I REUNIÓN INTERAUTONÓMICA EN ENFERMEDADES INFECCIOSAS 2023

Vigo, 27 y 28 de Octubre 2023

Patrocinio científico

AGIDEI
ASOCIACION GALLEGA PARA LA INVESTIGACION Y DOCENCIA EN ENFERMEDADES INFECCIOSAS

Patrocinador

GILEAD

9.30-9.50. **Comorbilidades ocultas y tratamiento antirretroviral.** ***Dra. Pilar Vázquez Rodriguez.*** *Unidad de Enfermedades Infecciosas.* Hospital Universitario de A Coruña. A Coruña.

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COMORBILIDADES OCULTAS Y TRATAMIENTO ANTIRRETROVIRAL

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SERVIZO GALEGO de SAÚDE | Complexo Hospitalario Universitario A Coruña
A Coruña

COMORBILIDADES “OCULTAS”

NIH National Institute on Drug Abuse
Advancing Addiction Science

La "comorbilidad", también conocida como "morbilidad asociada", es un término utilizado para describir dos o más trastornos o enfermedades que ocurren en la misma persona. Pueden ocurrir al mismo tiempo o uno después del otro. La comorbilidad también implica que hay una interacción entre las dos enfermedades que puede empeorar la evolución de ambas.

REAL ACADEMIA ESPAÑOLA

oculto, ta

Del lat. *occultus*.

1. adj. Escondido, ignorado, que no se da a conocer ni se deja ver ni sentir.

¿En qué situación estamos?

1981

SIDA
Sentencia de muerte

ENFERMEDAD
AGUDA
MORTAL

1996

CONFERENCIA DE
VANCOUVER
TARGA

Control infección por VIH
Disminuyen muertes

2006

STR
(Single Tablet Regimen)

COMODIDAD
SIMPLIFICACION
MENOS EFECTOS ADVERSOS

2014/15

ONUSIDA

90% 90% 90%

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection

The INSIGHT START Study Group*

ESTUDIO START

August 27, 2015

2021

CRONICIDAD

CUARTO
90

ENFERMEDAD
CRÓNICA

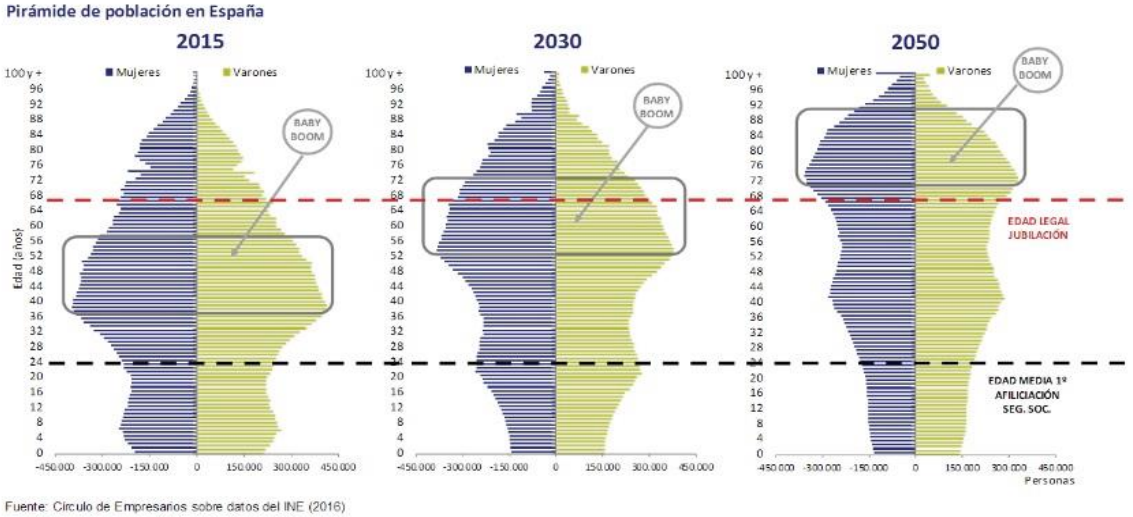
TRATAMIENTO PARA TODOS
1ª ESTRATEGIA OMS para el
FIN DE LA PANDEMIA

2023

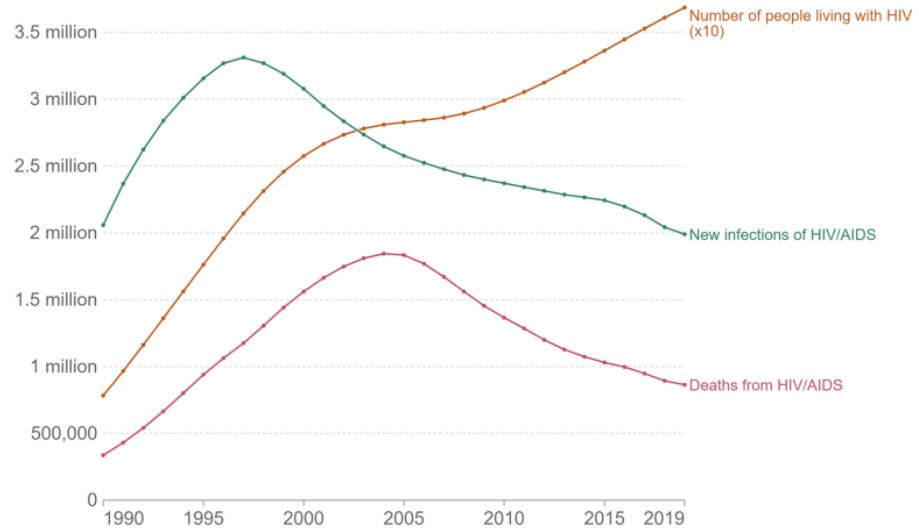
RETOS FUTUROS

- **AUMENTO EXPECTATIVA DE VIDA**
- **AUMENTO ENVEJECIMIENTO DE LA POBLACIÓN**
- **EFECTOS DE LA CRONICIDAD**
- **AUMENTO COMORBILIDADES**
- **AUMENTO DE FRAGILIDAD**
- **AUMENTO DIVERSIDAD POBLACIÓN PVVIH (problemáticas diferentes)**
- **POLIFARMACIA**
- **CONSUMOS**

CAMBIOS DEMOGRÁFICOS

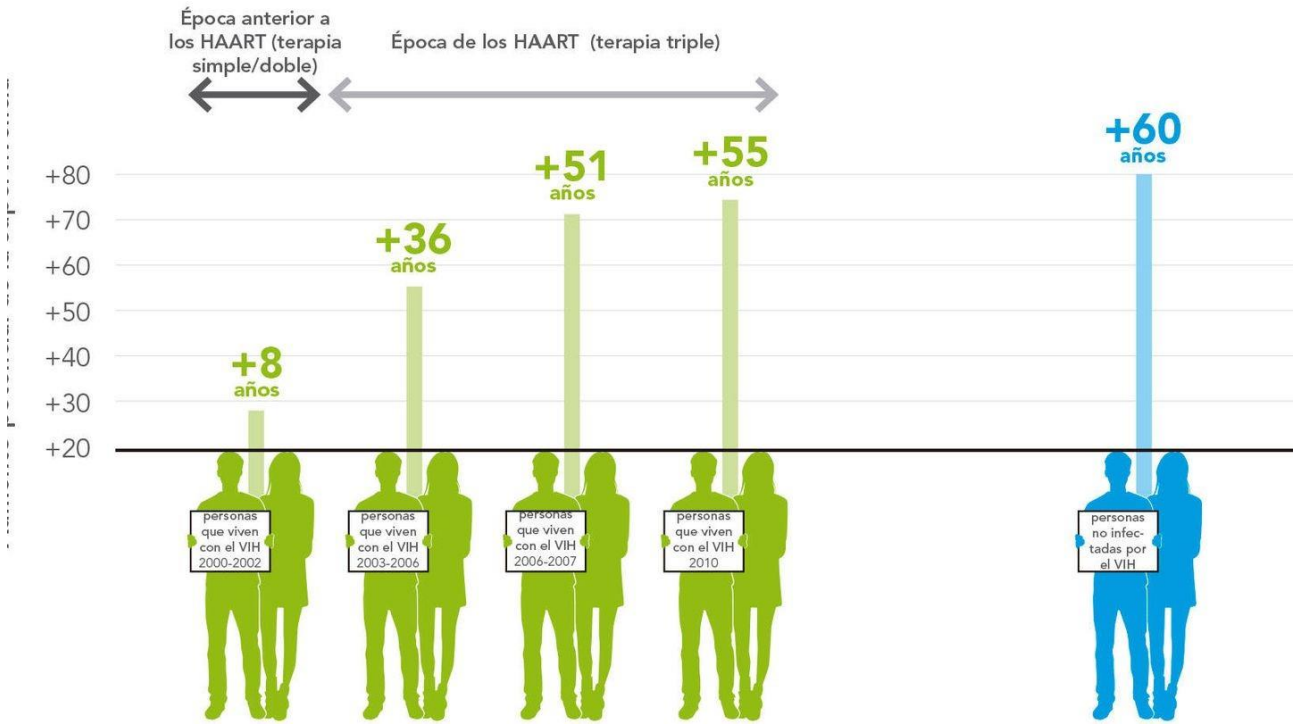


Fuente: Círculo de Empresarios sobre datos del INE (2016)



Beneficios del TAR

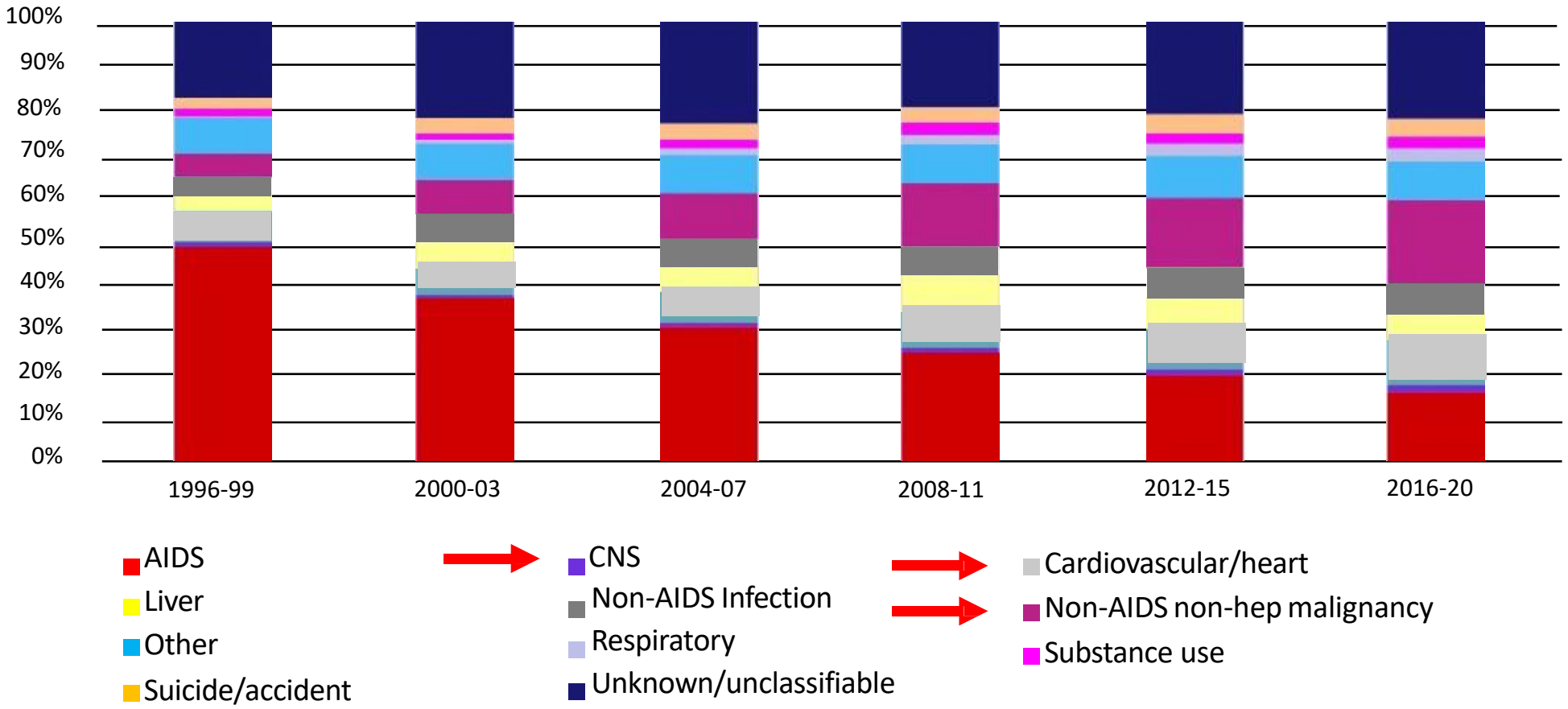
- Ha conseguido una gran **mejoría en la supervivencia** de nuestros pacientes hasta el punto que **más de la mitad** de nuestros pacientes se encuentra **por encima de los 50 años**



Beneficios del TAR. ART-CC. 1996-2019

- Ha **reducido las complicaciones relacionadas con el SIDA** con **tasas de mortalidad que descendieron a lo largo de los años:**
  - **1996-1999:** 16,8 (95% IC 15,4-18,4) 1.000 personas-año.
  - **2016-2020:** 7,9 (95% IC 7,6-8,2) 1.000 personas-año.

Causas de muerte por periodo



Trickey A. et al. 30th CROI. Seattle, Washington 2023. #156

Comorbilidad y envejecimiento

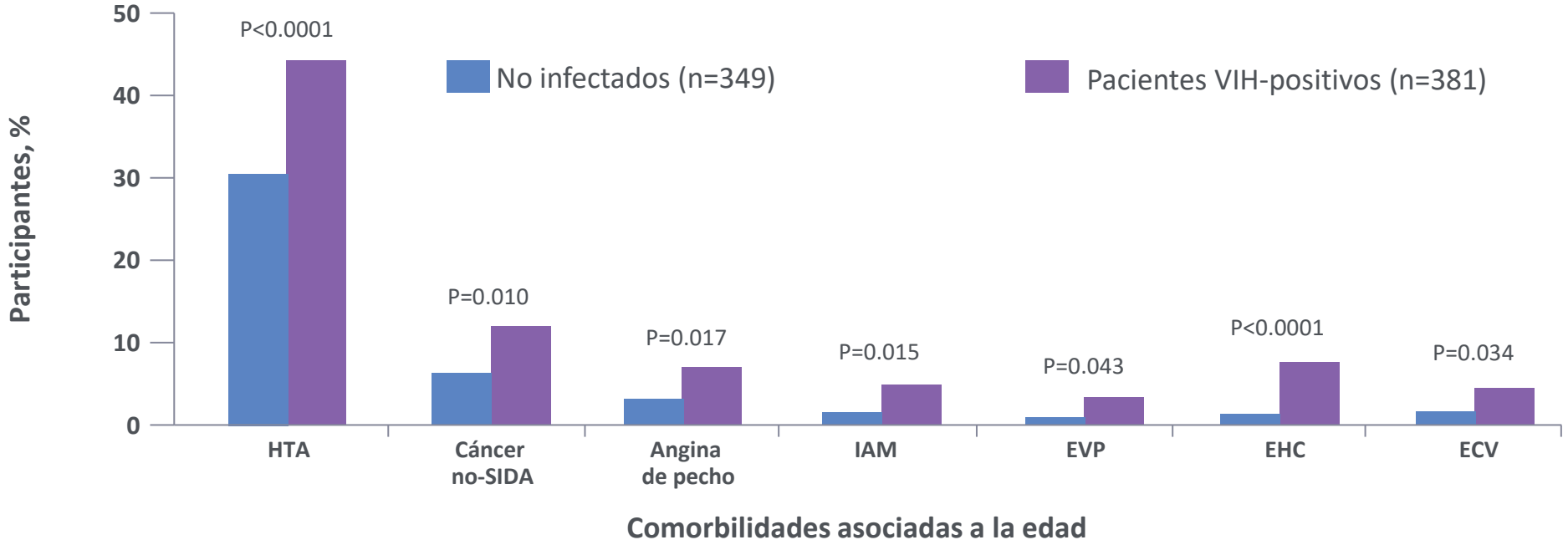
- Este aumento de la expectativa de vida ha provocado un **incremento de patología crónica, las comorbilidades y la polifarmacia** en comparación con la población general.

