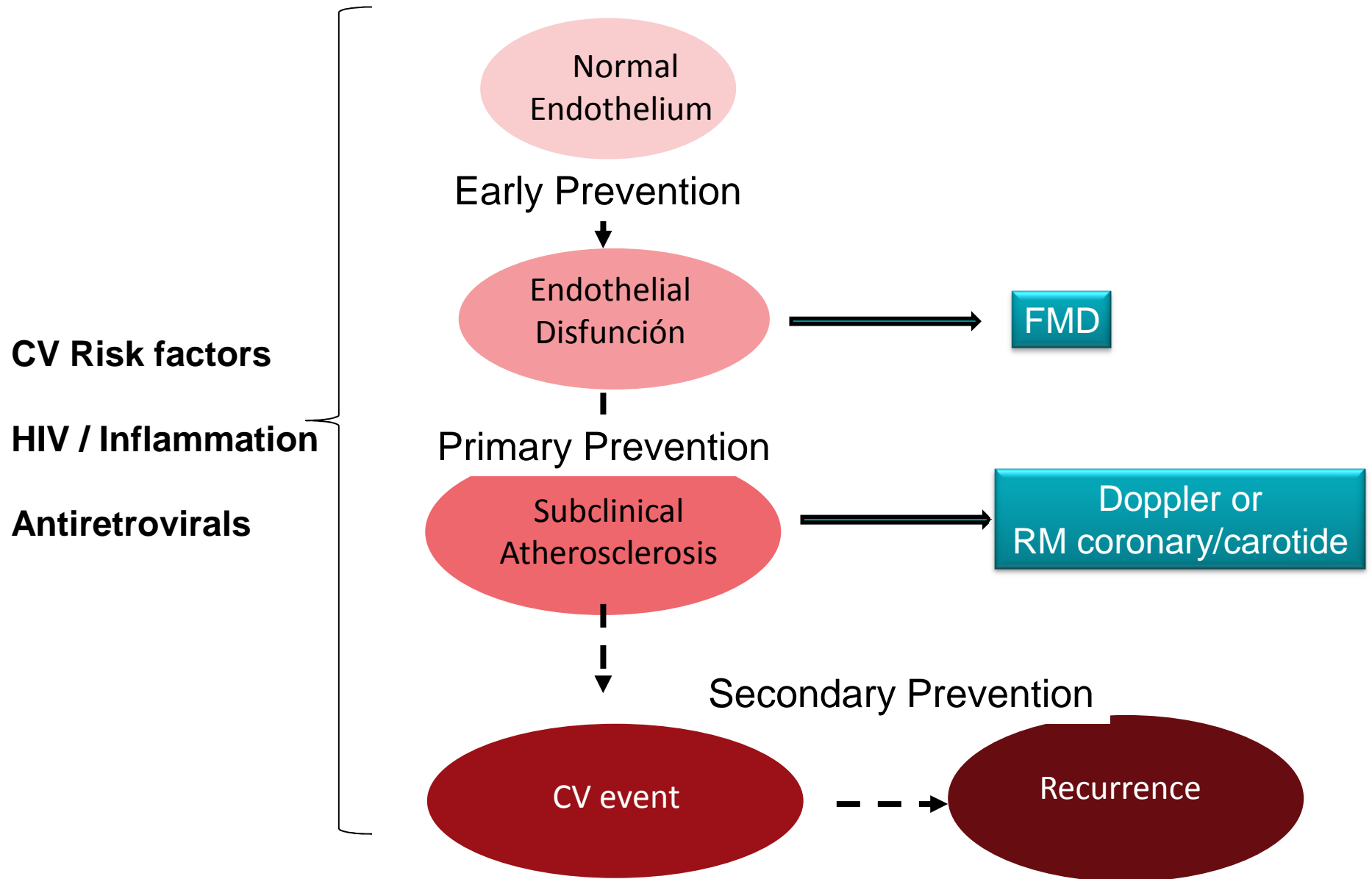
# ART decreases immune activation, but levels remain high vs HIV-negative subjects



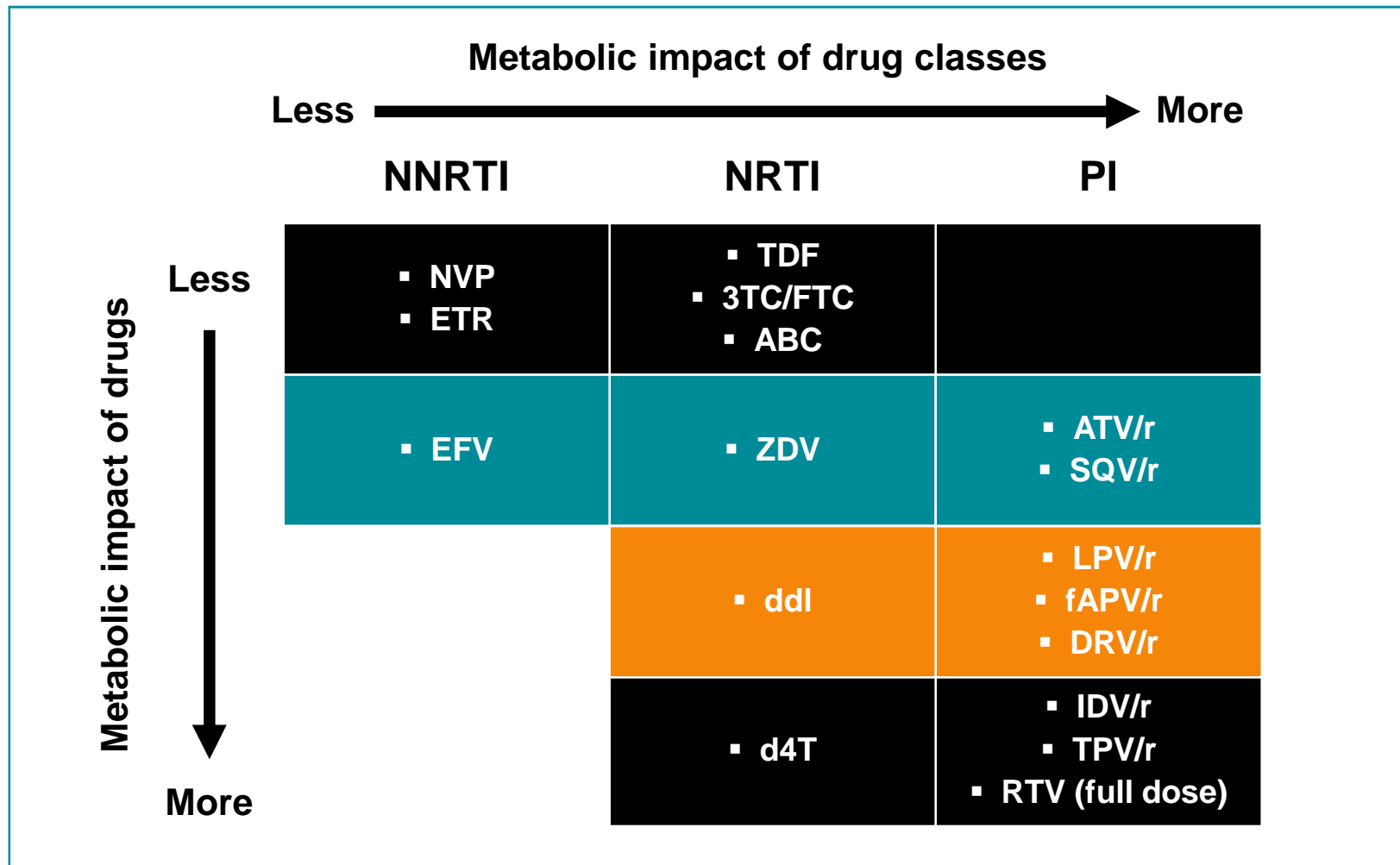
# Management

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# Management of CVD



# Metabolic impact of ARV drugs and classes



# Interacción farmacológica

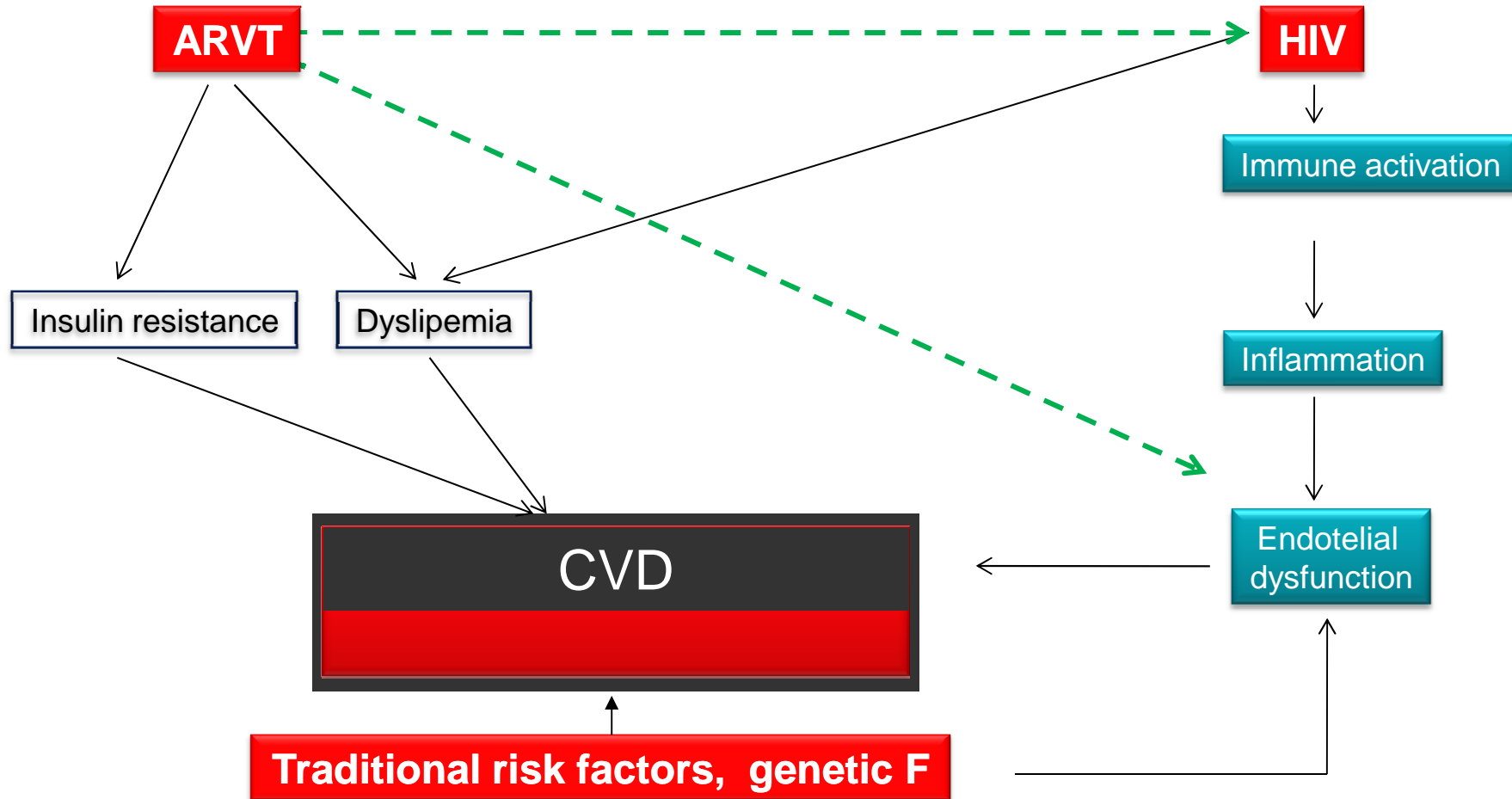
	Rosuvastatina	Atorvastatina	Pravastatina	Simvasatatina
ATV/r	↑conc. estatina*	↑conc. estatina*	NSC	Contraindicado
LPV/r	↑conc. estatina*	↑conc. estatina*	↑conc. estatina*	Contraindicado
DRV/r	↑conc. estatina*	↑conc. estatina*	NSC	Contraindicado
FPV/r	↑conc. estatina*	↑conc. estatina*	NSC	Contraindicado
EFV	NSC	↓ conc. estatina\$	↓ conc.estatina\$	↓conc estatina\$
NVP	NSC	NSC	NSC	NSC
ETR	NSC	NSC	NSC	NSC
MVC	NSC	NSC	NSC	NSC
RAL	NSC	NSC	NSC	NSC

NSC: no significación clínica (interacción)

\*Iniciar dosis bajas y subir según tolerancia. No utilizar dosis superiores a 40 mg atorvastatina

\$Requiere ajuste de dosis

# RCV en pacientes VIH



# Statins and mortality

## Johns Hopkins HIV Clinical Cohort

Subjects who achieved suppression within 180 days of starting HAART after January 1998. Assessment was continued until death in patients who maintained a virologic suppression, with right-censoring of their follow-up time if they had an HIV RNA >500 copies/ml.