- Los **mecanismos implicados** en el aumento de **comorbilidad** son **múltiples** y están relacionados con:
  - el propio VIH
  - toxicidad del TAR
  - activación inmunológica
  - inflamación crónica
  - determinantes sociales desfavorables de salud

Algunas comorbilidades son más prevalentes entre las PVVIH que en la población general

- La infección por **VIH** parece **acelerar el proceso de envejecimiento** y la **aparición de comorbilidades**[1]
- Una **mayor duración del TAR** (OR: 1,24 por cada 5 años de uso adicional de TAR) y un **nadir más bajo de CD4+** (OR: 1,12 por 100 células menos) se asocian con un **riesgo incrementado** de un **mayor número de comorbilidades**

Sujetos con ≥45 años con comorbilidades asociadas a la edad, según seroestado
(AGEhIV Study, 2010–2012)[2]

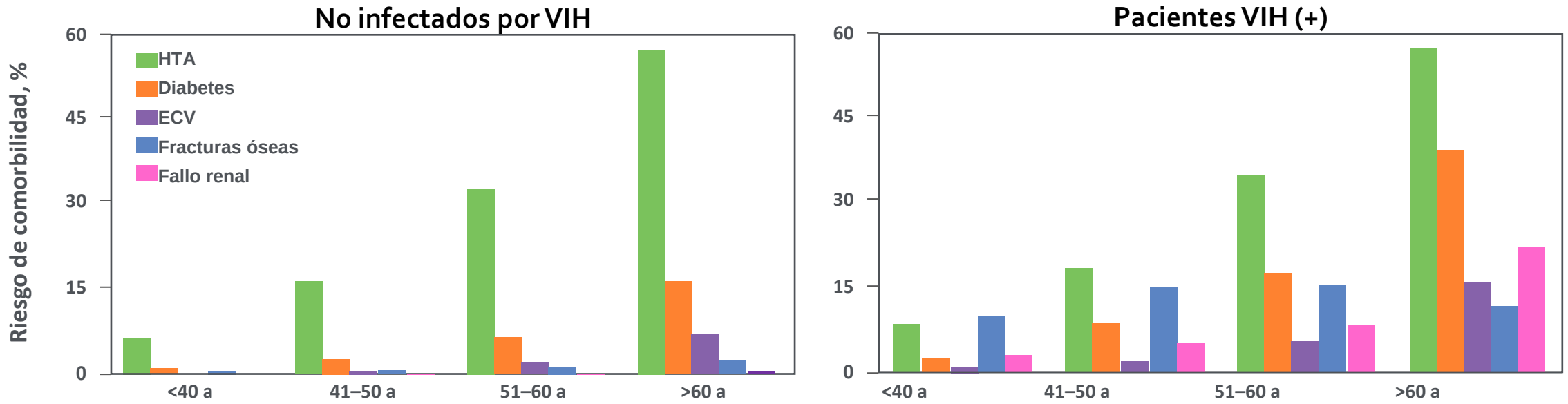


EHC, enfermedad hepática crónica; ECV, enfermedad cerebrovascular; HTA, hipertensión arterial; IAM, infarto agudo de miocardio; OR, odds ratio; EVP, enfermedad vascular periférica

1. Effros RB et al. Clin Infect Dis 2008;47:542–553; 2. Schouten J et al. IAC 2012. Washington, DC. THAB0205

Algunas comorbilidades parecen aparecer antes entre las PVVIH que en la población general

Prevalencia de comorbilidades no infecciosas en una cohorte de 2.854 pacientes VIH (+) y 8.562 personas no infectadas por VIH, según seroestado VIH y edad, 2009[1]



- Los pacientes **VIH (+)** tienen más tendencia a desarrollar **ECV, fracturas óseas y fallo renal** que las personas no infectadas por VIH[2]
- **Estas comorbilidades** a menudo se desarrollan **más temprano** en los pacientes **VIH (+)**[2]

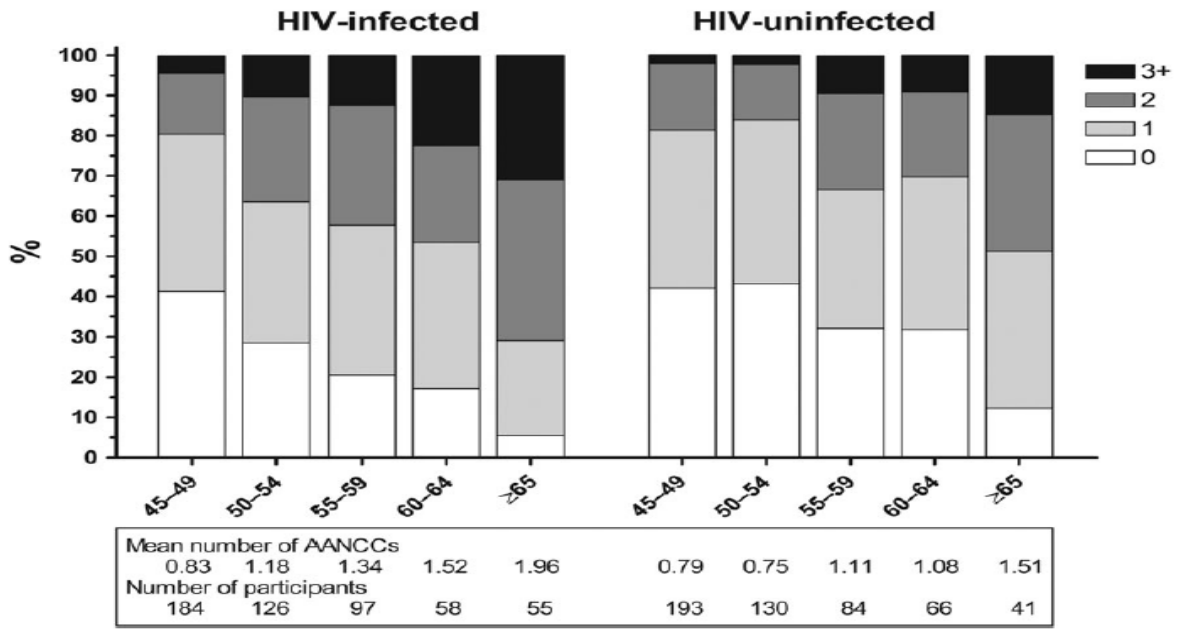
1. Guaraldi G et al. Clinicoecon Outcomes Res 2013;5:481–488;
2. Guaraldi G et al. Clin Infect Dis 2011;53:1120–1126

Las comorbilidades se acumulan en las PVVIH

AGEhIV Cohort Study

Prevalencia de CAENC (Comorbilidades asociadas a la edad no comunicables)

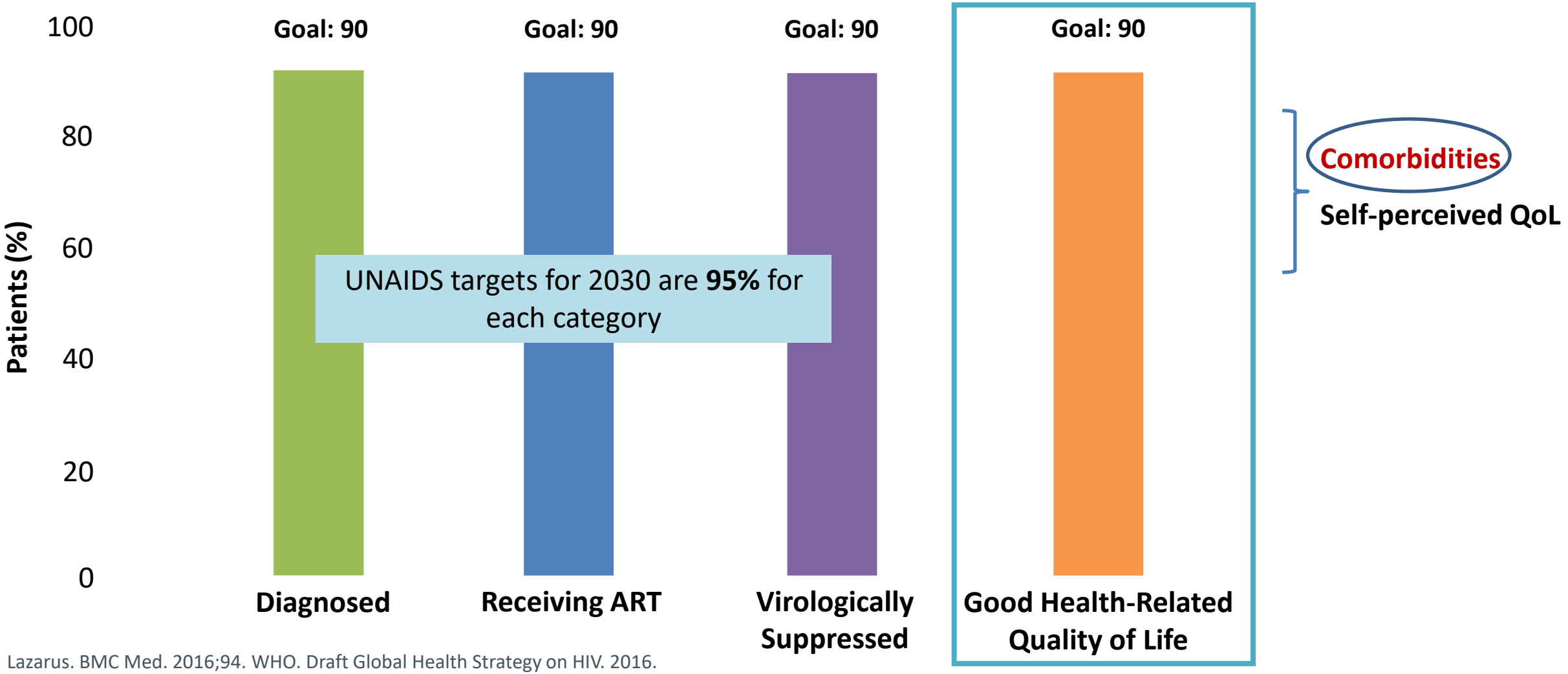
Distribución de la incidencia de CAENC según edad en ambos grupos del estudio.



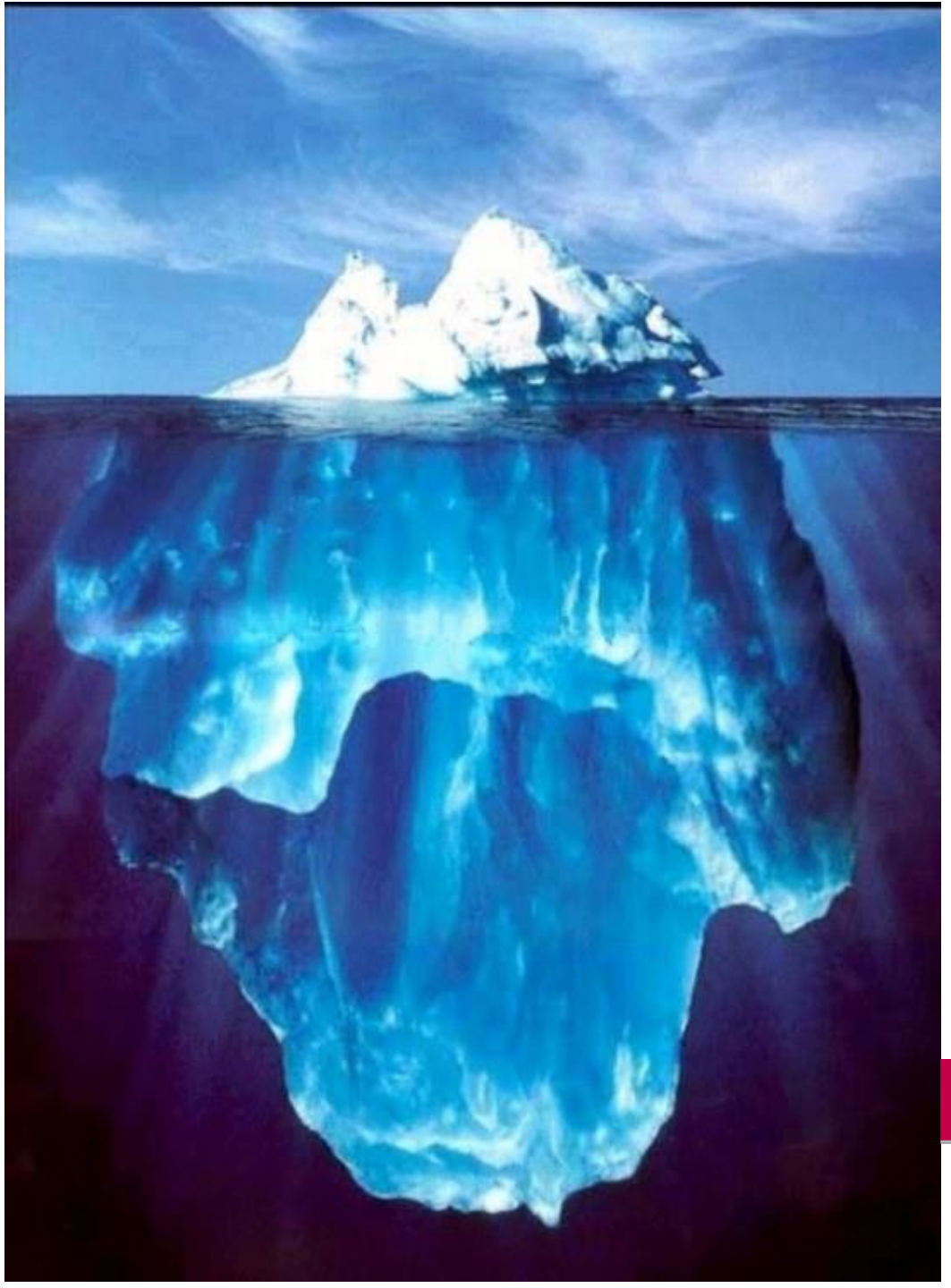
- Los sujetos **VIH (+)** presentan un **número significativamente mayor de CAENC** que los controles (1,3 [SD, 1,14] vs 1,0 [SD, 0,95]; P<0,001)
- La proporción de pacientes con **≥1 CAENC** también es **significativamente mayor entre los pacientes VIH (+)** (69,4% vs 61,8%; P=0,009)
- El **número medio de CAENC** en las categorías de edad 50–54 años, 60–64 años, y ≥65 años fue **significativamente mayor entre los pacientes VIH (+).**

Schouten J et al. Clin Infect Dis 2014:59:1787–1797

The “Fourth 90”: Health-Related Quality of Life

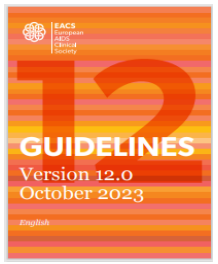


Lazarus. BMC Med. 2016;94. WHO. Draft Global Health Strategy on HIV. 2016. unaids.org/sites/default/files/media_asset/201506_JC2743_Understanding_FastTrack_en.pdf.