Category	Subcategory	Total N = 1538	Statin Use N = 238	No Statin Use N = 1300
Age (median years)		43 (36–49)	46 (40–53)	42 (36–47)**
Sex	Male	1034 (67.2%)	172 (72.3%)	862 (66.3%)
	Female	504 (32.7%)	66 (27.7%)	438 (33.7%)
Race	Black	1112 (72.3%)	138 (58.0%)	974 (74.9%)**
	White	292 (22.5%)	92 (38.7%)	292 (22.5%)**
	Other	40 (2.7%)	8 (3.4%)	34 (2.6%)
HIV Risk Group <sup>1</sup>	IDU	551 (34.3%)	48 (20.2%)	503 (38.7%)**
	MSM	445 (28.9%)	91 (38.2%)	354 (27.2%)**
	Heterosexual Contact	791 (51.7%)	106 (44.5%)	685 (52.7%)*
CD4 (median cells/mm <sup>3</sup> )		225 (80–358)	270 (153–461)	200 (70–339)**
HIV-1 RNA (median copies/ml)		36,186 (1,633–145,950)	11,149 (88–126,816)	39,879 (3,252–163,006)**
Hemoglobin (median g/dL)		12.7 (11.3–14.1)	13.2 (12.0–14.6)	12.7 (11.3–14.0)**
Total cholesterol (median mg/dL)		166 (141–194)	196 (168–238)	160 (134–188)**
Antihypertensive Use		407 (29.3%)	114 (46.3%)	293 (25.6%)**
Prior ART		933 (60.7%)	176 (73.9%)	757 (58.2%)**
Prior ADI		720 (46.8%)	132 (55.4%)	588 (45.2%)**
Viral hepatitis C co-infection		537 (34.9%)	61 (25.6%)	476 (36.6%)**
Year HAART started	< 2004	875 (56.9%)	159 (66.8%)	716 (55.1%)**
	≥2004	663 (43.1%)	79 (33.2%)	584 (44.9%)

# Statins and mortality

**Table 2.** Multivariate Cox Proportional Hazards Regression of statin use and other characteristics with survival.

Category	Subcategory	Relative Hazard (95% CI)	P-Value
Statin Use		0.33 (0.14,0.76)	0.009
Age (median years)		1.07 (1.05,1.10)	<0.0001
Race	Black	0.82 (0.47, 1.46)	0.51
	Others	1.0 (reference)	
HIV Risk Group	IDU	2.30 (1.30, 4.07)	0.004
	Heterosexual	1.50 (0.96, 2.35)	0.08
	MSM	1.0 (reference)	
CD4+ at HAART start (per 100 cell/mm <sup>3</sup> higher increments)		0.96 (0.84, 1.09)	0.52
HIV-1 RNA at HAART start (per log <sub>10</sub> higher increments)		0.96 (0.79, 1.18)	0.16
Hemoglobin at HAART start (per g/dL higher increments)		0.80 (0.71, 0.90)	0.0003
Total Cholesterol at HAART start (per 10 mg/dL higher increments)		0.98 (0.93, 1.03)	0.36
Year HAART started	<= 2004	1.20 (0.74, 2.06)	0.50
	> 2004	1.0 (reference)	
HAART Drug	NNRTI	1.23 (0.59, 1.52)	0.42
	Others	1.0 (reference)	
Prior ART		1.37 (0.82, 2.31)	0.23
Prior ADI		2.24 (1.39, 3.60)	0.001
Viral Hepatitis C Co-infection		1.07 (0.62, 1.84)	0.81

# Statins and mortality

**Table 3.** Causes of death.

Cause	Statin Use (#)	No Statin Use (#)
Malignancy	2	14
Infection (non-ADI)	2	12
Metabolic Complications of diabetes		1
Neuromuscular Disease Complications		2
End Stage or Acute Liver Failure		11
End Stage or Acute Renal Failure		6
Cardiovascular	2	10
Pulmonary Embolus		2
Trauma		3
Substance Overdose		3
Unknown*	1	14

\*Date of death confirmed: 6 were found dead at home but the cause was unknown; 9 others were confirmed dead but no further documentation could be obtained.

Statin use was associated with significantly lower hazard of dying in these HIV-infected patients who were being effectively treated with HAART.

# Therapeutic Interventions in Development

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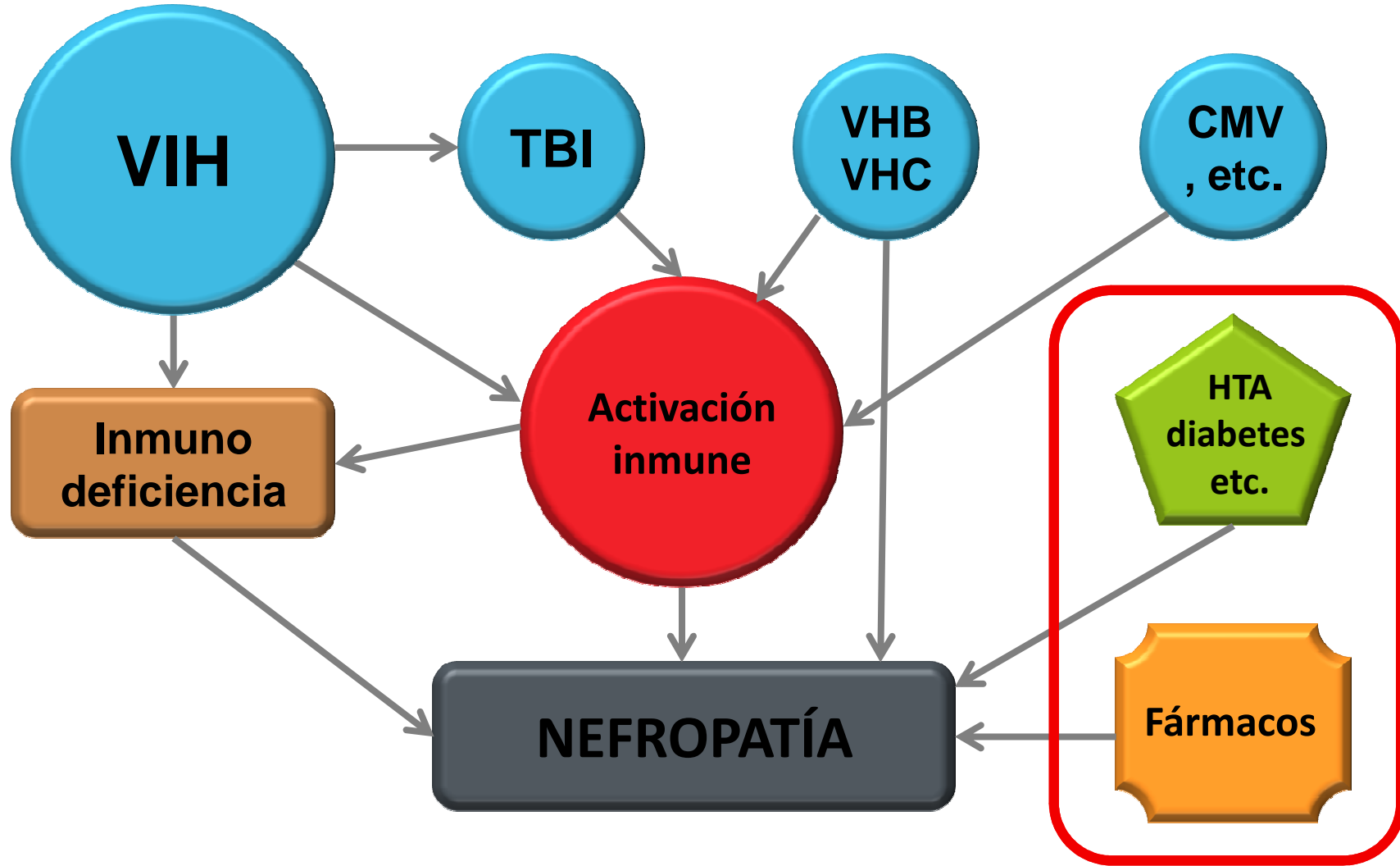
- Chemokine receptor inhibitors:
  - maraviroc, TB-652
- Anti-infective therapy:
  - CMV, EBV, HSV, HCV/HBV
- Microbial translocation:
  - sevelamer, colostrum, rifaximin
- Enhance T-cell renewal:
  - growth hormone, IL-7
- Antifibrotic drugs:
  - pirfenidone, ACEi, ARBs, KGF
- Anti-aging:
  - caloric restriction, sirtuin activators, vit. D, omega-3 fatty acids, rapamycin, diet, exercise (not recommended by me)
- Anti-inflammatory drugs:
  - chloroquine, hydroxychloroquine
  - minocycline
  - NSAIDs (COX-2i, aspirin)
  - statins
  - methotrexate
  - anakinra (IL-1Ra)
  - thalidomide, lenalidomide, pentoxifylline (weak TNF inhibitors)
  - biologics (TNFi, IL-6i, anti-IFNa, anti-PD1, anti-PDL1, JAKi, IDOi, Casp-1i)
- Anticoagulants:
  - warfarin, dabigatran, aspirin, clopidogrel

Combination therapy may be necessary.

# **Renal Damage and HIV Infection**

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# Etiología de las alteraciones renales en pacientes VIH+

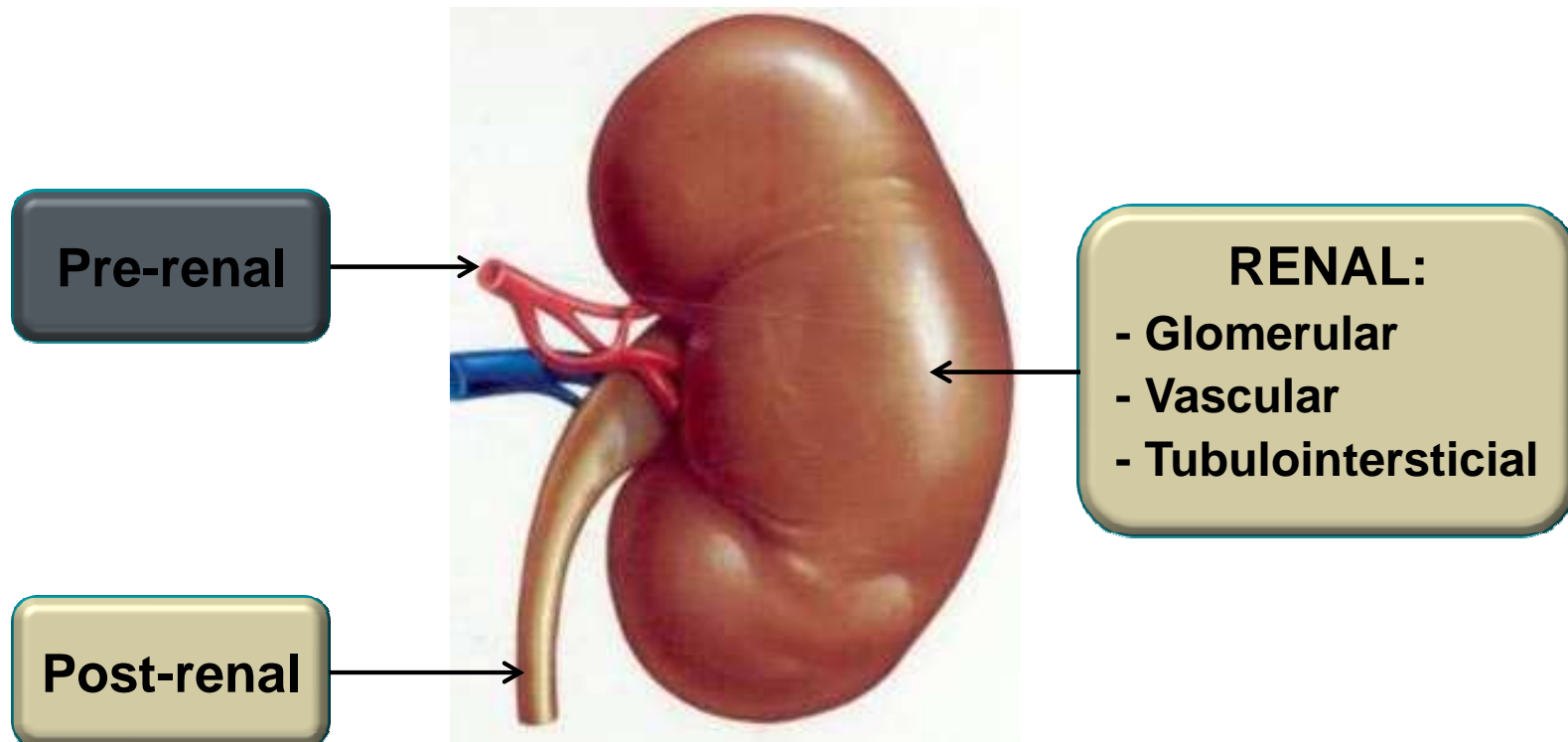


TBI: Translocación bacteriana intestinal

Modificada de Hsu C, et al. *AIDS Res Ther* 2013; 10:29.

# Espectro de la afectación renal en los pacientes VIH+

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# Espectro de la afectación renal en los pacientes VIH+ (1)

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- **Glomerular:**

- HIVAN (*HIV associated nephropaty*).
- HIVICK (*HIV immune complex kidney disease*).
  - Glomerulonefritis membranoproliferativa (VHC, crioglobulinemia).
  - Nefropatía IgA (VIH)
  - Glomerulonefritis segmentaria y focal no-colapsante (VIH)
  - Glomerulonefritis membranosa (VHB, VHC, VIH, sífilis)
  - Glomerulonefritis “lupus-like”
  - Glomerulonefritis agudas post-infecciosas
- Nefropatía de cambios mínimos
- Glomerulopatía diabética
- Nefropatía amiloidótica
- Glomerulonefritis fibrilar

## Glomerulopatías en VIH+: características

	NAVIH	GNMP	IgA	GSF	GNM	GNA	<i>Lupus-Like</i>
Síndrome nefrótico	++++	+++	-	+++	++++	+	++++
Hematuria macroscópica	-	++	++++	-	-	+++	++
Alteraciones urinarias persistentes (microhematuria/proteinuria no nefrótica)	+	++	++	+	+	-	+
Fracaso renal agudo	+	+	++	+	+	+++	+
Hipertensión arterial/hipertensión arterial maligna	+	+	+++	+	+	+	+
Hipocomplementemia	-	+++	-	-	-	+++	+
Crioglobulinas (+)	-	+++	-	-	-	+	+
Coinfección por VHC/VHB	-	++++	+	+	++	-	++

Panel de expertos de GESIDA/SEN/SEQC. Documento de consenso sobre evaluación y manejo de la afectación renal en los pacientes con infección por VIH (2014).

# Glomerulopatías en VIH+: Características

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- **Proteinuria, muy a menudo de rango nefrótico (>3 g/L).**
- **Hematuria.**
- **Reducción del filtrado glomerular.**
- **Importantes diferencias de evolución y tratamiento entre ellas:**

## HIVAN:

- Casi exclusiva en negros
- CV siempre detectable (> alta)
- Cifra baja CD4+ (<200/ $\mu$ L) o sida
- Muy rápida evolución
- Mayor incidencia ERCT (30%)
- Respuesta favorable al TAR
- Ttº: TAR, IECA y ARA

## HIVICK:

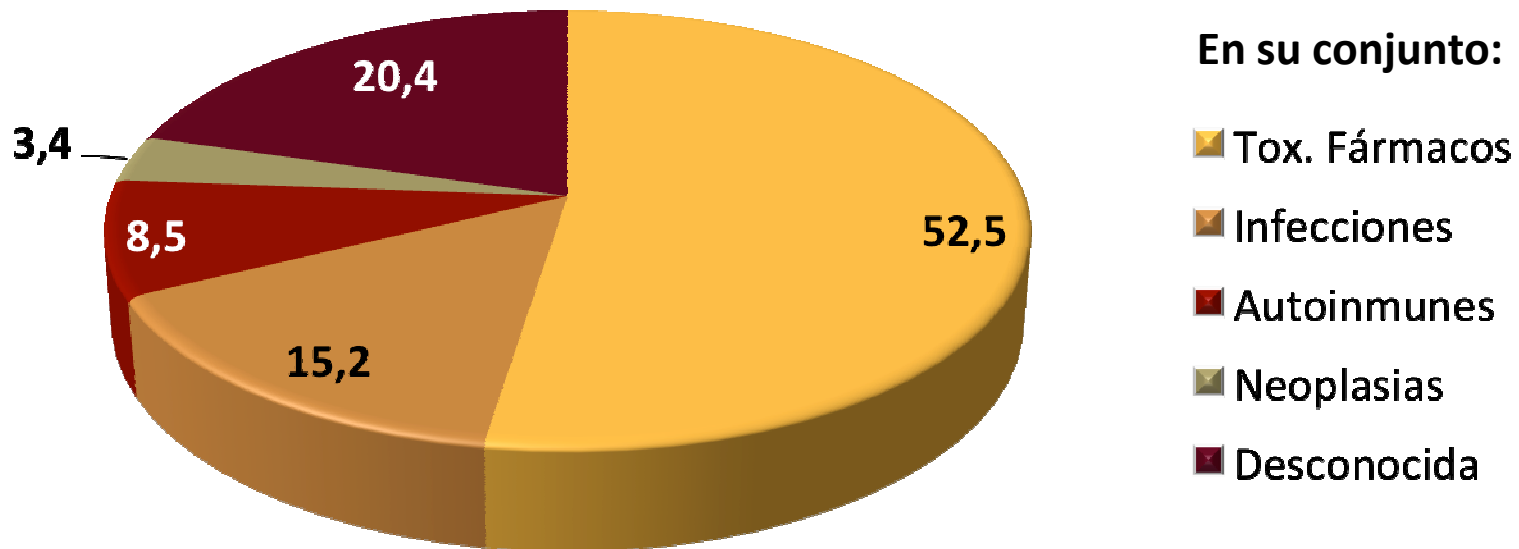
- Todas las razas (más la negra)
- Sin relación directa con CV
- Sin relación directa con CD4+
- Evolución menos agresiva
- Menor incidencia ERCT (8%)
- No hay relación entre el TAR y la incidencia de ERCT

1. Fine DM. *AIDS Pat Care & STDs* 2007; 21:813-24. 2. Estrella M, et al. *Clin Infect Dis* 2006; 43:377-380. 3. Atta MG, et al. *Nephrol Dial Transplant* 2006; 21:2809-2813. 4. Bigé N, et al. *Nephrol Dial Transplant* 2012; 27:1114-1121. 5. Foy MC, et al. *Clin J Am Soc Nephrol* 2013; 8:1524-1532.

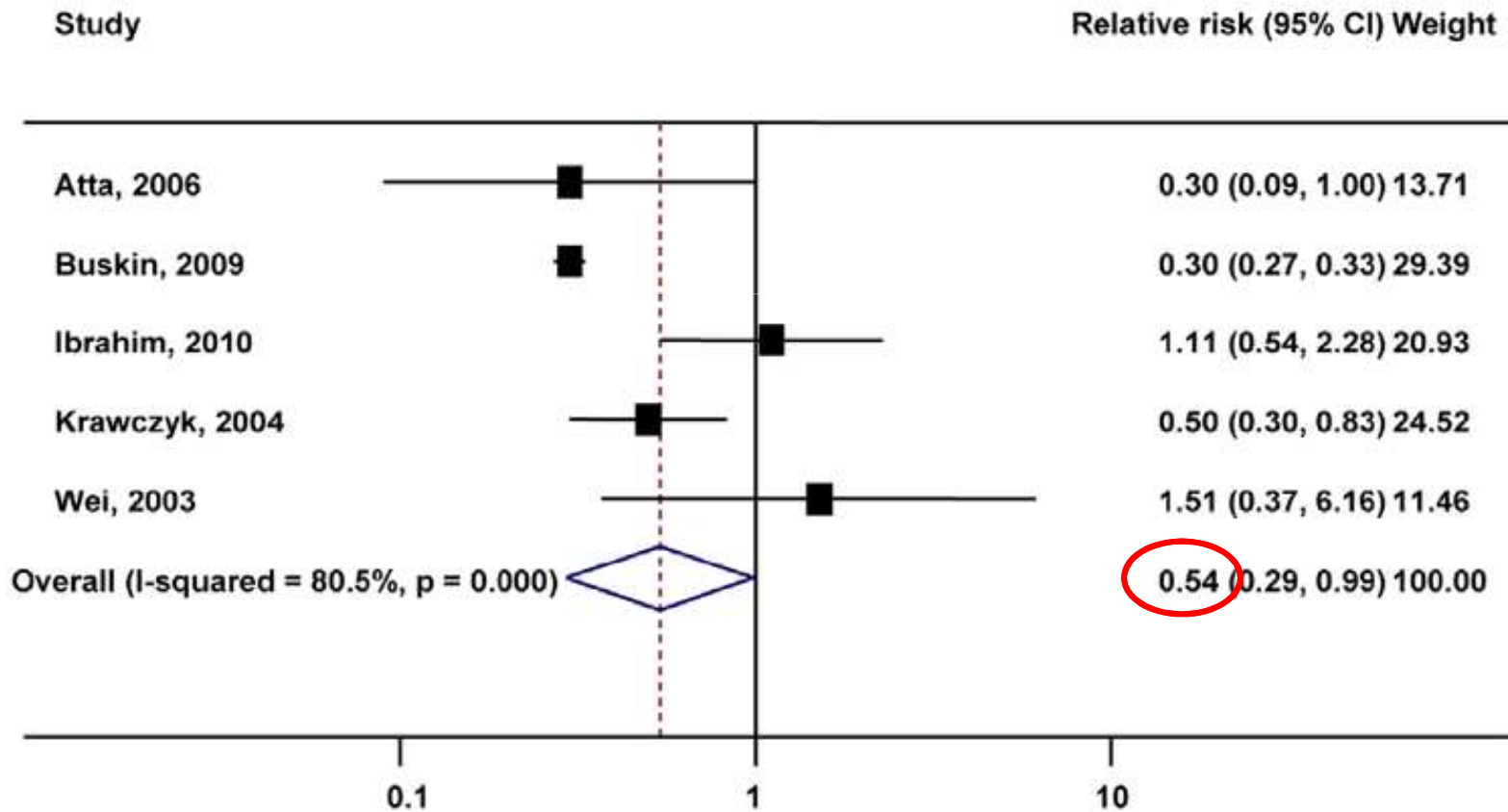
# Nefropatías tubulointersticiales en pacientes VIH+

En 59 (26,6%) de 222 biopsias renales efectuadas entre 1995 y 2011

- **Nefritis intersticial: 51%**
- **Tubulopatías: 49%**

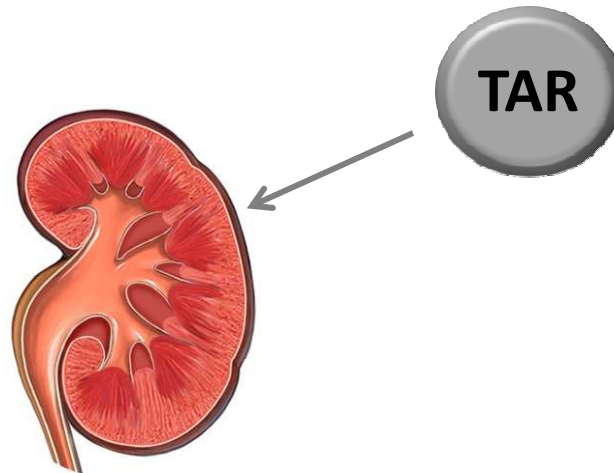


# Riesgo de FRA o ERC en pacientes con TAR vs. sin TAR Meta-análisis



# Impacto del TAR sobre la ERC

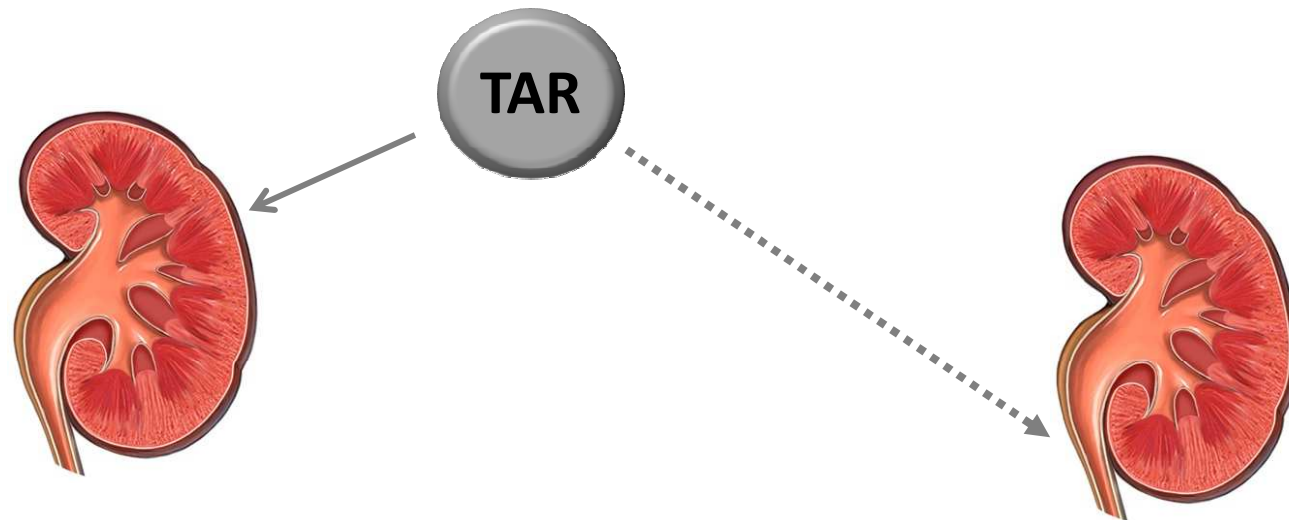
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## Estudios transversales retrospectivos

- Reducción de la incidencia de HIVAN
- Reversión o mejoría de HIVAN
- Reducción de la mortalidad por ERC
- Acción sobre otras nefropatías por VIH

# Impacto del TAR sobre la ERC



## Estudios transversales retrospectivos

- Reducción de la incidencia de HIVAN
- Reversión o mejoría de HIVAN
- Reducción de la mortalidad por ERC
- Acción sobre otras nefropatías por VIH