- Las **comorbilidades reconocidas** que **más afectan a las PVVIH** incluyen:
  - Trastornos cardiovasculares
  - Trastornos pulmonares
  - Trastornos hepáticos
  - Trastornos metabólicos
  - Neoplasias
  - Trastornos renales
  - Trastornos óseos
  - Trastornos del sistema nervioso
  - Disfunciones sexuales
  - Alteraciones Neuropsiquiátricas

Panel de expertos del Grupo de estudio de SIDA (GeSIDA) y de la Sociedad Española de Medicina de Familia y Comunitaria (semFYC). MANEJO COMPARTIDO DEL PACIENTE CON INFECCIÓN POR VIH ENTRE ATENCIÓN PRIMARIA Y HOSPITALARIA, MADRID; Feb 2022. disponible en: https://gesida-seimc.org/wp-content/uploads/2021/09/Documento_AP.pdf



Part IV

GeSIDA
GRUPO DE ESTUDIO DEL SIDA-SEIMC

MANEJO DE LA ENFERMEDAD HEPÁTICA EN PERSONAS QUE VIVEN CON VIH

MANEJO COMPARTIDO DEL PACIENTE CON INFECCIÓN POR VIH ENTRE ATENCIÓN PRIMARIA Y HOSPITALARIA

DOCUMENTO DE CONSENSO SOBRE EL MANEJO CLÍNICO DE LA COMORBILIDAD NEUROPSIQUIÁTRICA Y COGNITIVA ASOCIADA A LA INFECCIÓN POR VIH-1

DOCUMENTO DE CONSENSO DE GeSIDA PARA LA EVALUACIÓN Y EL TRATAMIENTO DE LAS ENFERMEDADES RENALES EN PACIENTES CON INFECCIÓN POR EL VIRUS DE LA INMUNODEFICIENCIA HUMANA

GUÍA DE PRÁCTICA CLÍNICA SOBRE LOS TUMORES NO DEFINITORIOS DE SIDA E INFECCIÓN POR EL VIH

DOCUMENTO DE CONSENSO SOBRE ALTERACIONES METABÓLICAS Y RIESGO CARDIOVASCULAR EN PACIENTES CON INFECCIÓN POR EL VIH

Actualización Febrero 2017

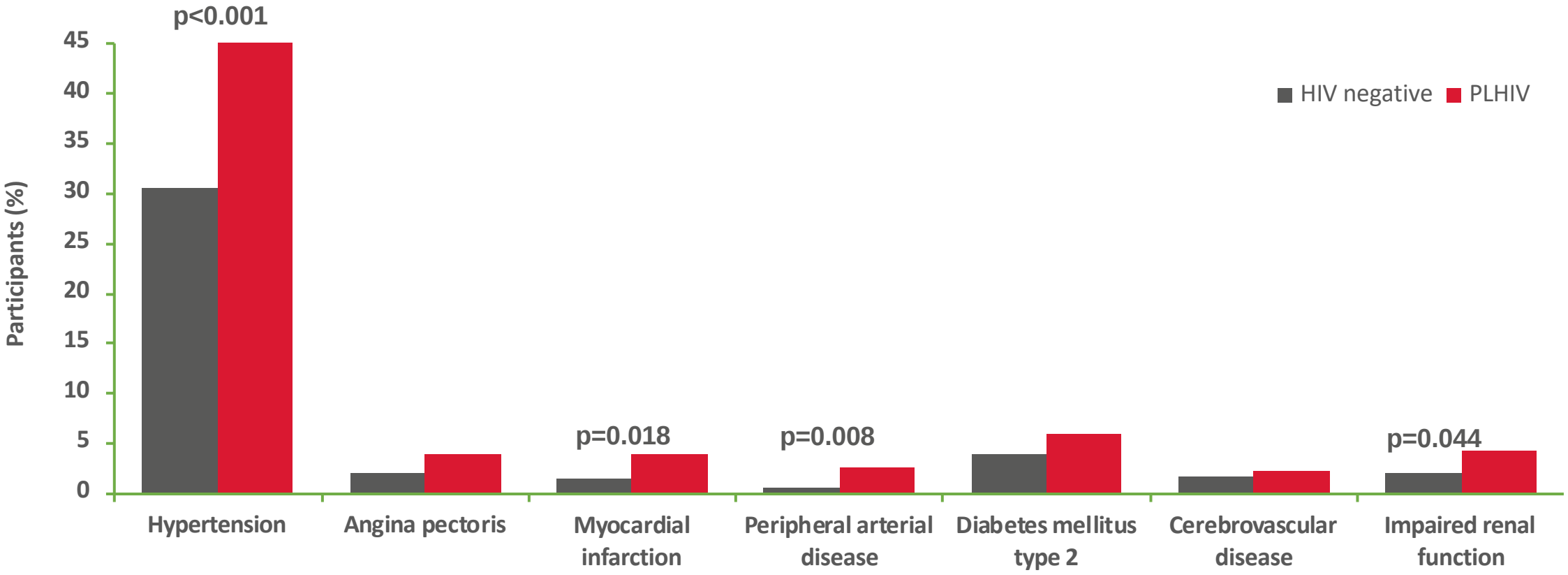
DOCUMENTO DE CONSENSO SOBRE LA OSTEOPOROSIS EN LA INFECCIÓN POR EL VIH.

MAYO 2016

E. Cardiovasculares

Cohorte AGEhIV: PVVIH tienen mayor riesgo de ECV que la población general.

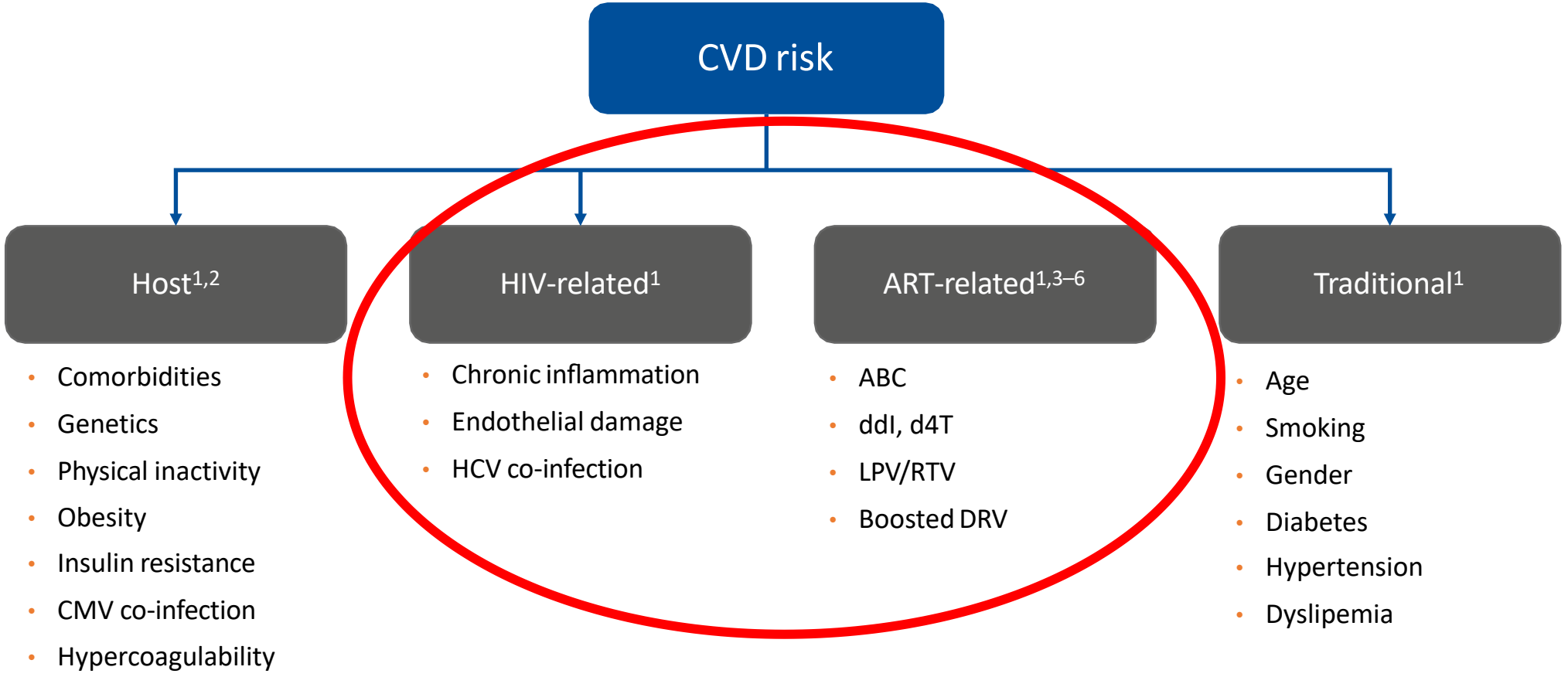
Group comparison of PLHIV aged ≥45 years and HIV-negative people attending a public sexual health clinic between October 2010 and September 2012



p-values obtained by chi-squared test.

CV, cardiovascular; PLHIV, people living with HIV.
Schouten J, et al. *Clin Infect Dis* 2014;59:1787–97.

Factores implicados

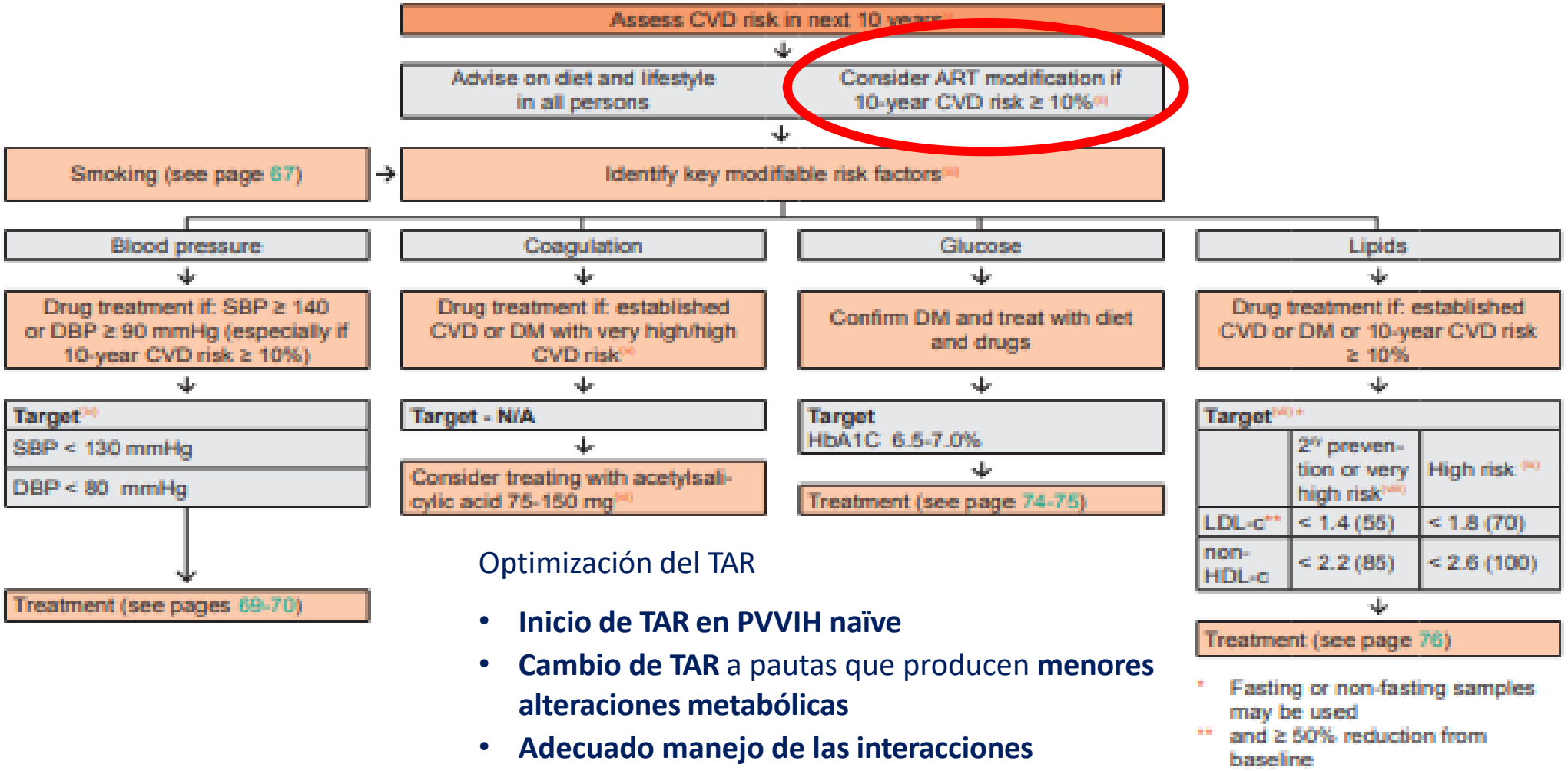


Debemos identificar los **FRCV modificables** y a los pacientes con RCV elevado para **implementar medidas preventivas y terapéuticas**

ABC, abacavir; CMV, cytomegalovirus; CVD, cardiovascular disease; d4T, stavudine; ddI, didanosine; DRV, darunavir; HCV, hepatitis C virus; LPV, lopinavir; PLHIV, people living with HIV; RTV, ritonavir.

1. De Gaetano Donati K, et al. *J Hematol Infect Dis* 2010;2:e2010034; 2. Lichtner M, et al. *J Infect Dis* 2015;211:178–86; 3. Shahbaz S, et al. *World J Cardiol* 2015;7:633–44. 4. Lundgren JD, et al. CROI 2009, #44LB; 5. Ryom L, et al. CROI 2017, #128LB; 6. Elion R. *J Acquir Immune Defic Syndr* 2018;78:62–72.