## Nefrotoxicidad

### ↑ Incidencia de ERC:

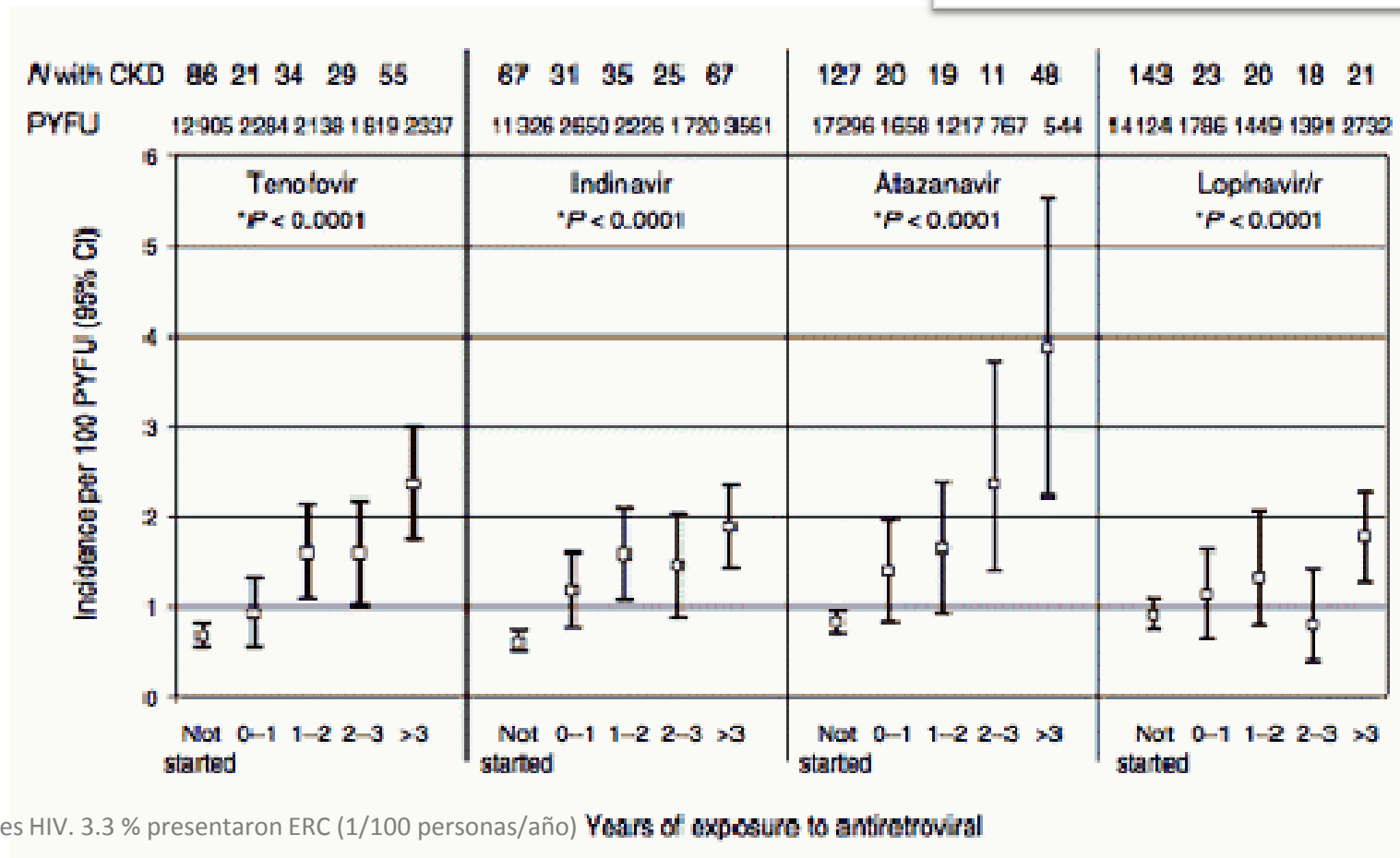
- ↑ Edad y supervivencia
- ↑ HTA
- ↑ Diabetes mellitus
- ↑ Nefrotoxicidad

# Incidencia de enfermedad renal crónica y ARV

## Cohorte EuroSIDA

Estimated glomerular filtration rate, chronic kidney disease and antiretroviral drug use in HIV-positive patients

Amanda Mocroft<sup>a</sup>, Ole Kirk<sup>b</sup>, Peter Reiss<sup>c</sup>, Stephane De Wit<sup>d</sup>, Dalibor Sedlacek<sup>e</sup>, Marek Beniowski<sup>f</sup>, Jose Gatell<sup>g</sup>, Andrew N. Phillips<sup>a</sup>, Bruno Ledergerber<sup>h</sup>, Jens D. Lundgren<sup>b,i</sup>, for the EuroSIDA Study Group



# Cohorte de veteranos

## Association of tenofovir exposure with kidney disease risk in HIV infection

Rebecca Scherzer<sup>a</sup>, Michelle Estrella<sup>b</sup>, Yongmei Li<sup>a</sup>, Andy I. Choi<sup>a</sup>, Steven G. Deeks<sup>c</sup>, Carl Grunfeld<sup>a</sup> and Michael G. Shlipak<sup>a</sup>

**Table 4.** Association of cumulative antiretroviral exposure (per year) with risk<sup>a</sup> of kidney disease outcomes, ordered by prevalence of use.

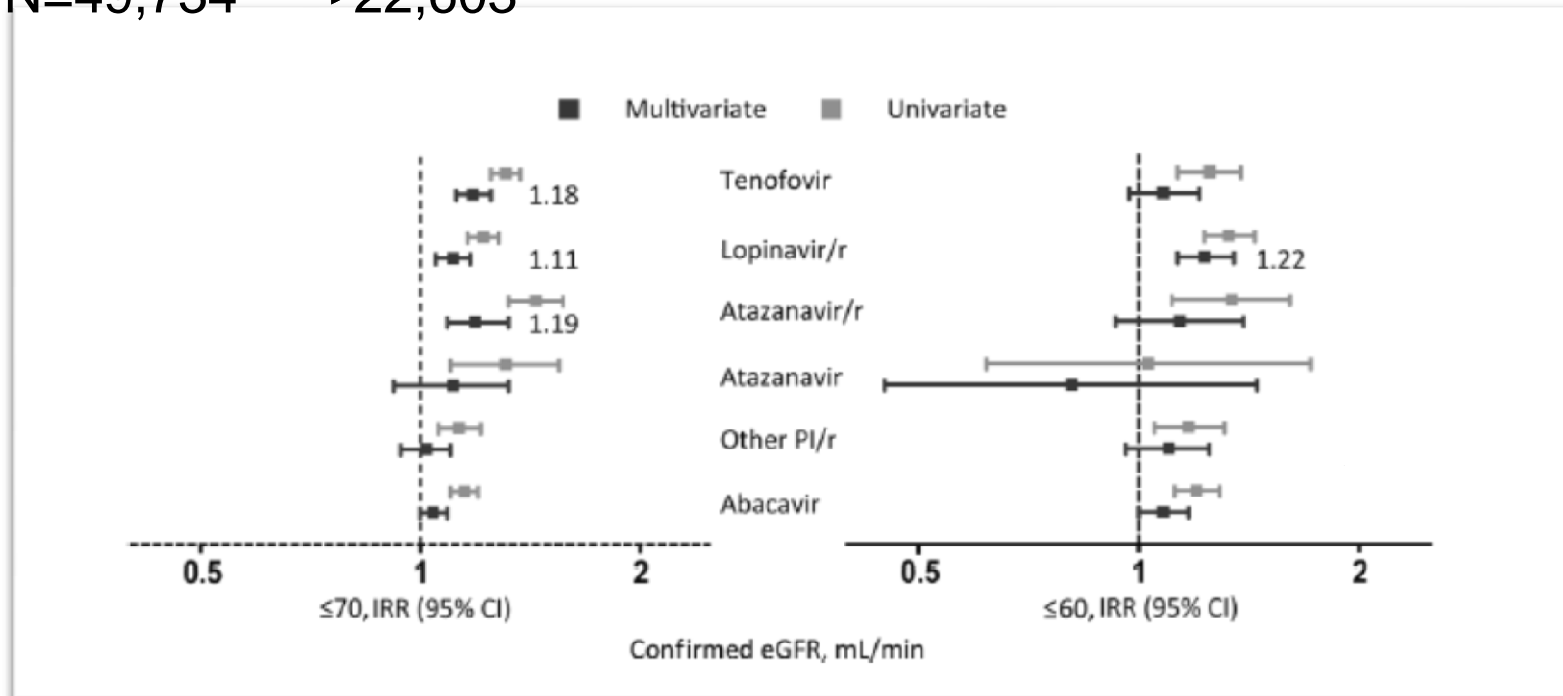
Antiretroviral	% of participants with any exposure at end of study	Proteinuria		Rapid Decline <sup>c</sup>		Chronic Kidney Disease	
		Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
Tenofovir	39.7	1.34 (1.25, 1.45)	<0.0001	1.11 (1.03, 1.18)	0.0033	1.33 (1.18, 1.51)	<0.0001
Atazanavir	17.1	0.93 (0.79, 1.08)	0.34	1.22 (1.07, 1.40)	0.0035	0.96 (0.77, 1.18)	0.69
Lopinavir/r	15.3	0.77 (0.68, 0.86)	<0.0001	1.05 (0.94, 1.17)	0.39	1.21 (0.91, 1.60)	0.18

In conclusion, this large, national sample of 10,841 HIV-infected persons indicates that tenofovir is associated with increased risk of proteinuria, rapid decline, and CKD. Clinicians treating HIV-infected patients should recognize that while traditional risk factors such as hypertension, older age, and diabetes may increase the risk for kidney disease, tenofovir is associated with elevated risk even in patients without pre-existing kidney risk factors.

## Cohorte D:A:D

# Association Between Antiretroviral Exposure and Renal Impairment Among HIV-Positive Persons With Normal Baseline Renal Function: the D:A:D Study<sup>a</sup>

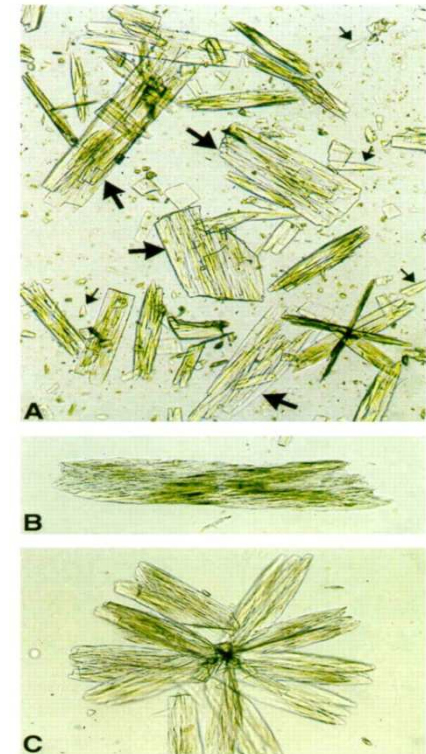
N=49,734 → 22,603



- TDF, ATV/r, and LPV/r use were independent predictors of chronic renal impairment in HIV-positive persons without pre-existing renal impairment.
- The proactive switch away from TDF in persons with deteriorating renal function may have limited our ability to fully address the potential association between TDF use and progression to CKD from an eGFR of  $\geq 90$  mL/min, since other parts of our analyses suggested that the TDF effect decreased after discontinuation.

# IDV, ATV

- Poorly soluble at physiologic urine pH
- Crystalluria in up to 2/3 of patients
- Classic presentation: crystalluria, obstruction, interstitial nephritis
- Clinic:
  - Asymptomatic
  - lumbar pain
  - hematuria
  - Increase of creatinine (nephritis)
  - obstruction: nephritis, hidronephrosis



# Tenofovir

- Classic presentation: proximal tubulopathy
- Tenofovir is linked with partial or full Fanconi's syndrome, which is characterized by:
  - proteinuria
  - normoglycemic glycosuria
  - hypokalemic renal tubular acidosis
  - phosphaturia
- 1-2% of patients develop significant toxicity
- More frequent sub-clinical abnormalities

## Incomplete Reversibility of Tenofovir-Related Renal Toxicity in HIV-Infected Men

*Karen Wever,\*† Michiel A. van Agtmael, MD,† and Andrew Carr, MBBS, MD\**

**Methods:** We determined the reversibility of TDF-related nephrotoxicity in 24 HIV-infected male outpatients who ceased TDF for renal impairment by retrospective assessment of estimated glomerular filtration rate (eGFR) using the Modified Diet in Renal Disease equation.

after TDF cessation. Only 10 (42%) patients reached their pre-TDF eGFR. Greater eGFR improvement was significantly associated with more rapid decline in eGFR on TDF therapy and in those who received TDF with a protease inhibitor, with a trend for shorter duration of TDF therapy.

*J Acquir Immune Defic Syndr* • Volume 55, Number 1, September 1, 2010

Short Communication

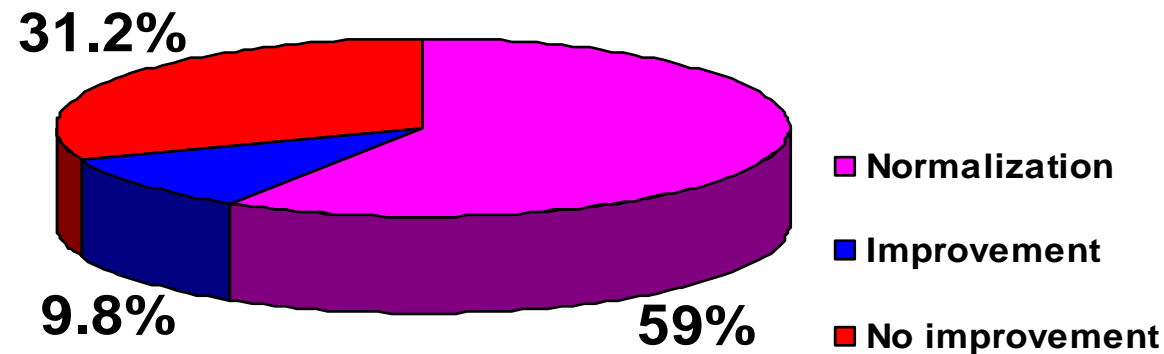
## High rate of reversibility of renal damage in a cohort of HIV-infected patients receiving tenofovir-containing antiretroviral therapy

Anna Bonjoch <sup>a,\*</sup>, Patricia Echeverría <sup>a</sup>, Núria Perez-Alvarez <sup>a,b</sup>, Jordi Puig <sup>a</sup>,  
Carla Estany <sup>a</sup>, Bonaventura Clotet <sup>a,c</sup>, Eugènia Negredo <sup>a</sup>

<sup>a</sup>Lluita contra la SIDA Foundation, Germans Trias i Pujol University Hospital, Autonomous University, Barcelona, Spain

<sup>b</sup>Statistics and Operations Research, Technical University of Catalunya, Barcelona, Spain

<sup>c</sup>IrsiCaixa Foundation, Barcelona, Spain



# **Osteoporosis and HIV Infection**

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# Bone remodeling

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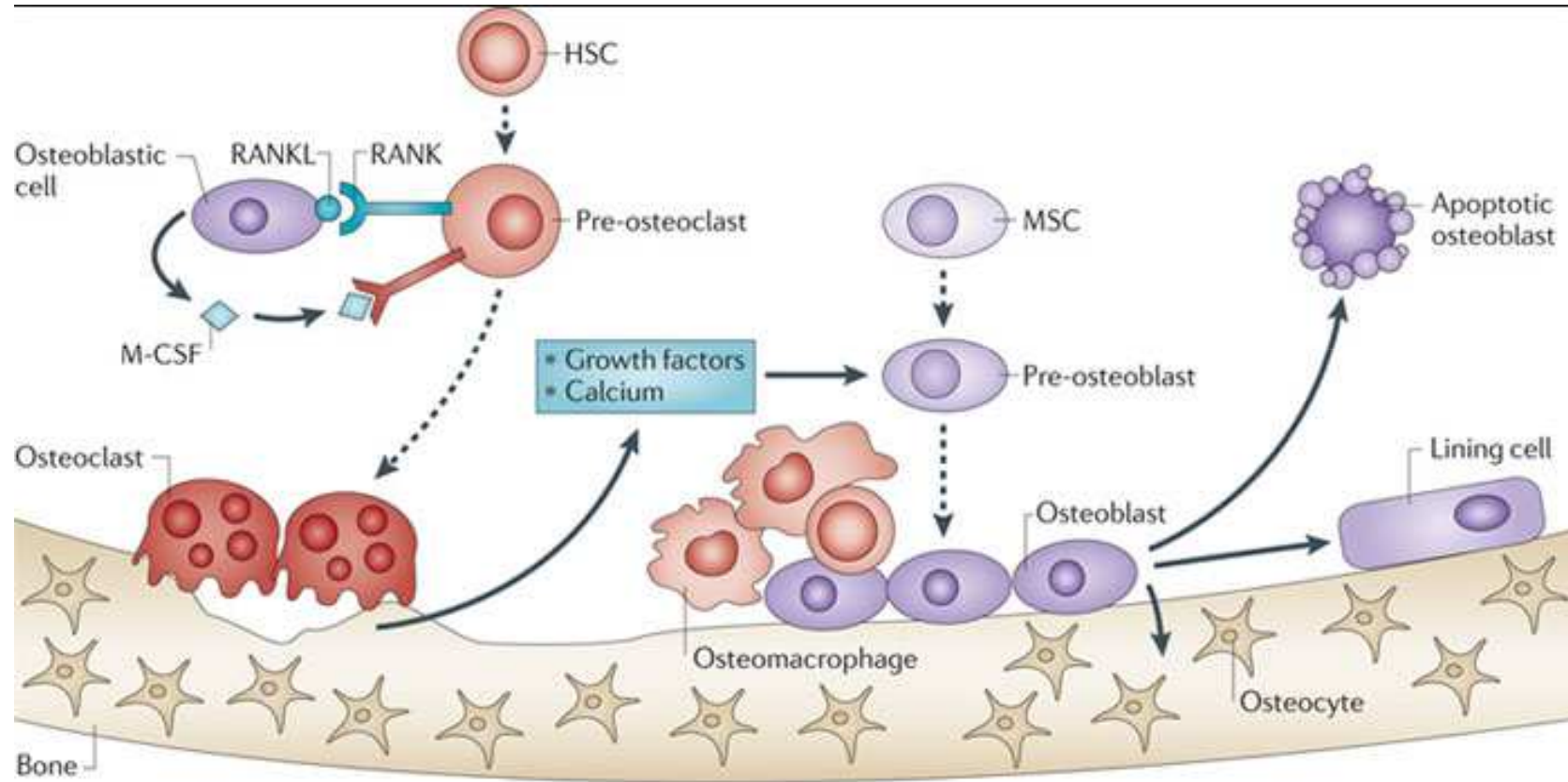
# Bone Cells

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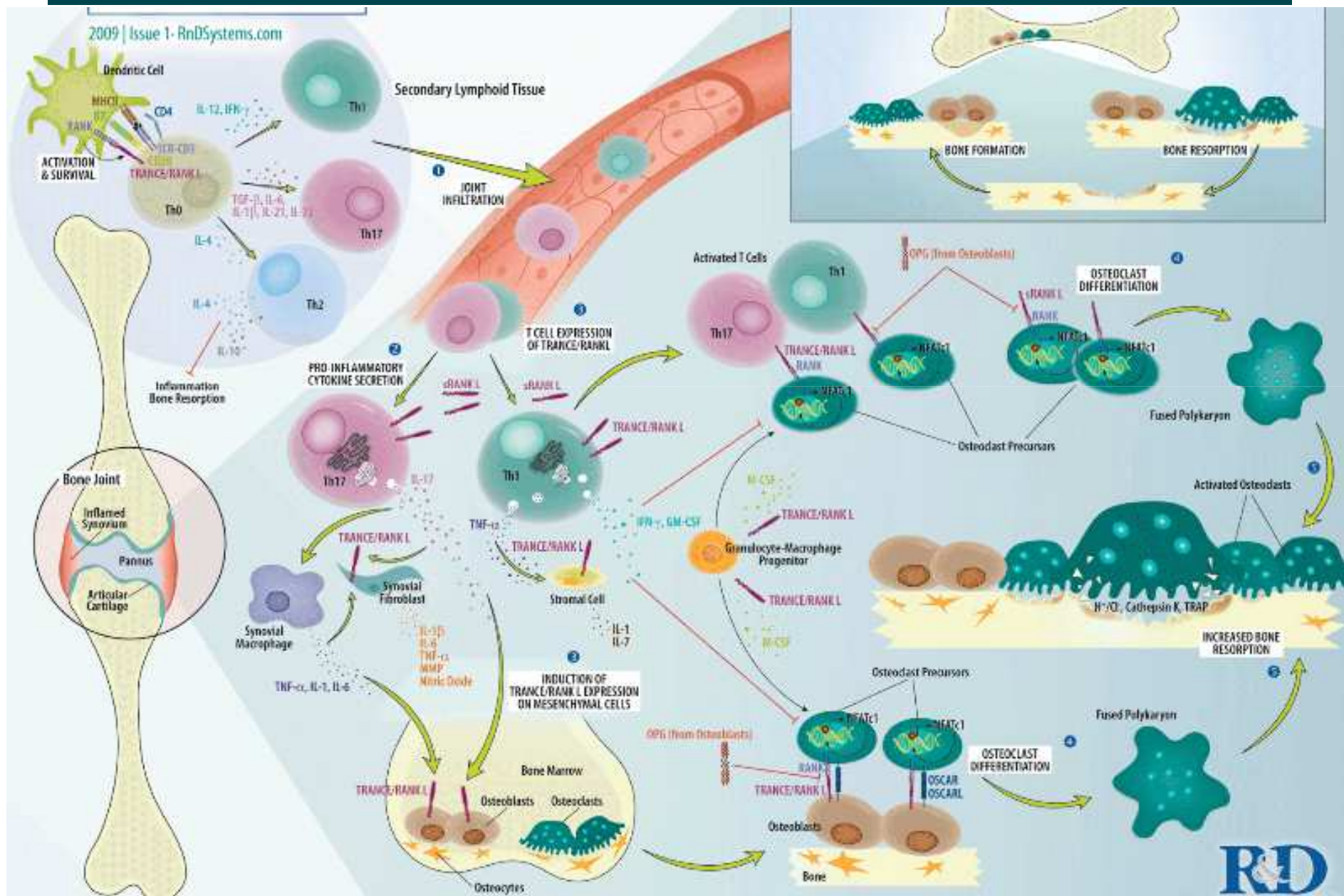
- **Osteoclast:** bone resorption
- **Osteoblast:** bone formation
- **Osteocyte:** Bone remodeling regulation



# Bone remodelling



# Bone remodelling



# Patogenia: Papel de la inflamación

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## Inflamación crónica

Artritis reumatoide, Lupus, Diabetes, Enfermedad inflamatoria intestinal,...

Osteoporosis postmenopáusica

Infección VIH



Disregulación del sistema inmunológico



**Linfocitos activados (Células B y T)**

→ Aumento de TNF- $\alpha$ , SOFAT...

→ Aumento de RANKL

**Células B disfuncionantes**

(Células B producen 64% del total de osteoprotegerina-OPG- en médula ósea)