Prevención de ECV



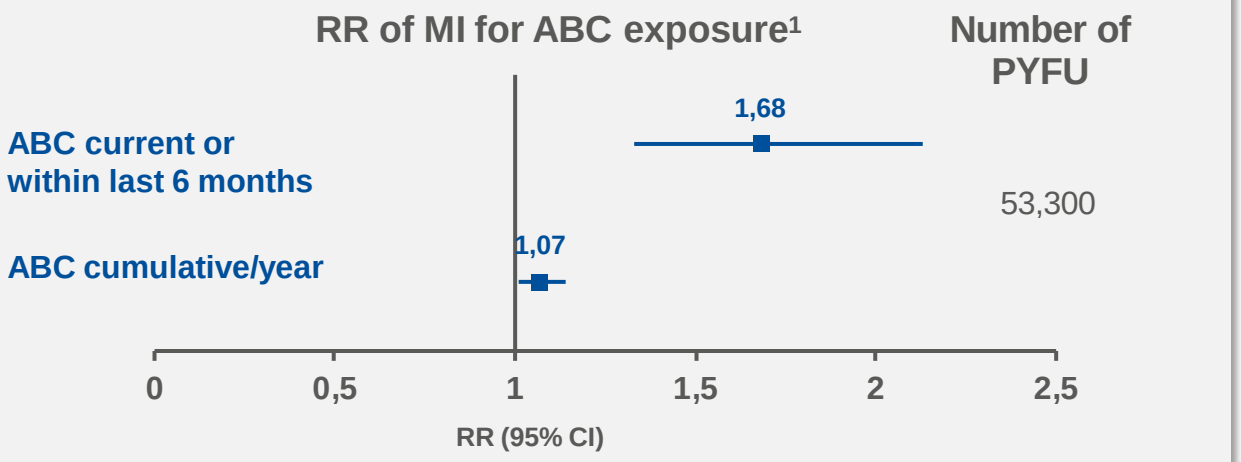
Optimización del TAR

- **Inicio de TAR en PVVIH naïve**
- **Cambio de TAR** a pautas que producen **menores alteraciones metabólicas**
- **Adecuado manejo de las interacciones**

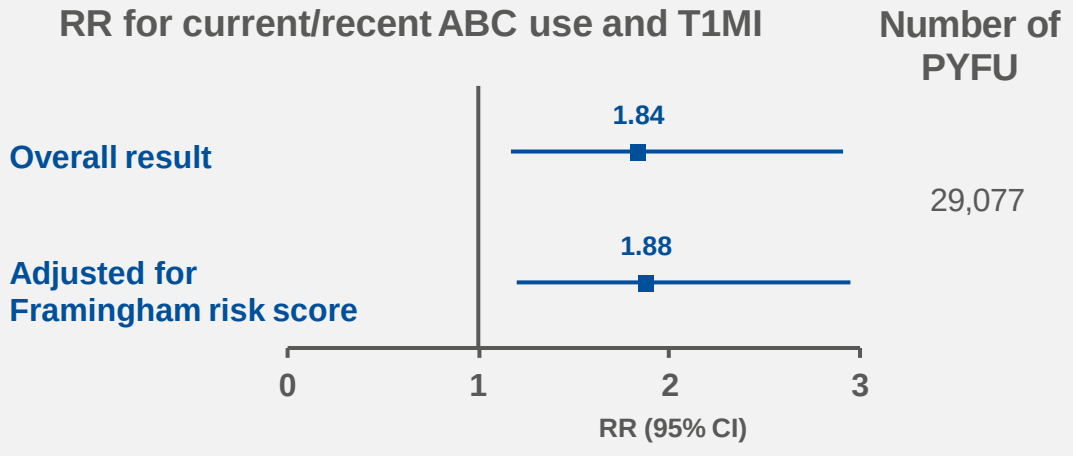
EACS Guidelines Version 12.0, October 2023. Available at: https://www.eacsociety.org/files/2019_guidelines-12.0_final.pdf. Last accessed: October 2023

Exposición reciente a ABC puede asociarse con aumento de riesgo de IM

D:A:D study population of 33,308 PLHIV, followed from enrolment until first MI event, February 2008 or 6 months after the last clinic visit[1]



NA-ACCORD study population of 8,265 PLHIV, observed to initiate ART, occurrence of MI (2001–2013)[2]



- There is additional evidence in favour of [3–9] and against[10–14] the association between ABC and CVD
- **No consensus** has been reached on the association between **ABC and MI**
- **ddI** has been significantly associated with **increased risk of MI[1]**
- **AZT** and **d4T** have been linked with the **development of CV risk factors[3]***

* CV risk factors linked to AZT and d4T include dyslipidaemia, insulin resistance, increased risk of diabetes mellitus and greater intima media thickness[3]

ABC, abacavir; ART, antiretroviral therapy; AZT, zidovudine; CI, confidence interval; CV, cardiovascular; CVD, cardiovascular disease; d4t, stavudine; ddI, didanosine; FDA, US Food and Drug Administration; T1MI, Type 1 myocardial infarction; PLHIV, people living with HIV; PYFU, person-years of follow-up; RCT, randomised control trial; RR, relative risk;

1. Lundgren JD, et al. CROI 2009; #441LB. 2. Elion RA, et al. *J Acquir Immune Defic Syndr.* 2018;78:62–72. 3. SMART/INSIGHT and D:A:D Study Groups. *AIDS.* 2008;22:F17–24. 4. Obel N, et al. *HIV Med.* 2010;11:130–6. 5. Choi AI, et al. *AIDS* 2011;25:1289–98; 6. Durand M, et al. *J Acquir Immune Defic Syndr* 2011;57:245–53; 7. Young J, et al. *J Acquir Immune Defic Syndr* 2015;69:413–21; 8. Marcus JL, et al. *J Acquir Immune Defic Syndr* 2016;71:413–9; 9. Sabin CA, et al. *BMC Med* 2016;14:61. 10. Lang S, et al. *Arch Intern Med* 2010;170:1228–38. 11. Brothers CH, et al. *J Acquir Immune Defic Syndr* 2009;51:20–8. 12. Bedimo RJ, et al. *Clin Infect Dis* 2011;53:84–91; 13. Ribaudo HJ, et al. *Clin Infect Dis* 2011;52:929–40; 14. Ding X, et al. *J Acquir Immune Defic Syndr* 2012;61:441–7.

El uso de IPs se ha asociado con un aumento del RCV

RTV

- Increase in levels of CV risk biomarkers[1,2]
- Platelet dysregulation[3]
- Cardiac dysfunction and fibrosis[4]

DRV

- 38% annual increase in coronary artery calcium[5]
- 26% annual increase in total plaque score[5]
- 59% CV risk increase per 5 years of exposure[6]

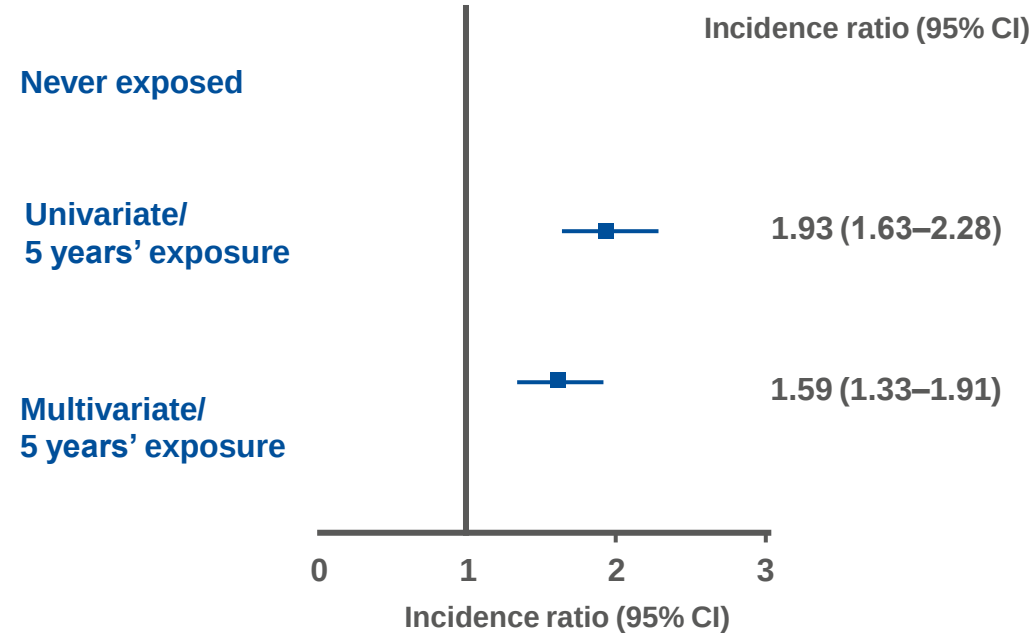
Older PIs

LPV and IDV:

- Increased risk of MI[7]
- Ischaemic heart disease[8]

D:A:D study population of 35,711 PLHIV (2009–2016)[6]

Association between CVD IRR and cumulative use of DRV/r**



*Large observational cohort studies have found an association between some PIs (ie., DRV/r, FPV, IDV, and LPV/r) and an increased risk of CV event; however this risk was not seen with ATV; †Primary model; baseline adjustment only for variables on the potential causal pathway between PI/RTV use and CVD; CVD defined as in previous D:A:D analyses as a composite endpoint including the following centrally adjudicated events: MI, stroke, sudden cardiac death and invasive cardiovascular procedures.
ART, antiretroviral therapy; CI, confidence interval; CV, cardiovascular; CVD, cardiovascular disease; D:A:D, Data Collection on Adverse Events of anti-HIV Drugs; DRV/r, darunavir/ritonavir; IRR, incidence rate ratio; MI, myocardial infarction; PLHIV, people living with HIV; RR, relative risk; RTV, ritonavir; SAD, sudden arrhythmic death.

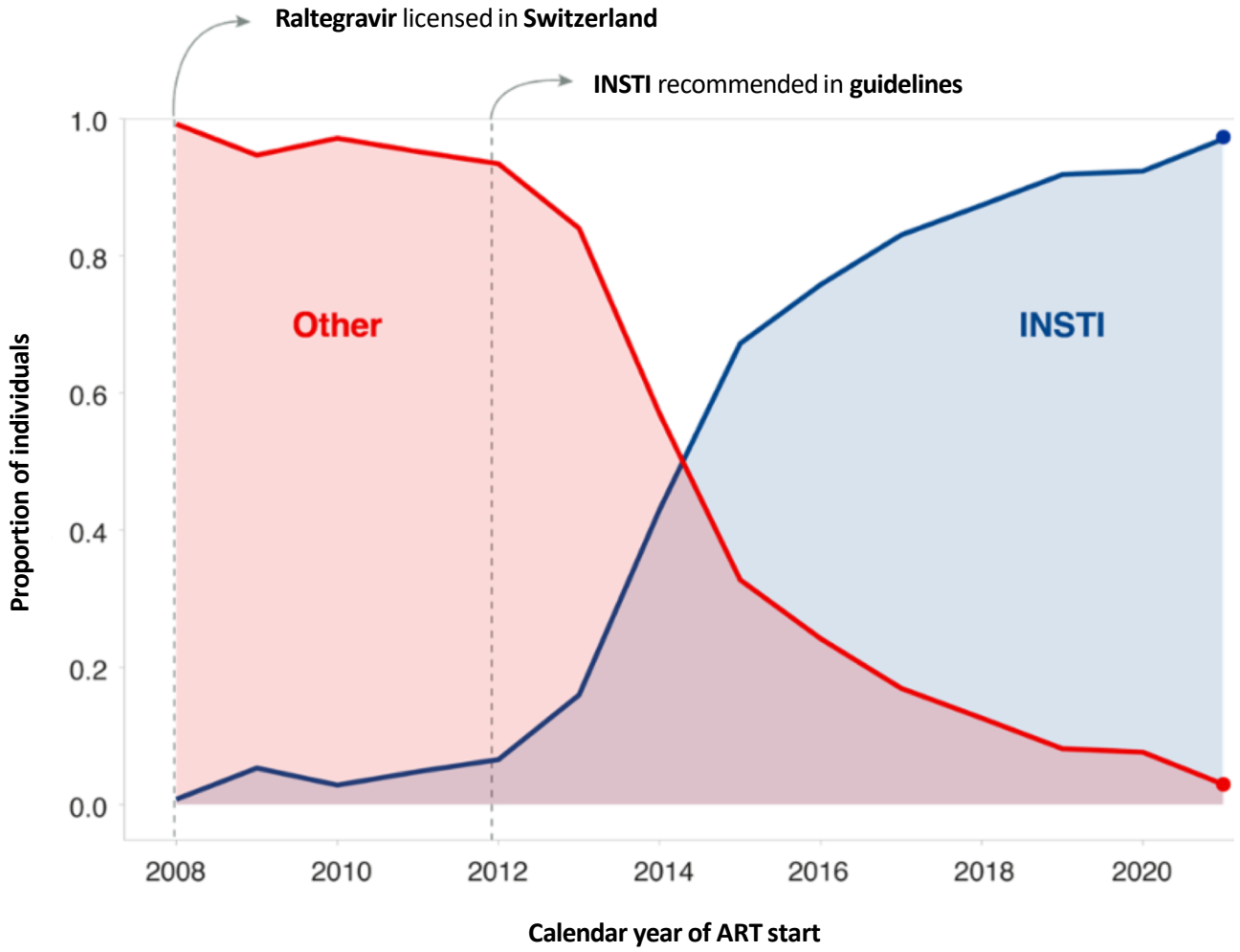
1. Mikhail N, et al. *Curr Hypertens Rep* 2003;5:117–21; 2. Lundgren J, et al. *Curr Opin Infect Dis* 2018;31:8–13; 3. Loelius SG, et al. *Thromb Res* 2018;169:96–104; 4. Laurence J, et al. *PLoS One* 2017;12:e0187185; 5. Ryom L, et al. *Lancet HIV* 2018;5:e291–e300; 6. Ryom L, et al. CROI 2017. #128LB.. 7. Lundgren JD, et al. CROI 2009. #44LB; 8. EACS guidelines. Version 9.1, October 2018. Available at: www.eacsociety.org/files/2018_guidelines-9.1-english.pdf. Last accessed: September 2019

Approximately one third of the PI-related excess risk for MI in D:A:D is due to DM, HT, or lipids

	Adjusted Model 1		Adjusted Model 2	
	Relative Rate (95% CI)	P Value	Relative Rate (95% CI)	P Value
Exposure to PIs (per year)	**1.16 (1.10-1.23)**	**<0.001**	**1.10 (1.04-1.18)**	**0.002**
Age (per 5 yr)	1.39 (1.31-1.46)	<0.001	1.32 (1.23-1.41)	<0.001
Male sex	1.91 (1.28-2.86)	0.002	2.13 (1.29-3.52)	0.003
BMI >30 kg/m^2	1.70 (1.08-2.69)	0.02	1.34 (0.77-2.34)	0.31
Family history of CHD	1.56 (1.10-2.23)	0.01	1.40 (0.96-2.05)	0.08
Smoking status				
Current	2.83 (2.04-3.93)	<0.001	2.92 (2.04-4.18)	<0.001
Former	1.65 (1.12-2.42)	0.01	1.63 (1.07-2.48)	0.02
Previous cardiovascular event	4.30 (3.06-6.03)	<0.001	4.64 (3.22-6.69)	<0.001
Diabetes mellitus	**-**	**-**	**1.86 (1.31-2.65)**	**<0.001**
Hypertension	**-**	**-**	**1.30 (0.99-1.72)**	**0.06**
Total cholesterol (per mmol/L increase)	**-**	**-**	**1.26 (1.19-1.35)**	**<0.001**
HDL cholesterol (per mmol/L increase)	**-**	**-**	**0.72 (0.52-0.99)**	**0.05**

D:A:D Study Group. Clin Infect Dis 2008

INSTI no se asocian con mayor riesgo de evento cardiovascular. HIV Swiss Cohort

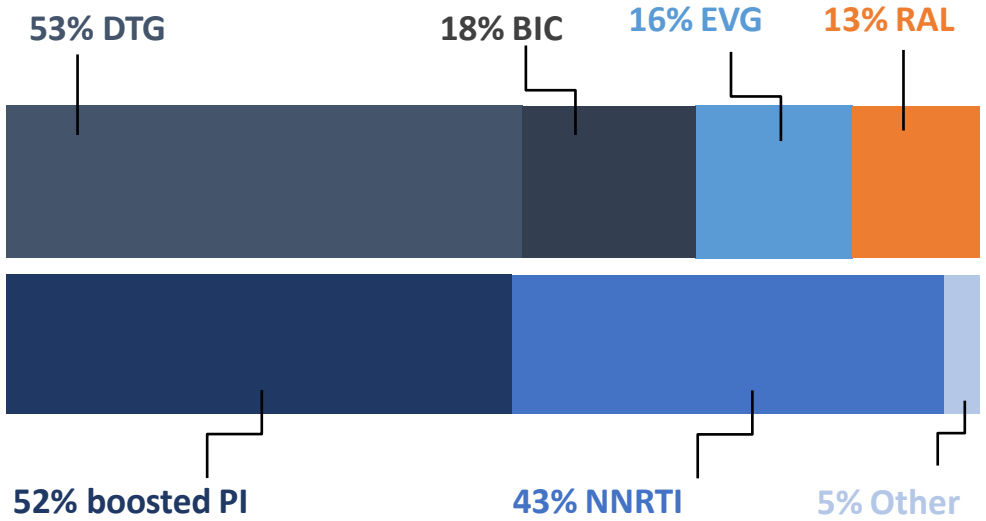


Características basales (5362 participantes naive -INI vs otra pauta-):

- ✓ Edad (39 años) Mujeres (40%)
- ✓ Historia CVD (2%)
- ✓ HTA (20%) DM (4%)
- ✓ Fumadores (47%)

Evento CV:

- ✓ IAM,
- ✓ ictus,
- ✓ cateterismo

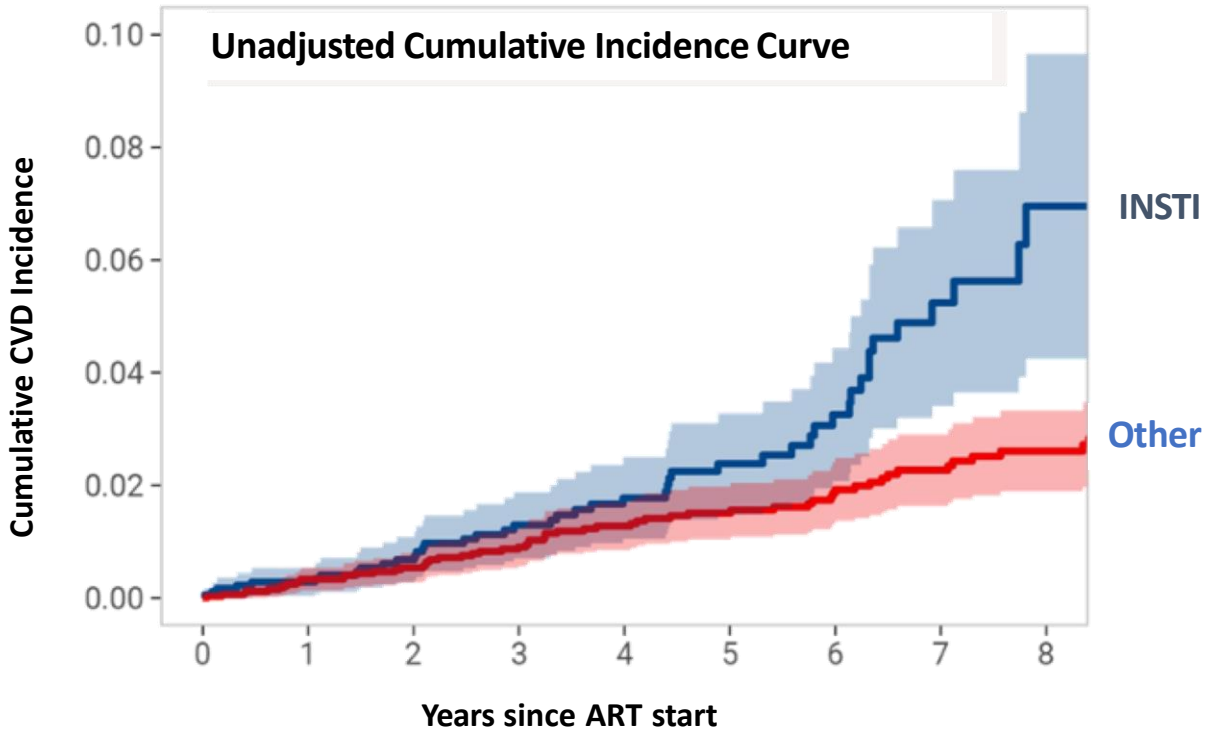


Integrasa: ABC (23%) TAF (40%)
Otros: ABC (12%) TAF (1.4%)

Surial B. et al. 30th CROI. Seattle, Washington 2023. #149

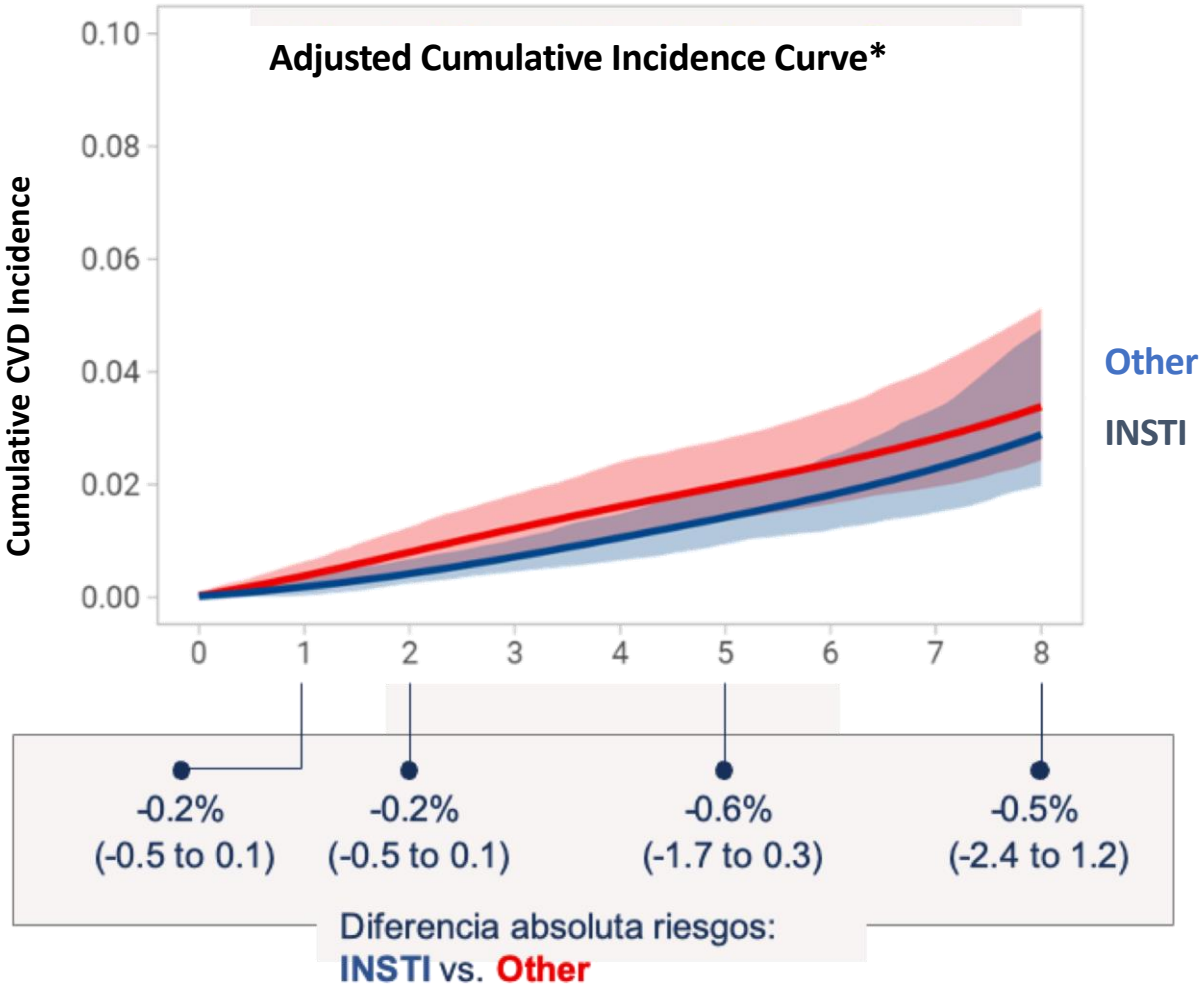
INSTI no se asocian con mayor riesgo de evento cardiovascular. HIV Swiss Cohort

116 events en 4’9 años (IQR 2’4-7,4)



Number at risk

INSTI	1813	1615	1398	1165	945	722	504	275	130
Other	3549	3161	2855	2522	2227	1933	1582	1261	976



Surial B. et al. 30th CROI. Seattle, Washington 2023. #149

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 24, 2023 VOL. 389 NO. 8

Pitavastatin to Prevent Cardiovascular Disease in HIV Infection

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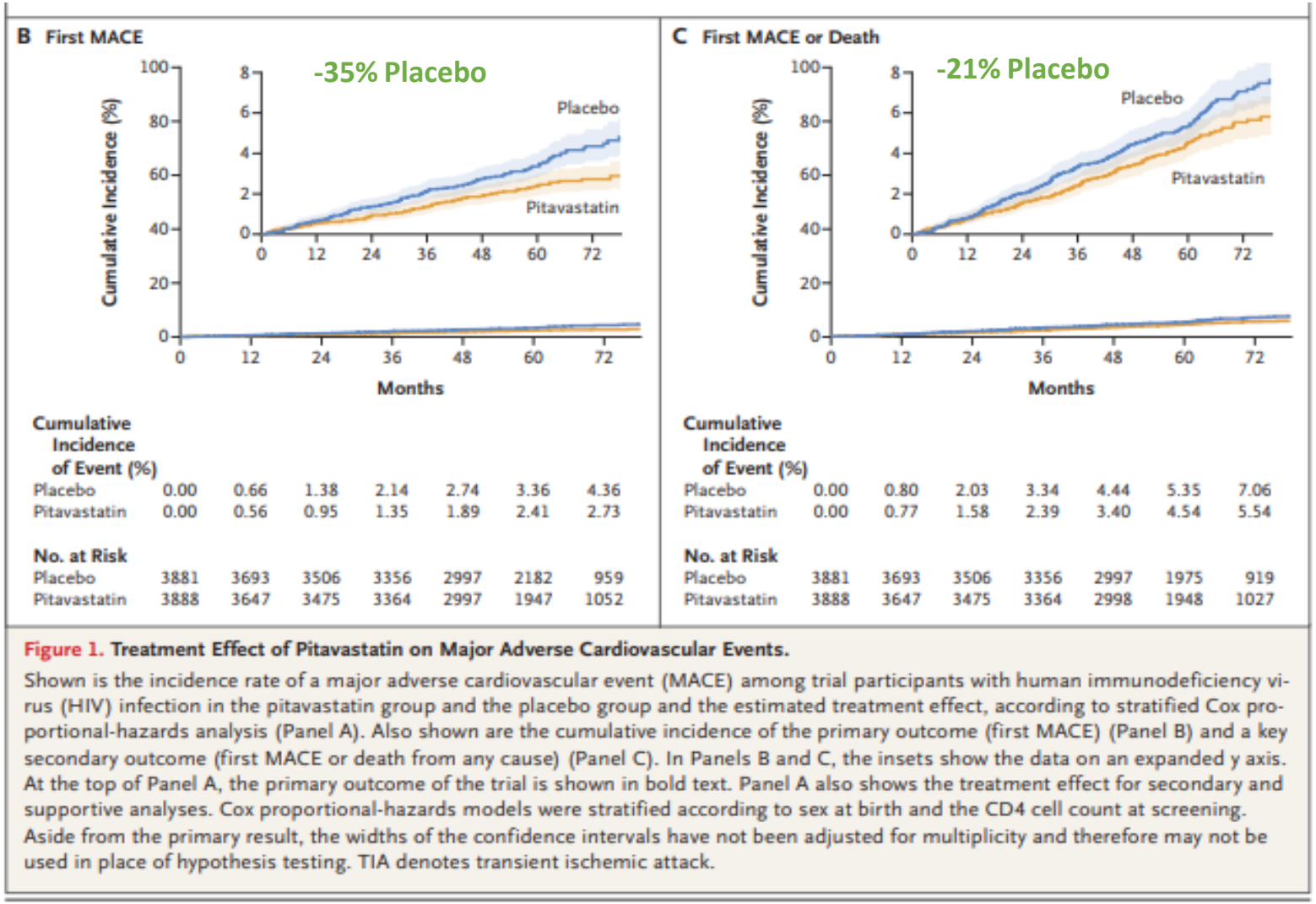
- **Estatina**:
  - Disminuye el LDL-C.
  - Actúa sobre la inflamación e inmuno-activación
- **Estatina** y **TAR** podrían reducir el RCV en PVVIH en TAR con RCV bajo/moderado
- **Otras estatinas** podrían tener efectos similares (se escogió la Pitavastatina por ser la estatina con menos interacciones con el TAR).

REPRIEVE

- RCV está aumentado en PVVIH.
- Estudio en fase 3, **7769 PVVIH** que reciben **TAR** con **RCV bajo-moderado:**
  - **PITAVASTATINA 4 mg al día**
  - **PLACEBO**
- Objetivo primario: **MACE** ("Major Adverse Cardiovascular Event": muerte cardiovascular, IAM, ingreso por ángor inestable, ACV, AIT, isquemia arterial periférica, revascularización).
- Media de edad 50 años (**40-75 años**), CD4 621, ARN-VIH indetectable en el 87,5% de los pacientes.
- **PVVIH TAR CON RCV BAJO/MODERADO QUE RECIBEN PITAVASTATINA TIENEN MENOR RIESGO DE MACE (seguimiento de 5,1 años)**



Cumulative Incidence of Event (%)							
Placebo	0.00	0.66	1.38	2.14	2.74	3.36	4.36
Pitavastatin	0.00	0.56	0.95	1.35	1.89	2.41	2.73
No. at Risk							
Placebo	3881	3693	3506	3356	2997	2182	959
Pitavastatin	3888	3647	3475	3364	2997	1947	1052

Cumulative Incidence of Event (%)							
Placebo	0.00	0.80	2.03	3.34	4.44	5.35	7.06
Pitavastatin	0.00	0.77	1.58	2.39	3.40	4.54	5.54
No. at Risk							
Placebo	3881	3693	3506	3356	2997	1975	919
Pitavastatin	3888	3647	3475	3364	2998	1948	1027

Figure 1. Treatment Effect of Pitavastatin on Major Adverse Cardiovascular Events.

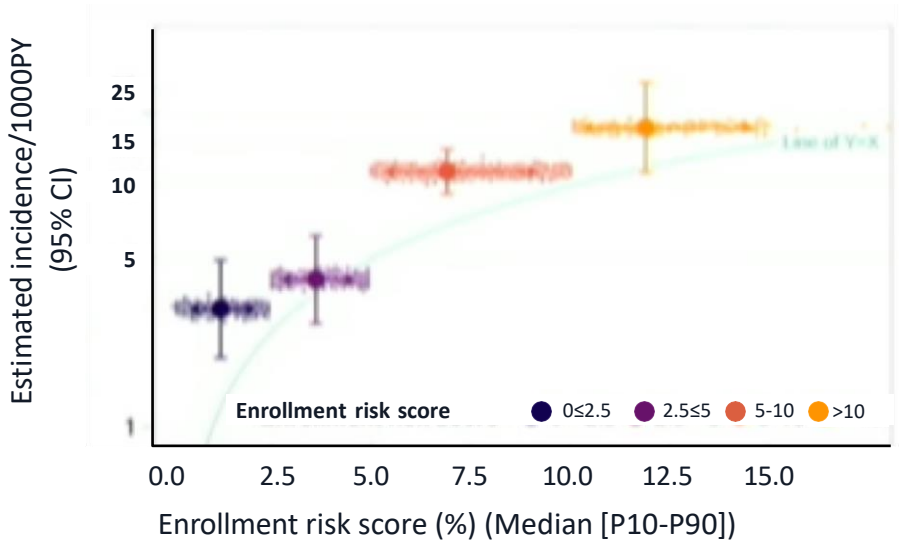
Shown is the incidence rate of a major adverse cardiovascular event (MACE) among trial participants with human immunodeficiency virus (HIV) infection in the pitavastatin group and the placebo group and the estimated treatment effect, according to stratified Cox proportional-hazards analysis (Panel A). Also shown are the cumulative incidence of the primary outcome (first MACE) (Panel B) and a key secondary outcome (first MACE or death from any cause) (Panel C). In Panels B and C, the insets show the data on an expanded y axis. At the top of Panel A, the primary outcome of the trial is shown in bold text. Panel A also shows the treatment effect for secondary and supportive analyses. Cox proportional-hazards models were stratified according to sex at birth and the CD4 cell count at screening. Aside from the primary result, the widths of the confidence intervals have not been adjusted for multiplicity and therefore may not be used in place of hypothesis testing. TIA denotes transient ischemic attack.