→ Descenso de OPG

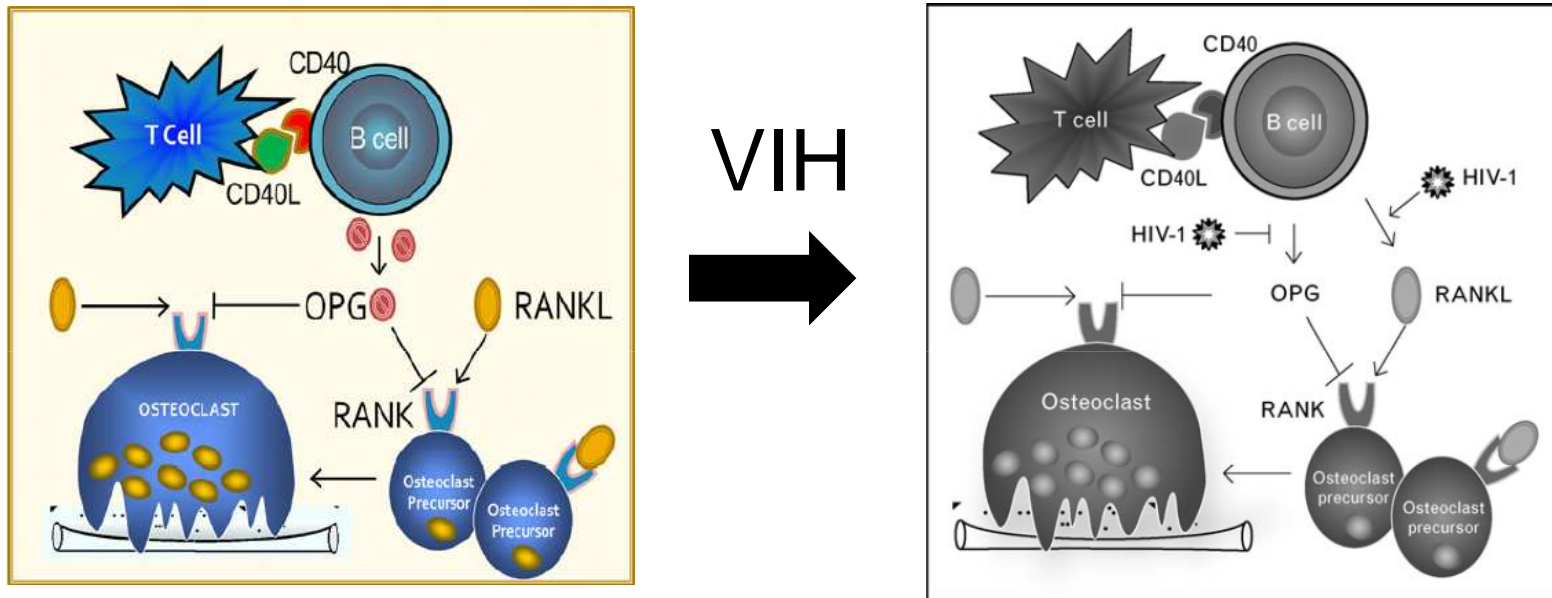


**Elevación del ratio RANKL/OPG**



**Pérdida DMO**

# Patogenia: Papel del virus

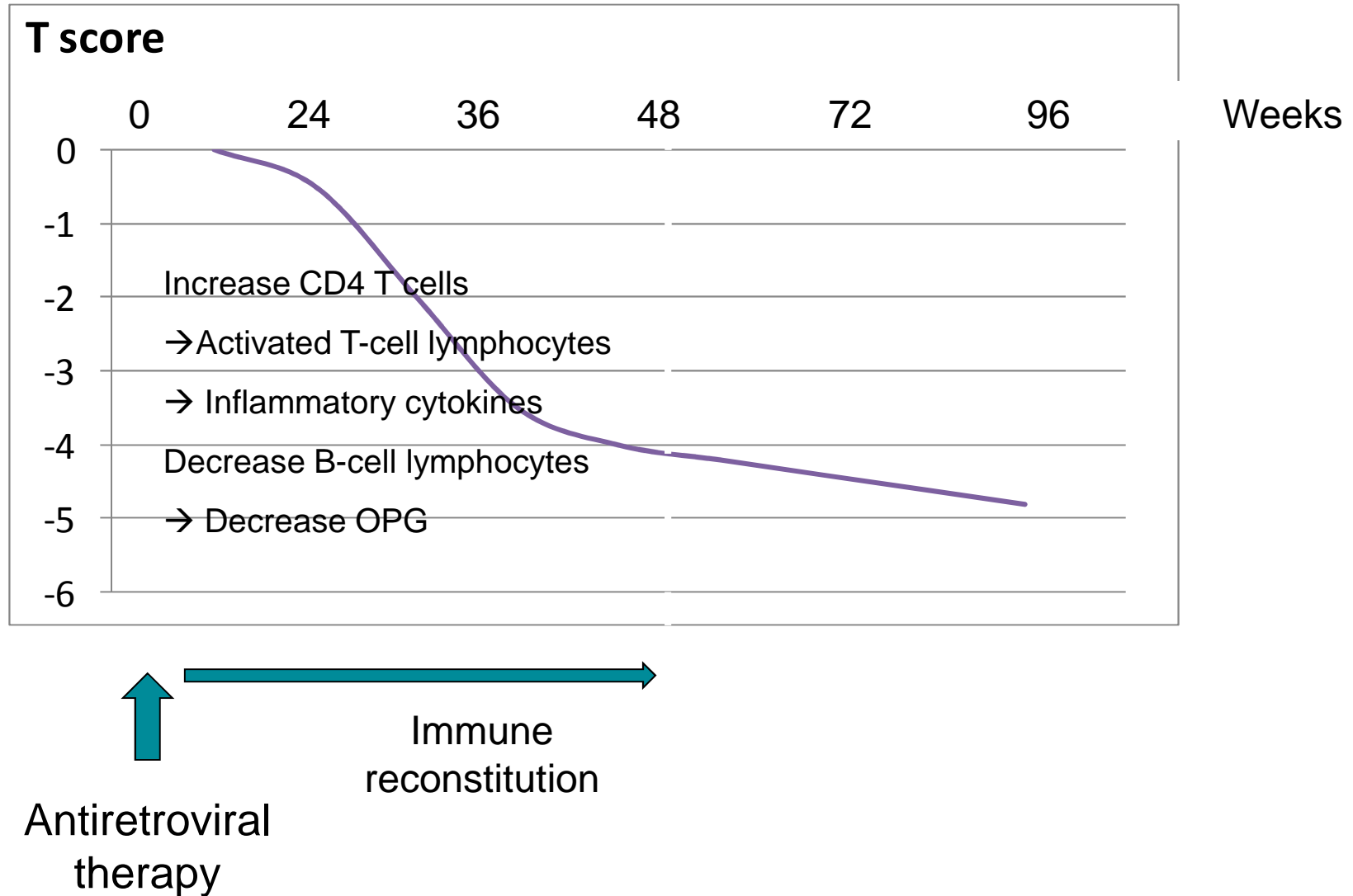


VIH bloquea la OPG y activa RANKL



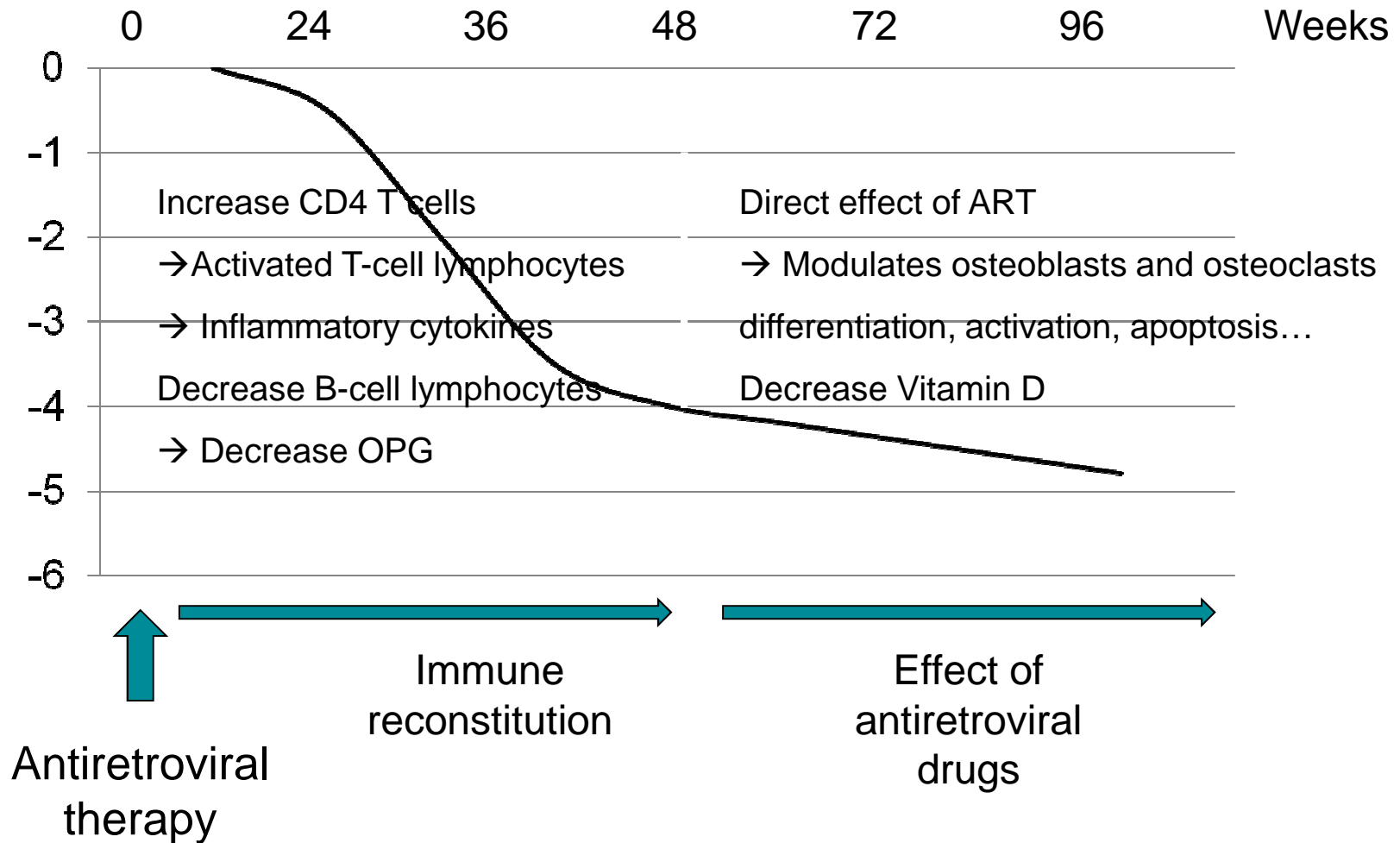
**Elevación del ratio RANKL/OPG ratio**

# Patogenia: Papel del tratamiento



# Patogenia: Papel del tratamiento

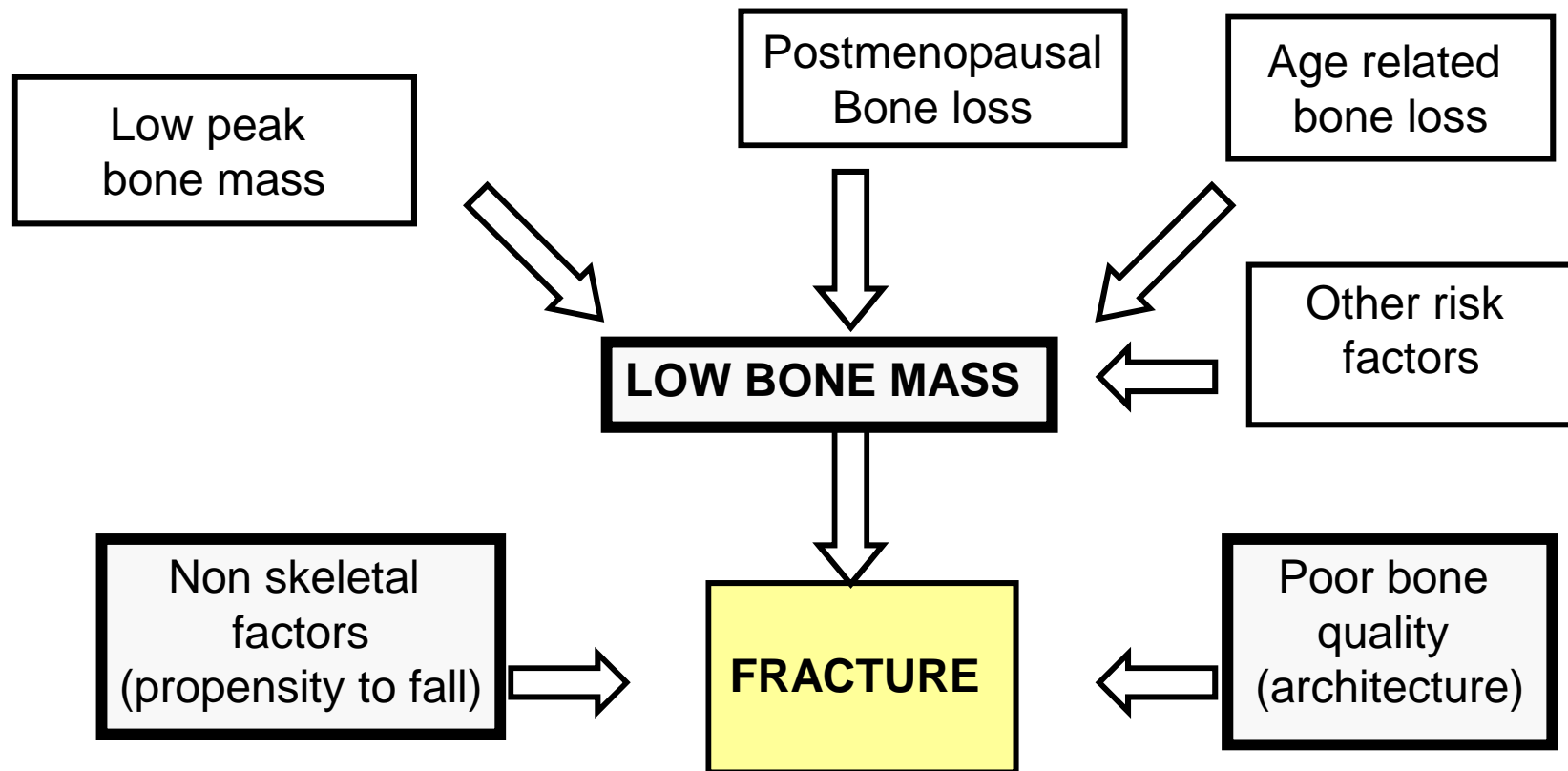
**T score**



# Patogenia: Factores tradicionales

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**LOW BMD = ↓ PBM or ↑ Loss**



# Prevalence and Management

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# Prevalence

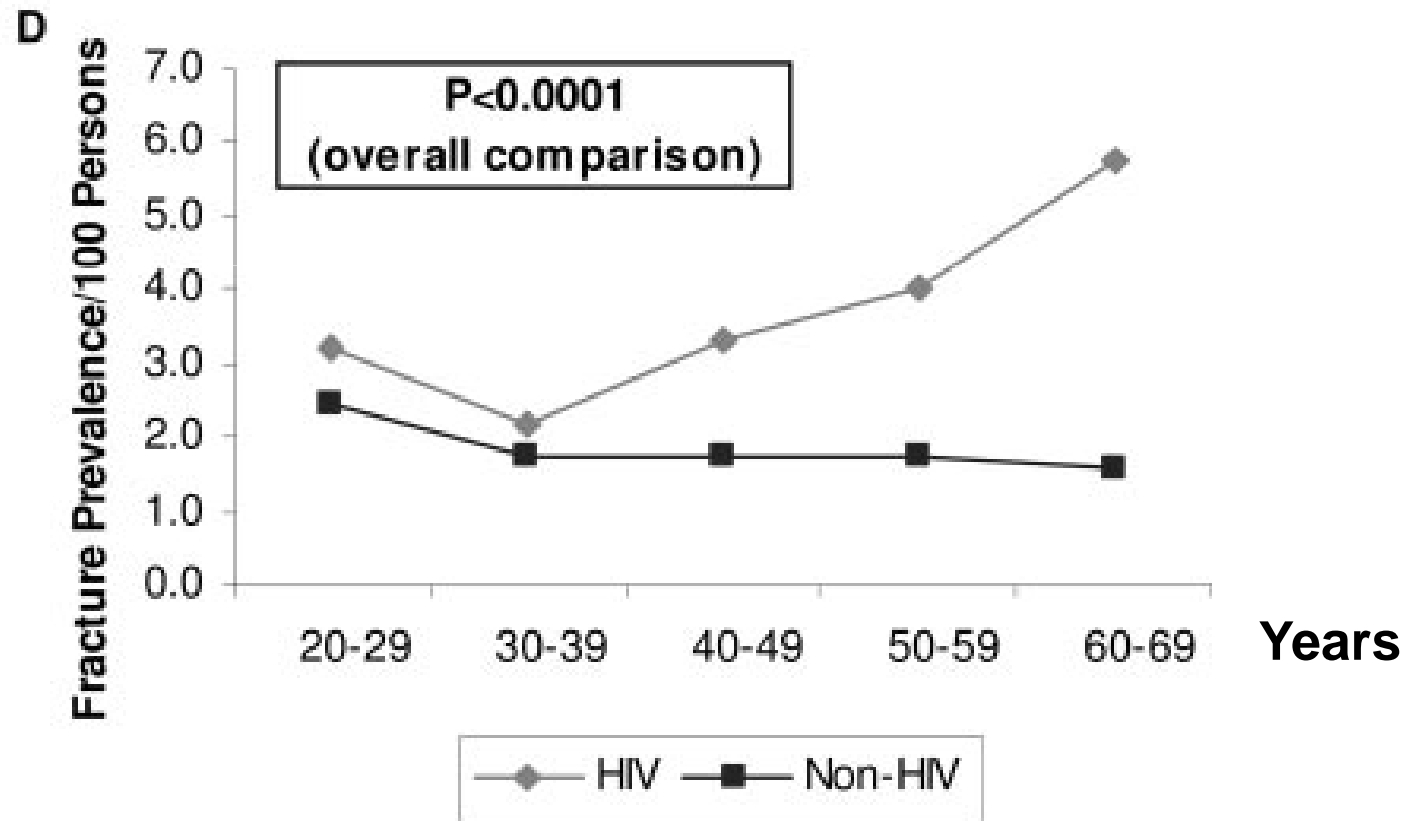
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n=671 patients (1982 dexas)