Reducción en un 35% el riesgo de MACE y en un 21% de MACE o muerte:

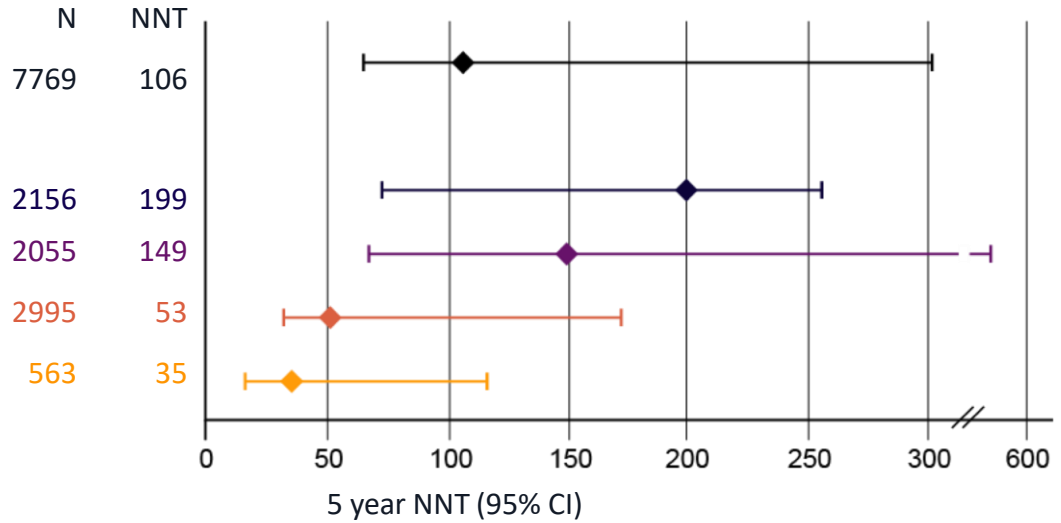
- Independiente de sexo (varones y mujeres).
- Independiente de los niveles de LDL basales.
- Mayor efecto en Asia y Sudeste asiático.

REPRIEVE

- **Número de personas a tratar para evitar 1 MACE <u>mucho menor</u>** que la NNT de la aspirina o de los fármacos para la hipertensión (NNT en el orden de 100).



Increasing MACE events with increasing ASCCVD risk score



Decreasing NNT with increasing ASCCVD risk score

NNT: number needed to treat

S. Grinspoon, et al. IAS 2023; July 23-26, 2023. Abstract SY06

Smoking contributes to myocardial infarction in HIV patients almost twice as much as in the overall population

Population attributable risk

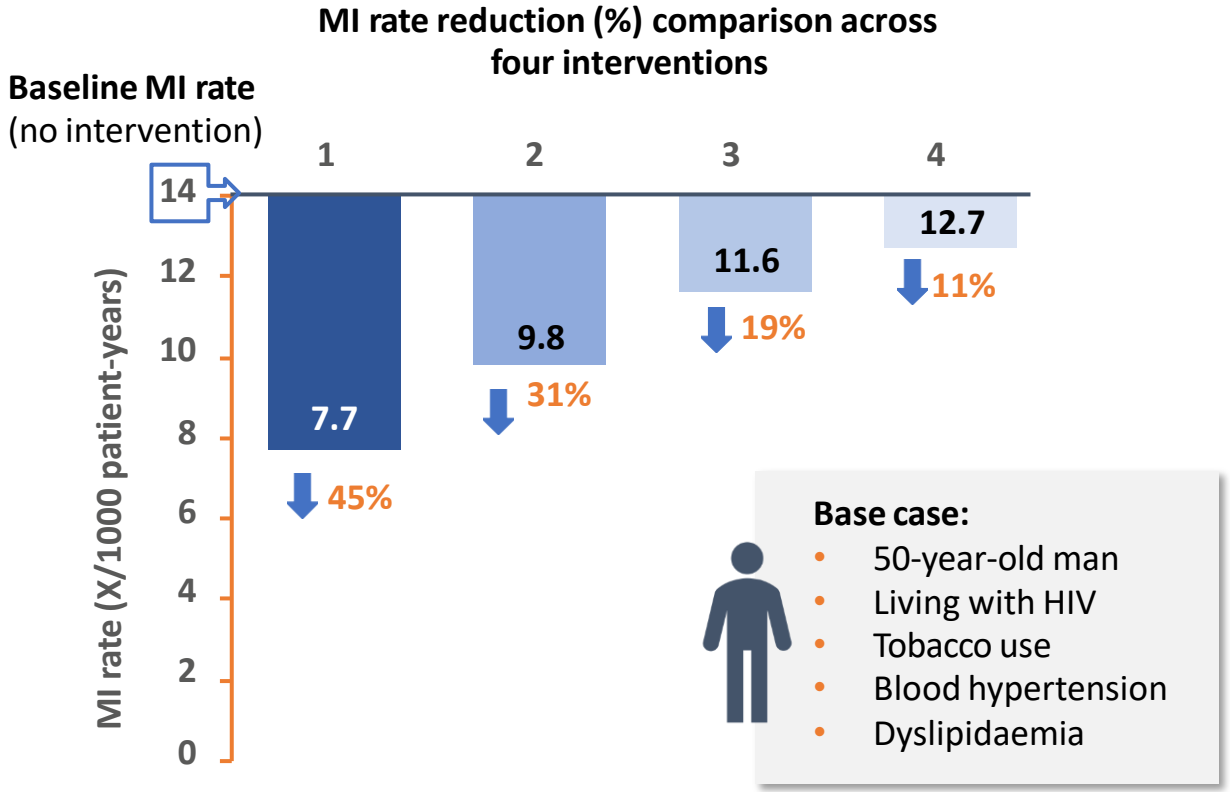
	Smoking	Diabetes	Hypertension	Combination of all 3 factors
HIV+	54.35%	6.57%	9.07%	60.00%
HIV-	30.58%	17.24%	38.81%	68.75%

Calvo M et al. HIV Med 2013

Comparación de las distintas medidas de reducción del riesgo

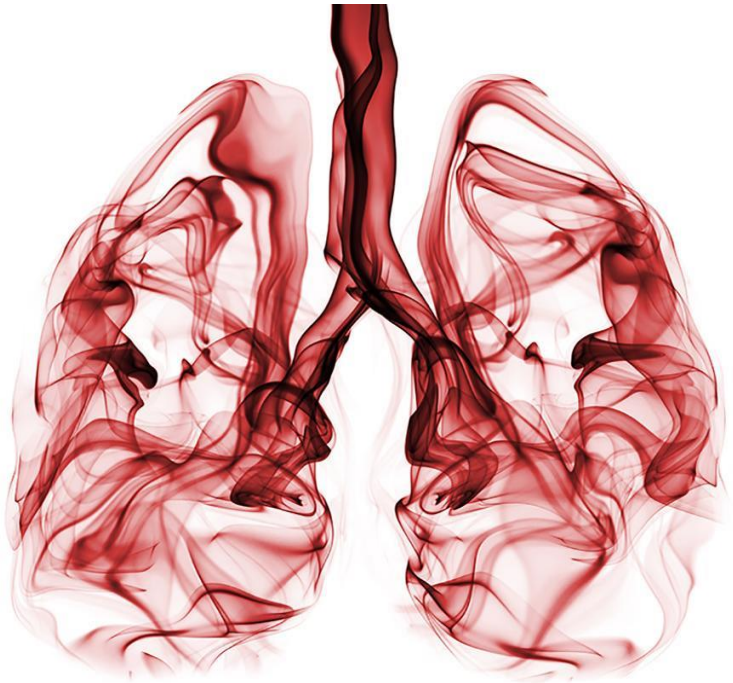
- Decision tree model to estimate the 10-year impact of different interventions on predicted MI rates, based on RWD (publications from the HIV or general population)
- Model adjusted for age, gender and four strategies to reduce MI risk:

1	Substitution of ABC with an alternative agent
2	Lipid-lowering medication use
3	Anti-hypertensive medication use
4	Smoking cessation counselling



Replacing ABC has a greater impact on MI risk than interventions solely based on attempting to modify each of three traditional risk factors

ABC, abacavir; MI, myocardial infarction; PLHIV, people living with HIV; RWD, real-world data.
Hsue P, et al. CROI 2018, #692.

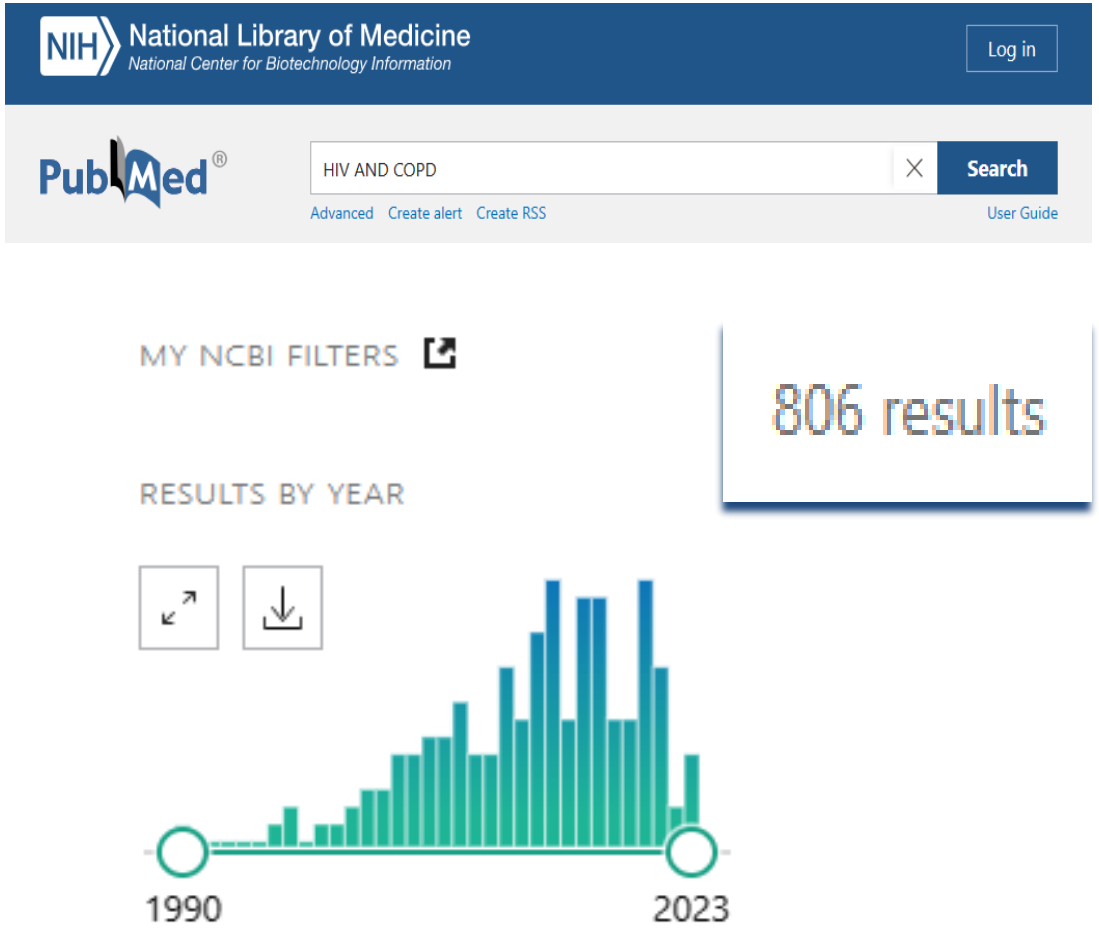


EPOC

EPOC y VIH

Importancia del EPOC en el VIH

- ¿ Es una comorbilidad olvidada en los estudios de cohortes?
- ¿Es frecuente en los pacientes con VIH? y ¿en comparación con lo no VIH?
- El VIH ¿es un factor de riesgo más?
- ¿Está infradiagnosticado?



Chronic obstructive pulmonary disease: an emerging comorbidity in HIV-infected patients in the HAART era?

G. Madeddu · A. G. Fois · G. M. Calia · S. Babudieri · V. Soddu Infection (2013) 41:347–353

Abstract

Purpose The objective of our study was to evaluate the presence of respiratory symptoms and chronic obstructive pulmonary disease (COPD) in a human immunodeficiency virus (HIV)-infected outpatient population and to further investigate the role of highly active antiretroviral therapy (HAART) and other possibly associated risk factors.

Methods We consecutively enrolled in a cross-sectional study HIV-infected patients and HIV-negative age, sex and smoking status matched controls. All participants completed a questionnaire for pulmonary symptoms and underwent a complete spirometry.

Results We enrolled 111 HIV-infected patients and 65 HIV-negative age- and sex-matched controls. HIV-infected patients had a significantly higher prevalence of any respiratory symptom ($p = 0.002$), cough ($p = 0.006$) and dyspnoea ($p = 0.02$). HIV-infected patients also had a significantly higher prevalence of COPD in respect of HIV-negative controls ($p = 0.008$). Furthermore, HIV-infected individuals had significantly ($p = 0.002$) lower forced expiratory volume at one second (FEV1) and FEV1/forced vital capacity (FVC) ratio (Tiffeneau index) ($p = 0.028$), whereas the total lung capacity (TLC) was significantly higher ($p = 0.018$). In the multivariate analysis, significant predictors of respiratory symptoms were current smoking [adjusted odds ratio (AOR) 11.18; 95 % confidence interval (CI) 3.89–32.12] and previous bacterial pneumonia (AOR 4.41; 95 % CI 1.13–17.13), whereas the only significant predictor of COPD was current smoking (AOR 5.94; 95 % CI 1.77–19.96). HAART receipt was not associated with respiratory symptoms nor with COPD.

Conclusions We evidenced a high prevalence of respiratory symptoms and COPD among HIV-infected patients. HIV infection, current cigarette smoking and previous bacterial pneumonia seem to play a significant role in the development of respiratory symptoms and COPD. Thus, our results suggest that the most at-risk HIV-infected patients should be screened for COPD to early identify those who may need specific treatment.

PVVIH tienen una prevalencia significativamente más alta de **cualquier síntoma respiratorio**, tos y disnea, así como de **EPOC.**
Importante “buscarlo” en PVVIH con “alto riesgo”

Review › Curr HIV/AIDS Rep. 2016 Jun;13(3):140-8. doi: 10.1007/s11904-016-0313-0.

Non-infectious Pulmonary Diseases and HIV

M Triplette [1], K Crothers [2], E F Attia [2]

Affiliations + expand

PMID: 27121734 DOI: 10.1007/s11904-016-0313-0

Abstract

Pulmonary complications remain among the most frequent causes of morbidity and mortality for individuals with HIV despite the advent of antiretroviral therapy (ART) and improvement in its efficacy and availability. The prevalence of non-infectious pulmonary diseases is rising in this population, reflecting both an increase in smoking and the independent risk associated with HIV. The unique mechanisms of pulmonary disease in these patients remain poorly understood, and direct effects of HIV, genetic predisposition, inflammatory pathways, and co-infections have all been implicated. Lung cancer, chronic obstructive pulmonary disease (COPD), and pulmonary hypertension are the most prevalent non-infectious pulmonary diseases in persons with HIV, and the risk of each of these diseases is higher among HIV-infected (HIV+) persons than in the general population. This review discusses the latest advances in the literature on these important complications of HIV infection.

Keywords: ART; Antiretroviral therapy; Chronic obstructive pulmonary disease; Complications; Genetic predisposition; Pulmonary complications; Pulmonary disease; Review.