Patients, n (%)			
	Normal	Osteopenia	Osteoporosis
Total	174 (25.93%)	323 (48.14%)	174 (25.93%)
Men	104 (21.53%)	246 (50.93%)	133 (27.54%)
<65 years	104 (21.80%)	244 (51.15%)	129 (27.04%)
>65 years	0 (0.0%)	2 (33.33%)	4 (66.67%)
Women	70 (37.23%)	77 (40.96%)	41 (21.81%)
<55 years	69 (38.76%)	74 (41.57%)	35 (19.66%)
>55 years	1 (10.00%)	3 (30.00%)	6 (60.00%)

# Fractures

## Triant Study



# Radiology

## Radiology (spine)

- Only in case of osteoporosis
- Diagnosis of complications (vertebral fracture)

# Biochemical markers

## Resorption Markers

- Pyridinoline (Pyr)
- Deoxypyridinoline (dPyr)
- Amino terminal telopeptide of type I collagen (NTX)
- Carboxyl terminal telopeptide of type I collagen (CTX)

## Formation Markers

- Osteocalcin (OC)
- Bone-specific alkaline phosphatase (BAP)
- Amino terminal propeptide of type I collagen (PINP)
- Carboxyl terminal propeptide of type I collagen (PICP)

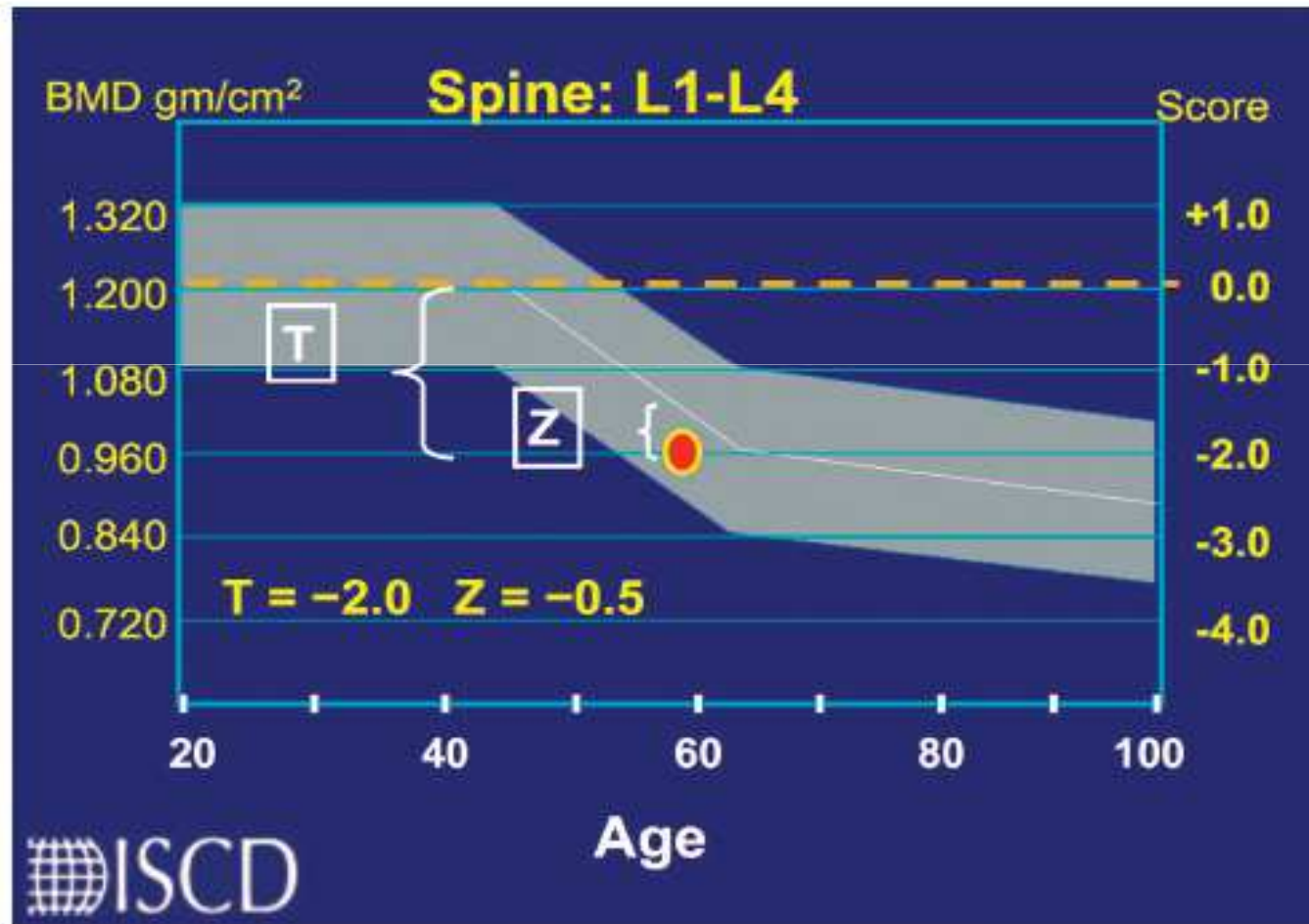
# Biochemical parameters

- Ca+, P+, Vitamin D
- Secondary causes in case of osteopenia/osteoporosis
  - TSH, T4
  - Testosterona (varones)
  - Prolactina
  - PTH
  - FSH, LH.....

## FRAX ([www.shef.ac.uk/FRAX](http://www.shef.ac.uk/FRAX))

# DEXA

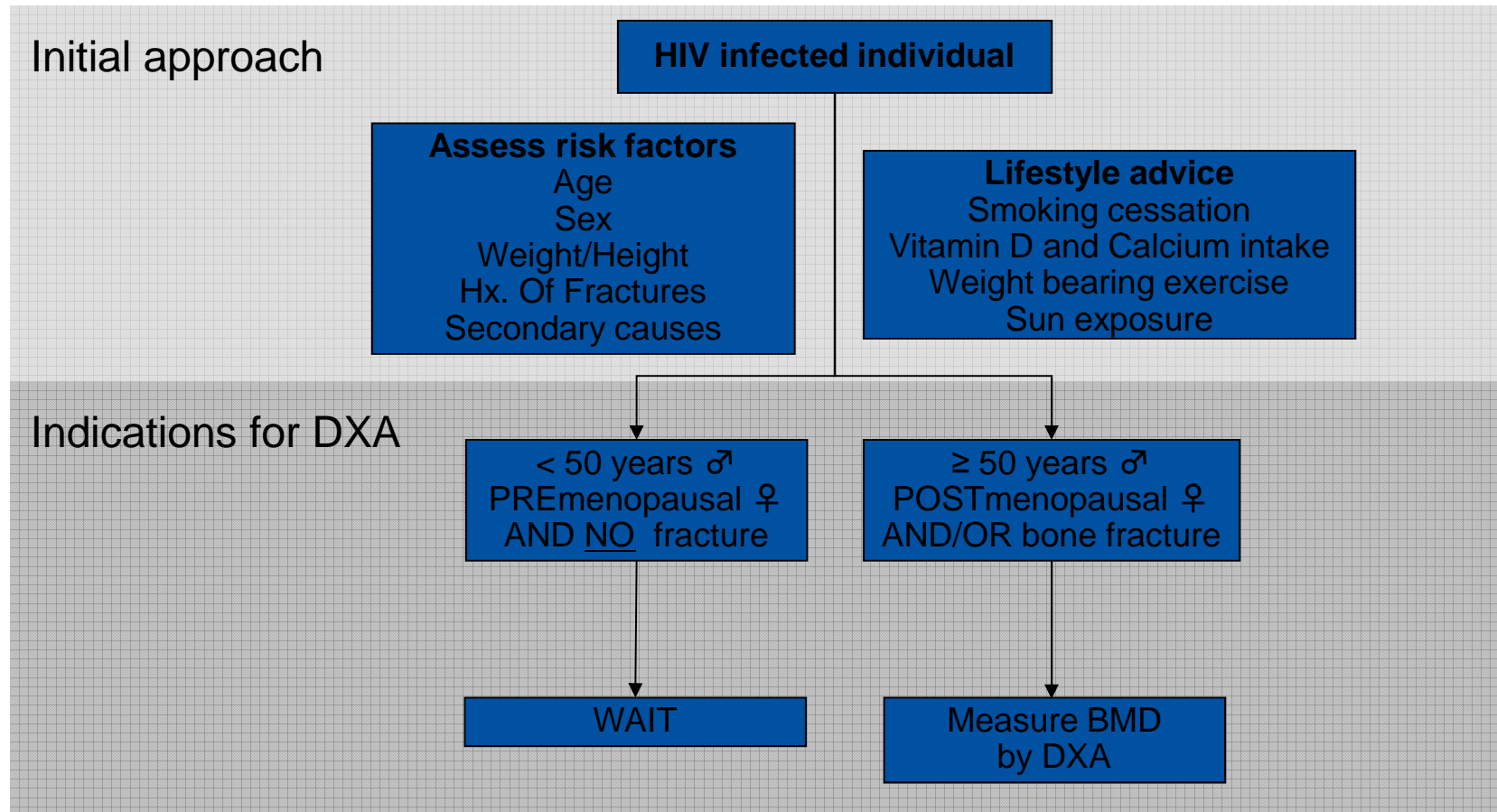
FIGURE 3. Z- and T-Scores



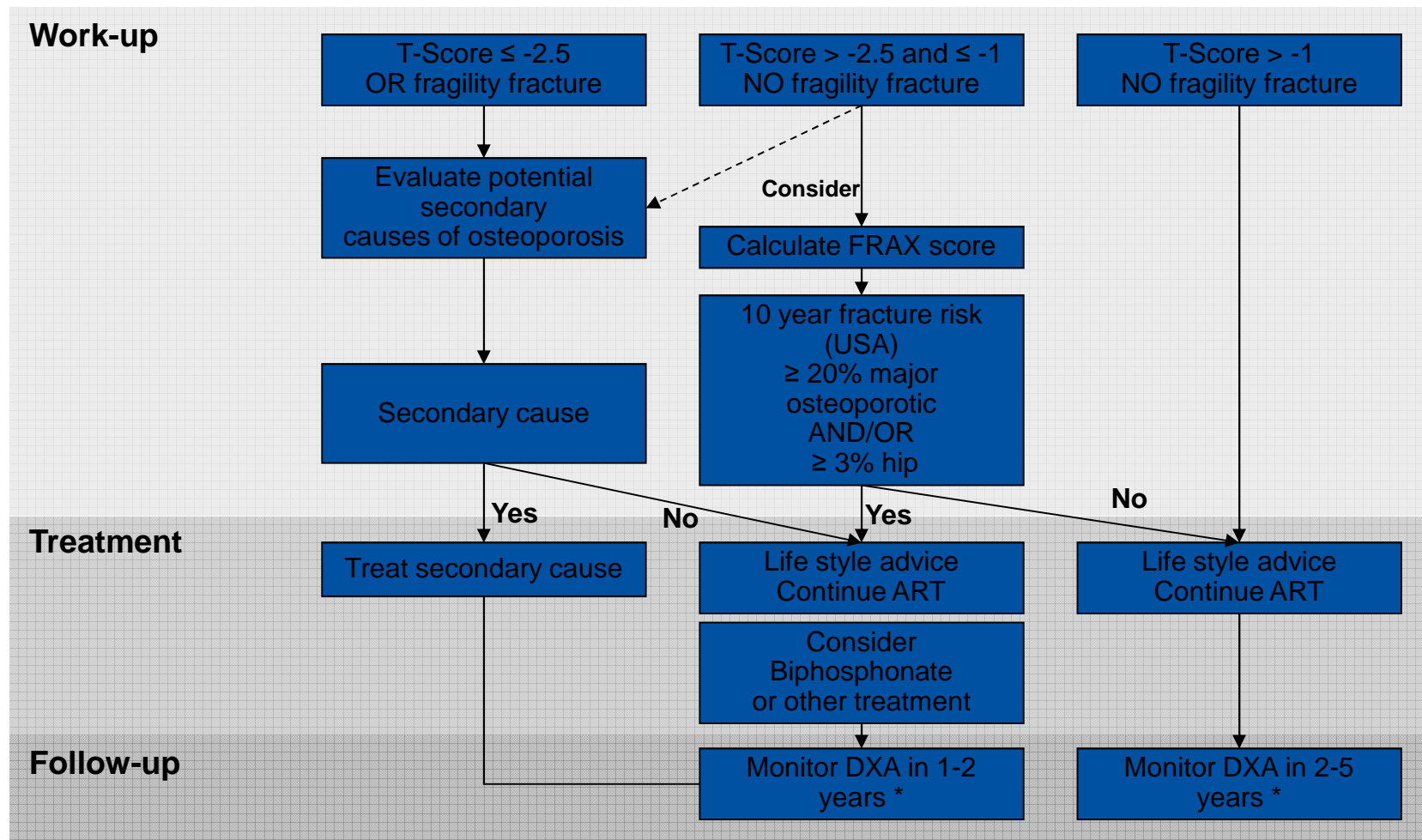
From: ISCD Bone Densitometry Clinician Course. Lecture 5 (2008).

# Management

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# Management



Treatment

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# Secondary causes of osteoporosis

DXA	n=1199	Osteoporosis 10%	Osteopenia 52%	Normal 36%	P value
1 <sup>st</sup> Hyperparathyroidism	1073	0%	0%	0%	1
2 <sup>nd</sup> Hyperparathyroidism					
High PTH, low vitamin D	723	8%	6.3%	5.6%	0.7
High PTH, low GFR*	1005	3%	1.3%	1.1%	0.3
Hyperthyroidism	1072	0.9%	0.7%	0.3%	0.56
Vitamin D deficiency	723	46%	25%	22%	<.0001
Hypogonadism (males)	428	5.3%	8.7%	11.4%	0.4
BMI less than 20 kg/m <sup>2</sup>	1156	34%	20%	10%	<.0001

Guaraldi et al. Lipodystrophy 2006

Biochemical determinations	Low BMD (n=149)	Normal BMD (n=36)	p value
25(OH)D, ng/mL	23.2±9.5	26.93±7.5	0.118
Min-max, ng/mL	5.5-46.8	10.9- 47	
<10 ng/mL, %	7.4	0	0.13
<30 ng/mL, %	83	75	0.60
PTH, pg/mL	45.06±18.42	--	
PTH > 65 pg/mL, %	14.6	--	
TSH, µIU/mL	2.14±1.2	--	
TSH > 4.2 µIU/mL, %	5.4	--	
T4, ng/dL	1.12±0.16	--	
Testosterone (in men), ng/dL	641.7±244.5	--	
Testosterone < 249 ng/dL, % of men	2.65	--	
Calcium, mmol/L	2.33±0.09	--	

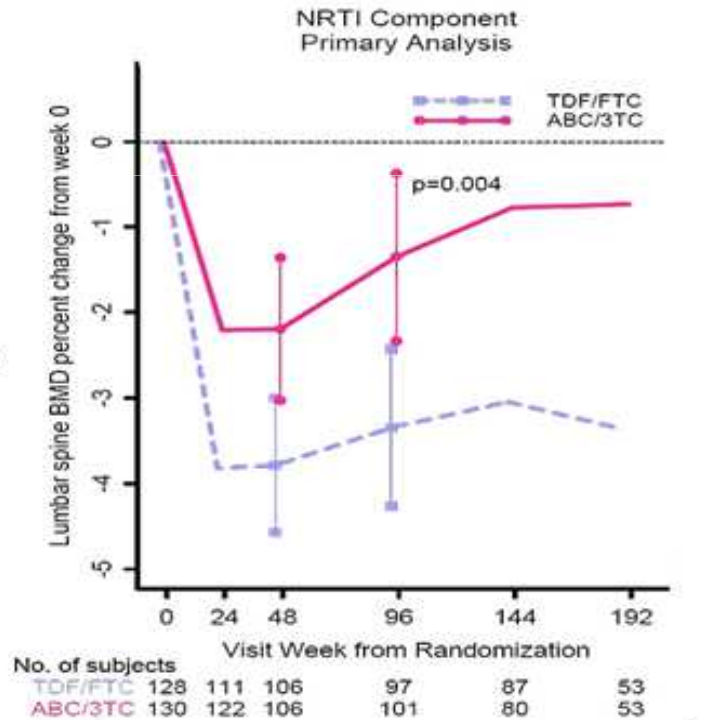
Negredo et al.

Future Medicine 2012.

# Role of antiretroviral drugs

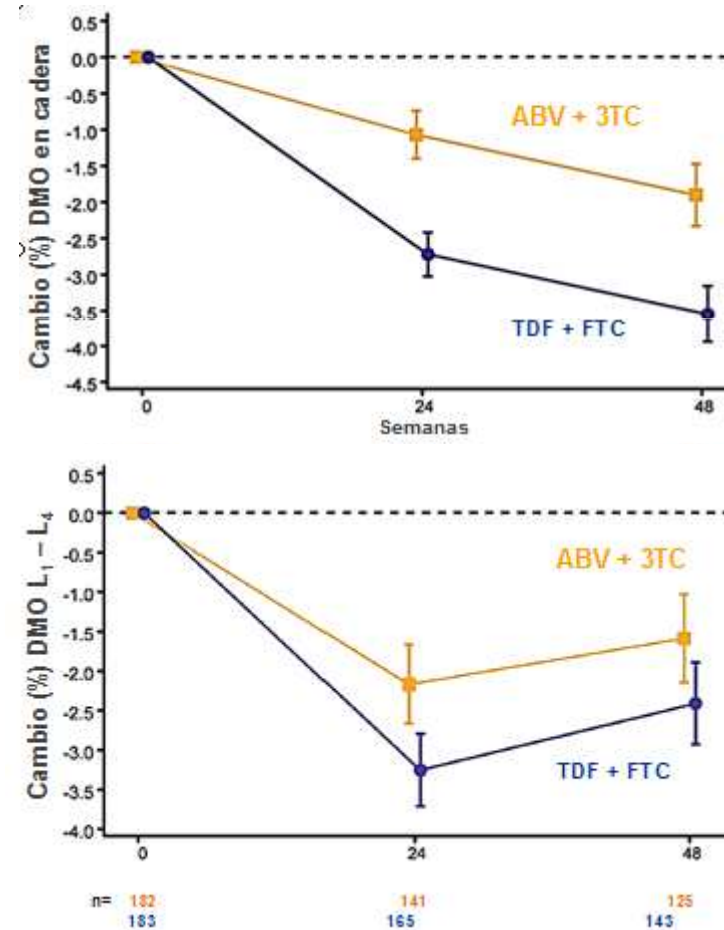
## Role of tenofovir

ACTG A5224s: ABC/3TC vs TDF/FTC + EFV o ATV/r



Mc Comsey G, et al. CROI 2010

ASSERT: ABC/3TC vs TDF/FTC + EFV



Stellbrink HJ, et al. Clin Infect Dis. 2010

# Role of antiretroviral drugs

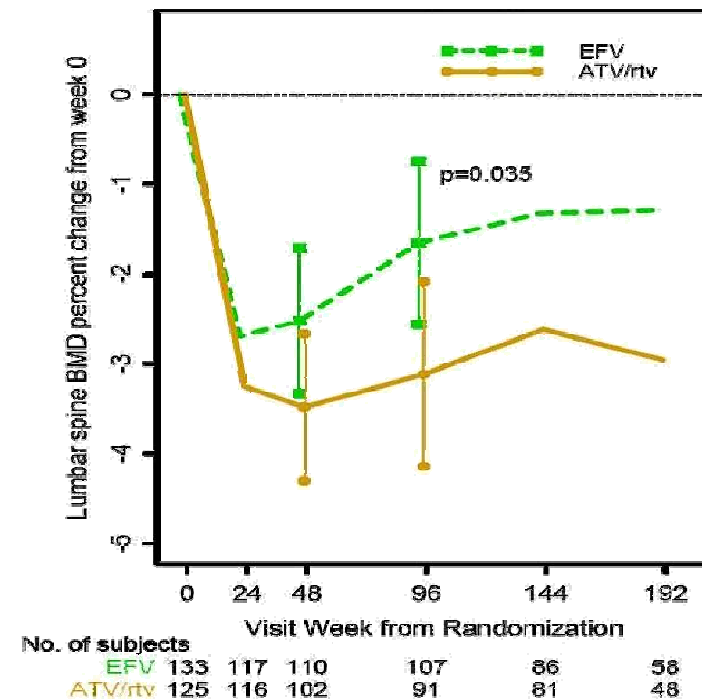
## Role of protease inhibitors

**Cohorte Germans Trias**  
n=671 patients (1982 dexas)

### Factores asociados a baja DMO)

Variable	Estimate	Standard Error	P value
Age	-0.0526	0.0062	<0.0001
BMI	0.0971	0.0155	<0.0001
Gender (female vs male)	-0.3343	0.1252	0.0078
<b>Time with PI</b>	<b>-0.0837</b>	<b>0.0192</b>	<b>&lt;0.0001</b>
ART at the last DXA (no vs yes)	-0.5944	0.1752	0.0007
Creatinine	-0.0101	0.0036	0.0047
Time with ART (<25% vs 25-50)	0.5958	0.2595	0.0221
(<25% vs 50-75)	0.6146	0.2534	0.0156
(<25% vs ≥75%)	0.7029	0.2432	0.0040

**ACTG A5224s:** (randomizado, multicéntrico, 192 sem)  
ABC/3TC versus TDF/FTC + EFV versus ATV/r



# Pharmacological treatment

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¿Who should receive pharmacological treatment?

- Post-menopausal women + osteoporosis,
- Men >60 years + osteoporosis,
- Osteoporosis (t-score <-2,5 DS) + bone fracture,
- Severe osteoporosis (t-score < -4).

# Pharmacological treatment

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## Biphosphonates in VIH

### Alendronato en VIH:

- Guaraldi G HIV Clin Trials 2004;5:269-77.
- Negrodo E, AIDS 2005;21:2473-82.
- McComsey GA, AIDS 2007;21:2473-82.
- Mondy K, JAIDS 2005;38:426-31.

### Zoledronato en VIH:

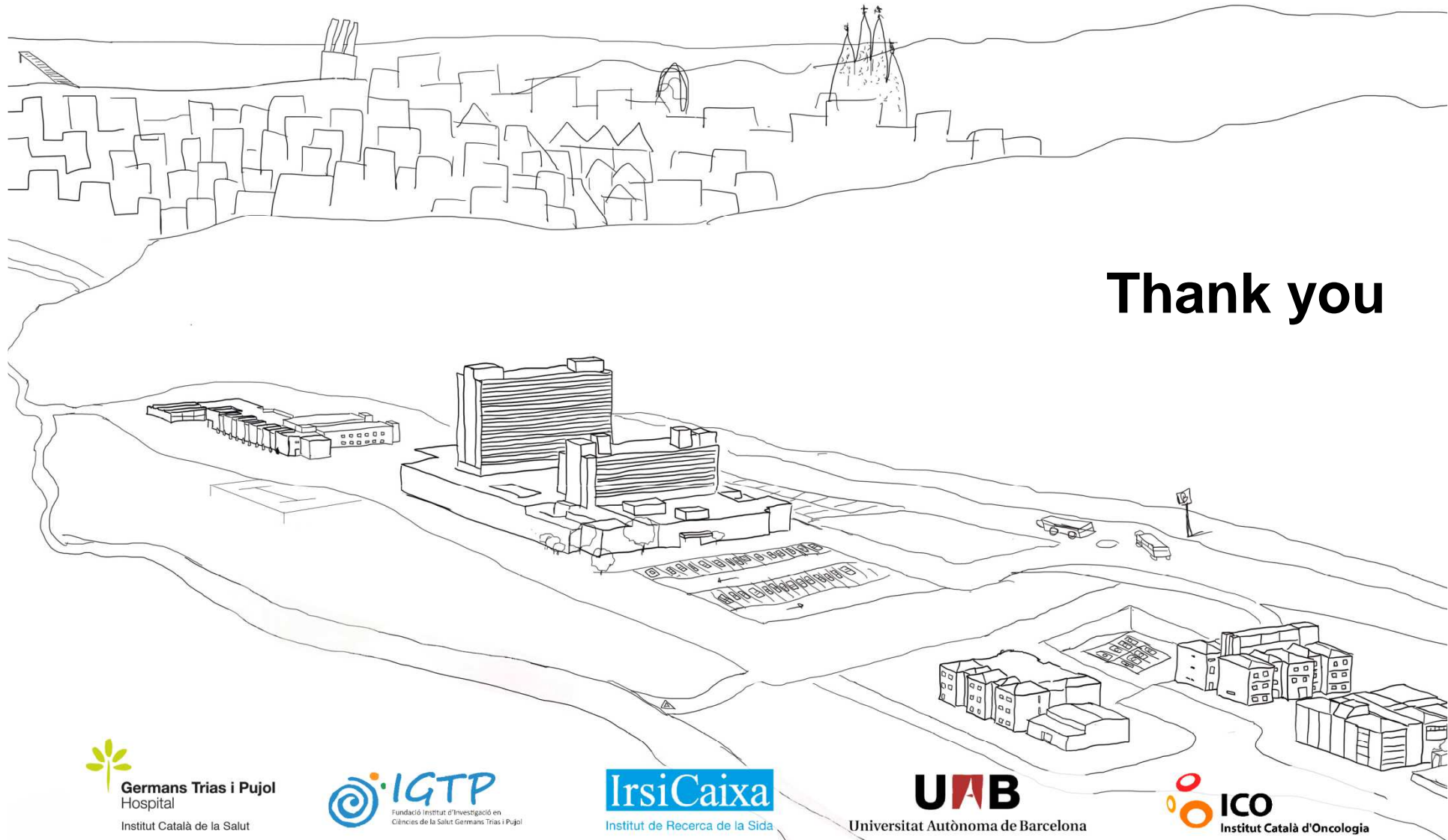
- Bolland MJ. J Clin Endocrinol Metab 2007;92:1283-8
- Bolland, et al. J Bone and Mineral Res 2008
- Huang J. AIDS 2009;23:51-7.
- Negrodo et al. CROI 2014, Boston. #782

### **Pros:**

- ✓ Increase in lumbar and hip BMD
- ✓ Good tolerability

### **Contras:**

- ✓ Small studies
- ✓ Short follow-up (mostly 1-2 years)
- ✓ No data about the clinical benefit (fractures).



**Thank you**



Il·lustració: Cristina González Castro. Escola d'art i superior de disseny Pau Gargallo de Badalona