Enfermedades pulmonares no infecciosas más prevalentes en VIH:
- **Cáncer de pulmón**
- **EPOC**
- **HTAP**

* mayor gravedad

Enfermedades pulmonares **suponen una de las causas más frecuentes de morbi-mortalidad** en pacientes con VIH a pesar de la TAR

PREVALENCIA E INCIDENCIA

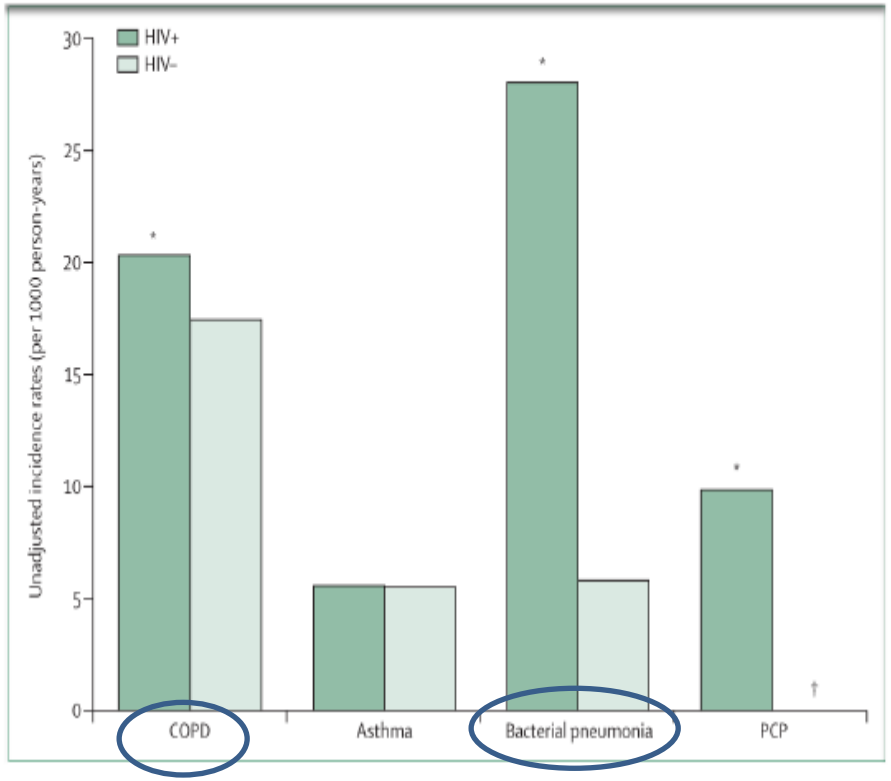
Prevalence of chronic obstructive pulmonary disease in the global population with HIV: a systematic review and meta-analysis

Jean Joel Bigna, Angeladine Malaha Kenne, Serra Lem Asangbeh, Aurelie T Sibetcheu

Findings Of 4036 studies identified, we included 30 studies (151686 participants) from all WHO regions in the meta-analysis of COPD prevalence. 23 studies (77%) had low risk of bias, six (20%) had moderate risk of bias, and one (3%) had high risk of bias in their methodological quality. The overall prevalence of COPD was 10·5% (95% CI 6·2–15·7; I^2=97·2%; six studies) according to the lower limit of normal definition of COPD, and 10·6% (6·9–15·0; 94·7%; 16 studies) according to the fixed-ratio definition. COPD prevalence was higher in Europe and among current and ever smokers, and increased with level of income and proportion of participants with detectable HIV viral load. Prevalence of COPD was significantly higher in patients with HIV than in HIV-negative controls (pooled odds ratio 1·14, 95% CI 1·05–1·25, I^2=63·5%; 11 studies), even after adjustment for tobacco consumption (2·58, 1·05–6·35, 74·9%; four studies).

Mayor prevalencia EPOC en pacientes con VIH.
Prevalencia de EPOC en VIH en Europa y Norte América varía entre 6,8% y 21% .

Cohorte de Veteranos. Incidencia del EPOC en pacientes VIH vs. no VIH



Crothers K, Butt AA, Gibert CL, et al. Increased COPD among HIV-positive compared to HIV-negative veterans. Chest. 2006;130:1326–33.
Gingo MR, George MP, Kessinger CJ, et al. Pulmonary function abnormalities in HIV-infected patients during the current antiretroviral therapy era. Am J Respir Crit Care Med. 2010;182:790–6.
George MP, Kannass M, Huang L, et al. Respiratory symptoms and airway obstruction in HIV-infected subjects in the HAART era. PLoS One. 2009;4:e6328.
Samperiz G, Guerrero D, Lopez M, et al. Prevalence of and risk factors for pulmonary abnormalities in HIV-infected patients treated with antiretroviral therapy. HIV Med. 2014;15:321–9.

Official Journal of the Asian Pacific Society of Respirology
Respirology

INVITED REVIEW SERIES:
UNRAVELLING THE MANY FACES OF COPD TO OPTIMIZE ITS CARE AND OUTCOMES
SERIES EDITORS: GREGORY G KING AND DON SIN

HIV and COPD: a conspiracy of risk factors

UMESH G. LALLOO,[1] SANDY PILLAY,[1] ROSIE MNGQIBISA,[1] SABEER ABDOOL-GAFFAR[2] AND ANISH AMBARAM[3]

[1]*Durban University of Technology,* [2]*Kingsway Hospital, and* [3]*Gateway Private Hospital, Durban, South Africa*

Respirology (2016) **21**, 1166–1172

Entidad **infradiagnosticada** en pacientes con infección por VIH. Se estima que **más del 25%** de los VIH pueden tener EPOC. Aparece a **edades más tempranas**.

AIDS CARE, 2016
VOL. 28, NO. 10, 1338–1343
http://dx.doi.org/10.1080/09540121.2016.1189499

Routledge
Taylor & Francis Group

Chronic obstructive pulmonary disease and HIV: are we appropriately screening?

Bahareh Ghadaki[a], Nadine Kronfli[b], Thuva Vanniyasingam[c] and Shariq Haider[d]

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ABSTRACT

Individuals with human immunodeficiency virus (HIV) represent a population that is at a higher risk of developing chronic obstructive pulmonary disease (COPD). In this study, we sought to determine the effects of smoking on respiratory symptoms and diseases among HIV-positive patients and to determine if symptomatic patients are being appropriately screened for COPD. HIV-positive individuals completed a self-administered questionnaire. The effects of smoking on respiratory symptoms and diseases were reported as odds ratios (ORs). The COPD screening criteria were adapted from the Canadian Thoracic Society (CTS) guidelines. Two hundred and forty-seven participants were recruited. The median age was 49 years; 75% were male and 92% were on highly active antiretroviral therapy. Smokers represented 66% of the population. Smoking had a statistically significant effect on respiratory symptoms including wheeze (OR 4.8 [95% confidence interval (CI) 1.6–14.2]), phlegm production (OR 4.9 [95% CI: 2.2–10.5]), cough (OR 7.0 [95% CI: 3.0–16.2]), and dyspnea (OR 7.2 [95% CI: 1.7–31.2]). Smoking had a higher odds of respiratory diseases including COPD (OR 4.9 [95% CI: 1.1–21.9]) and bronchitis (OR 3.8 [95% CI: 1.9–7.7]). Among HIV-positive smokers, 40% met the CTS screening criteria, while only 12% self-reported a diagnosis of COPD. The burden of smoking in the HIV population is significant. HIV-positive smokers are more likely to report both respiratory symptoms and diseases than HIV-positive non-smokers. A discrepancy exists between patients who met the CTS screening criteria and those who were diagnosed with COPD, raising the concern for under-recognition and under-diagnosis of COPD in this population.

ARTICLE HISTORY
Received 2 November 2015
Accepted 9 May 2016

KEYWORDS
HIV; smoking; COPD; screening

VIH-Fumadores: 40% criterios de EPOC, de ellos, sólo un 12% tenía el diagnóstico de EPOC.
INFRADIAGNÓSTICO EPOC.

HIV and Chronic Obstructive Pulmonary Disease

Is It Worse and Why?

Alison Morris[1], M. Patricia George[1], Kristina Crothers[2], Laurence Huang[3], Lorrie Lucht[1], Cathy Kessinger[1], and Eric C. Kleerup[4] on behalf of the Lung HIV Study

[1]Departments of Medicine and Immunology, University of Pittsburgh, Pittsburgh, Pennsylvania; [2]Department of Medicine, University of Washington, Seattle, Washington; [3]Department of Medicine, University of California, San Francisco, California; and [4]Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, California

PROCEEDINGS OF THE AMERICAN THORACIC SOCIETY VOL 8 2011

Smoking-related diseases, such as chronic obstructive pulmonary disease (COPD), are of particular concern in the HIV-infected population. Smoking rates are high in this population, and long-term exposure to cigarette smoke in the setting of HIV infection may increase the number of complications seen. Before the era of combination antiretroviral therapy, HIV-infected persons were noted to have an accelerated form of COPD, with significant emphysematous disease seen in individuals less than 40 years old. Unlike many of the AIDS-defining opportunistic infections, HIV-associated COPD may be more common in the current era of HIV because it is frequently reported in patients without a history of AIDS-related pulmonary complications and because many aging HIV-infected individuals have had a longer exposure to smoking and HIV. In this review, we document the epidemiology of HIV-associated COPD before and after the institution of combination antiretroviral therapy, review data suggesting that COPD is accelerated in those with HIV, and discuss possible mechanisms of HIV-associated COPD, including an increased susceptibility to chronic, latent infections; an aberrant inflammatory response; altered oxidant-antioxidant balance; increased apoptosis associated with HIV; and the effects of antiretroviral therapy.

EPOC: **“evolución más acelerada”** en VIH.

“FACTORES DE RIESGO”

Official Journal of the Asian Pacific Society of Respirology
Respirology

INVITED REVIEW SERIES:
UNRAVELLING THE MANY FACES OF COPD TO OPTIMIZE ITS CARE AND OUTCOMES
SERIES EDITORS: GREGORY G KING AND DON SIN

HIV and COPD: a conspiracy of risk factors

UMESH G. LALLOO,[1] SANDY PILLAY,[1] ROSIE MNGQIBISA,[1] SABEER ABDOOL-GAFFAR[2] AND ANISH AMBARAM[3]

[1]*Durban University of Technology,* [2]*Kingsway Hospital, and* [3]*Gateway Private Hospital, Durban, South Africa*

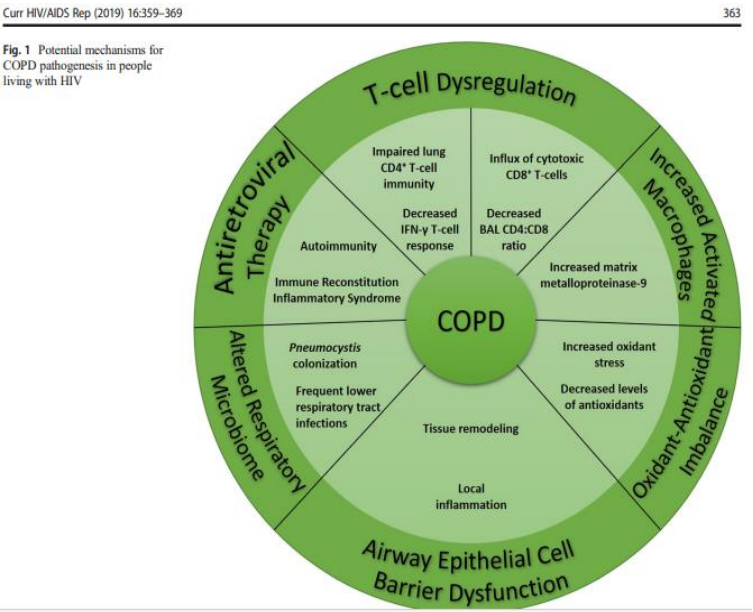


Fig. 1 Potential mechanisms for COPD pathogenesis in people living with HIV

- ✓ **Tabaquismo.**
- ✓ **Inflamación crónica.**
- ✓ **Carga viral VIH** (podría modular la severidad de EPOC en VIH).
- ✓ **CD4** (<200: descenso DLCO y FEV1, enfisema).
- ✓ **TAR** (IRIS, autoinmunidad).
- ✓ Presencia de **VIH “residual” en el pulmón** a pesar del TAR y de la carga vírica indetectable en sangre (macrófagos alveolares como reservorio).
- ✓ **Alteración del microbioma pulmonar** (asociación entre colonización por P. jirovecii y obstrucción al flujo aéreo, independientemente de la historia de tabaquismo).

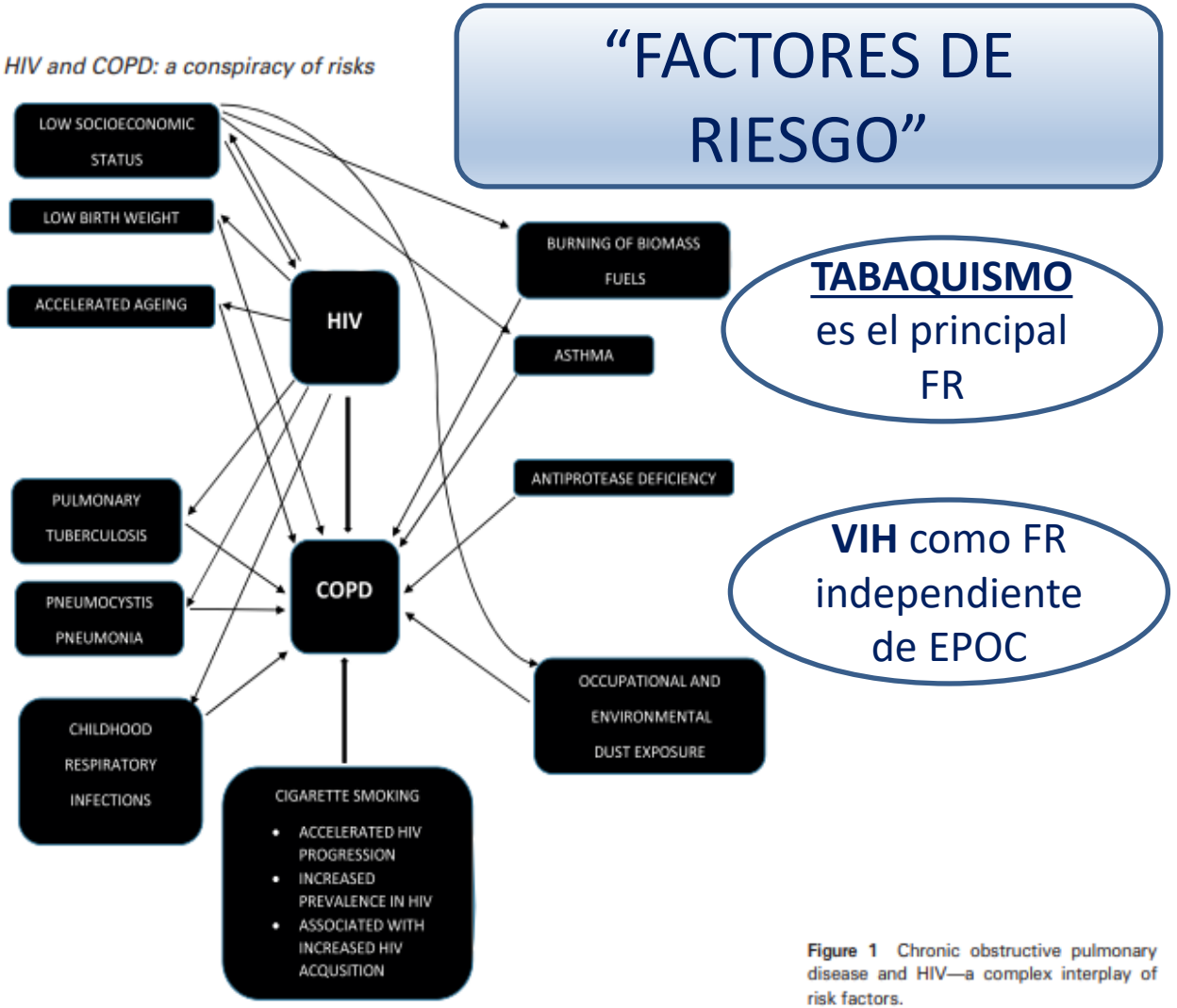


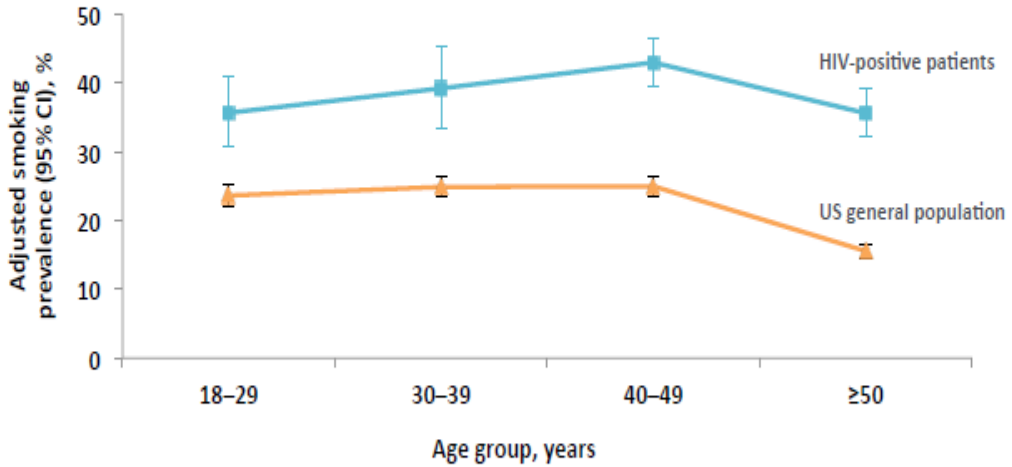
Figure 1 Chronic obstructive pulmonary disease and HIV—a complex interplay of risk factors.

TABAQUISMO es el principal FR

VIH como FR independiente de EPOC

La prevalencia del tabaquismo es el doble entre los pacientes VIH (+) que en la población general

Prevalencia de consumo de cigarrillos entre pacientes VIH (+) que recibieron cuidados médicos vs la población general (NHIS) en Estados Unidos, 2009[1]

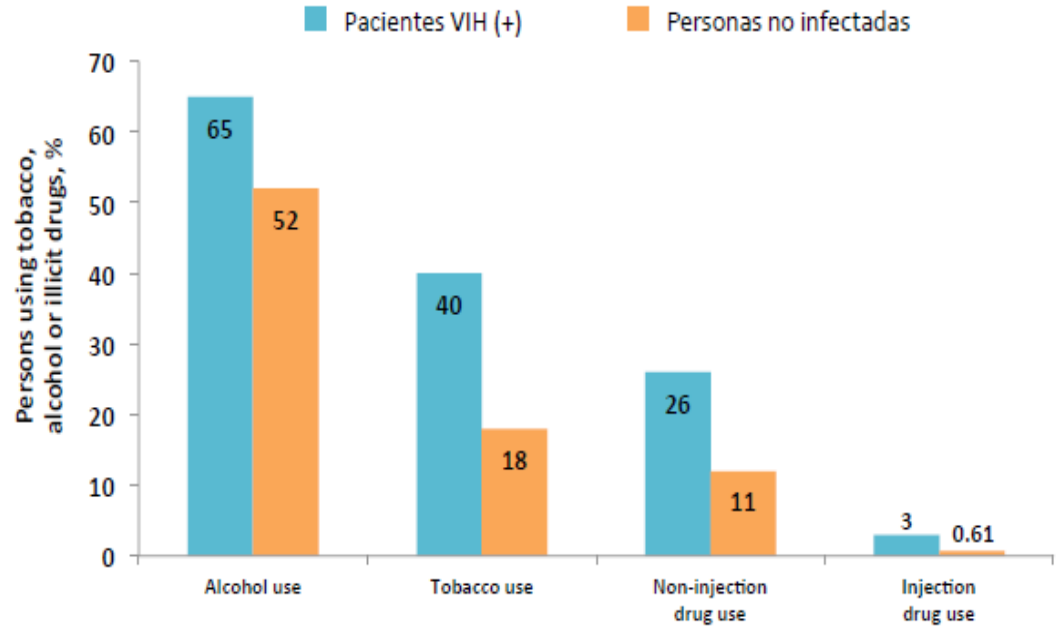


- Las personas VIH (+) que fuman cigarrillos tienen un mayor riesgo de mortalidad por cualquier causa cuando se comparan con pacientes VIH (+) que nunca han fumado[2,3]

1. Mdodo R et al. Ann Intern Med 2015;162:335–344; 2. Feldman JG et al. Am J Public Health 2006;96:1060–1065; 3. Crothers K et al. J Gen Intern Med 2005;20:1142–1145

Algunos pacientes VIH (+) tienen conductas de riesgo de forma más frecuente que la población general

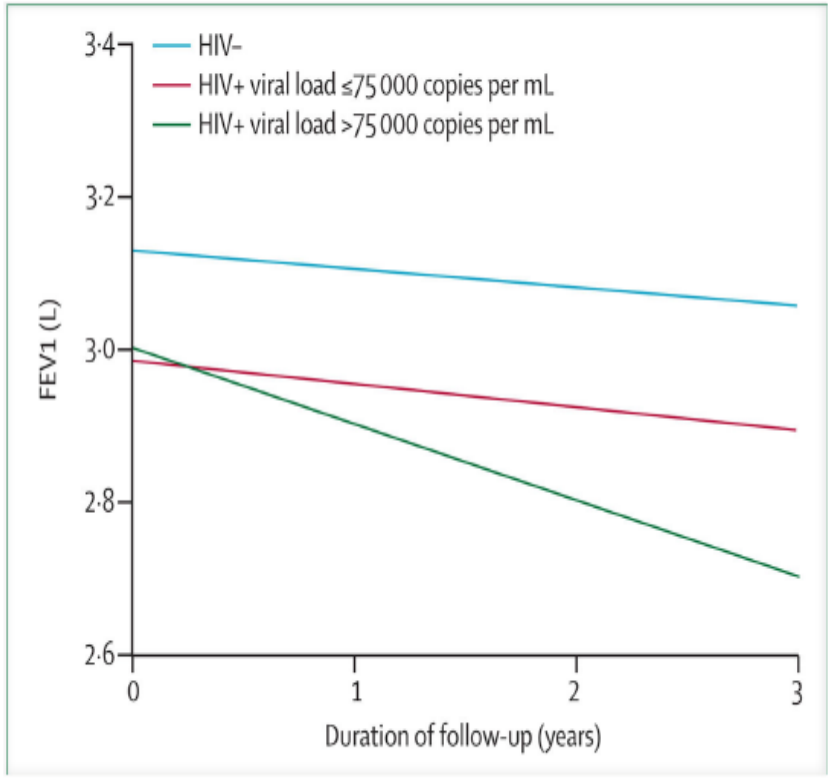
Prevalencia del uso de tabaco, alcohol, y drogas ilícitas entre pacientes VIH (+) e individuos no infectados[1–3]



- El uso de tabaco, alcohol y drogas ilícitas es mayor entre los pacientes VIH (+)

1. CDC. Behavioral and Clinical Characteristics of Persons Receiving Medical Care for HIV Infection—Medical Monitoring Project, United States, 2011. HIV Surveillance Special Report 10; 2. CDC. Summary Health Statistics for US Adults: National Health Interview Survey, 2012; 3. United Nations Office on Drugs and Crime, World Drug Report 2014

Higher viral load is associated with more rapid annual FEV1 decline



Drummond MB, et al. AIDS. 2013; 27:1303–11.

Decreased Lung Function and All-Cause Mortality in HIV-infected Individuals

Matthew R. Gingo[1], Mehdi Nouraie[1], Cathy J. Kessinger[1], Ruth M. Greenblatt[2,3], Laurence Huang[3], Eric C. Kleerup[4], Lawrence Kingsley[5], Deborah K. McMahon[1], and Alison Morris[1,6]

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Abstract

Rationale: Human immunodeficiency virus (HIV) infection is associated with pulmonary disease and worse lung function, but the relationship of lung function with survival in HIV is unknown.

Objectives: To determine whether lung function is associated with all-cause mortality in HIV-infected individuals.

Methods: HIV-infected participants from cohorts in three locations underwent pre- and post-bronchodilator spirometry and determination of single-breath diffusing capacity of the lung for carbon monoxide (D_{LCO}) in 2008–2009, computed tomographic (CT) scanning of the chest for quantitative emphysema and airway measures, and echocardiography for estimated left ventricular systolic and diastolic function and tricuspid regurgitant velocity. Bivariate analysis and multivariable Cox proportional hazards models were used to determine whether decreased lung function was independently associated with increased all-cause mortality. Models were adjusted for covariates including age, sex, body mass index, smoking status, self-reported hepatitis C status, HIV viral levels, $CD4^+$ T-cell counts, hemoglobin, antiretroviral therapy, and illicit drug use.

Results: Overall, 396 HIV-infected participants underwent pulmonary function testing. Thirty-two participants (8%) died during a median follow-up period of 69 months. A post-bronchodilator FEV_1-to-FVC ratio less than 0.7 (hazard ratio [HR], 2.47; 95% confidence interval [CI], 1.10–5.58) and a D_{LCO} less than 60% (HR, 2.28; 95% CI, 1.08–4.82) were independently associated with worse mortality. Also, hepatitis C (HR, 2.68; 95% CI, 1.22–5.89) and baseline plasma HIV RNA level (HR per ln RNA copies/ml, 1.50; 95% CI, 1.22–1.86) were associated with mortality in HIV-infected participants. The only CT or echocardiographic measure associated with greater mortality in univariate analysis was greater wall thickness of medium-sized airways (HR for wall area percent, 1.08; 95% CI, 1.00–1.18; $P = 0.051$), but none of the CT or echocardiogram measures were associated with mortality in multivariable analysis.

Conclusions: Airflow obstruction and impaired diffusing capacity appear to be associated with all-cause mortality in HIV-infected persons over an average of 6 years of follow-up. These data highlight the importance of lung dysfunction in HIV-infected persons and should be confirmed in larger cohorts and with extended follow-up periods.

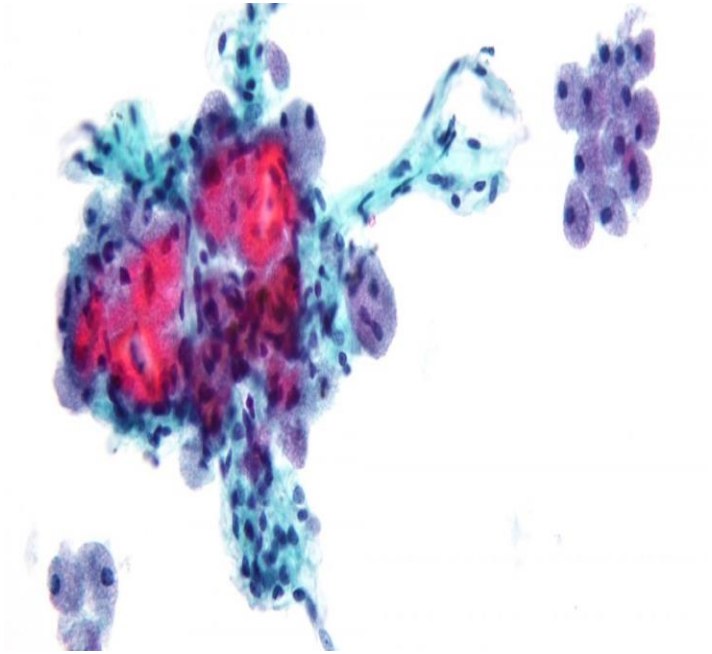
Clinical trial registered with www.clinicaltrials.gov (NCT00869544, NCT01326572).

Keywords: HIV; acquired immunodeficiency syndrome; chronic obstructive pulmonary disease

OCFA y **empeoramiento de DLCO** se asocian con **mortalidad de cualquier causa** en **PVVIH** (seguimiento durante 6 años)

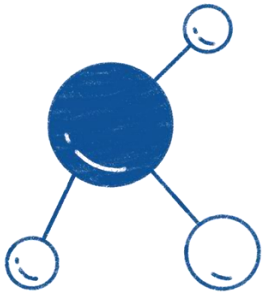
Importancia del EPOC en el VIH

¿ Es una comorbilidad olvidada en los estudios de cohortes?	SI
¿Es frecuente en los pacientes con VIH? y ¿en comparación con lo no VIH?	SI
El VIH ¿es un factor de riesgo más?	SI
¿Está infradiagnosticado?	SI



Neoplasias

EPIDEMIOLOGÍA DEL CÁNCER NO SIDA EN LAS PVVIH



Las **neoplasias malignas** son en la actualidad una de las **principales causas de hospitalización** y **muerte** en la personas que viven con VIH.

CÁNCERES DEFINITORIOS DE SIDA

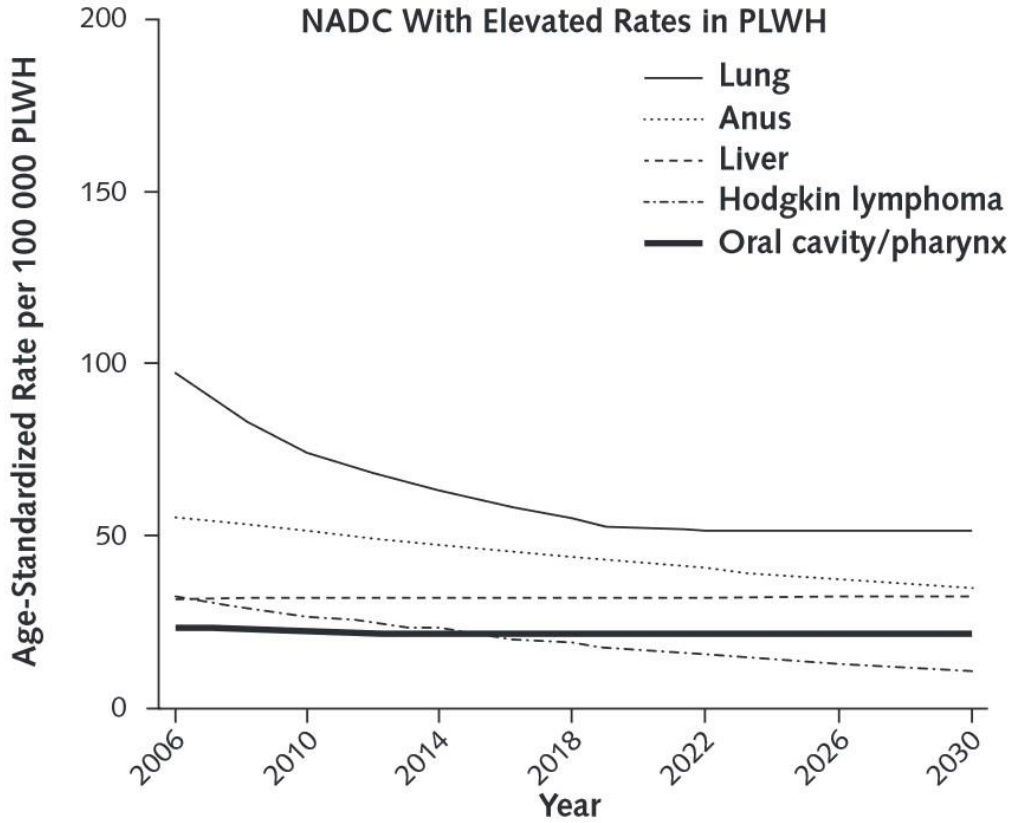
- Linfoma no Hodgkin
- Sarcoma de Kaposi
- Cáncer cervical

CÁNCERES NO DEFINITORIOS DE SIDA

- Cáncer de pulmón
- Cáncer de hígado
- Linfoma de Hodgkin
- Cáncer anal
- …

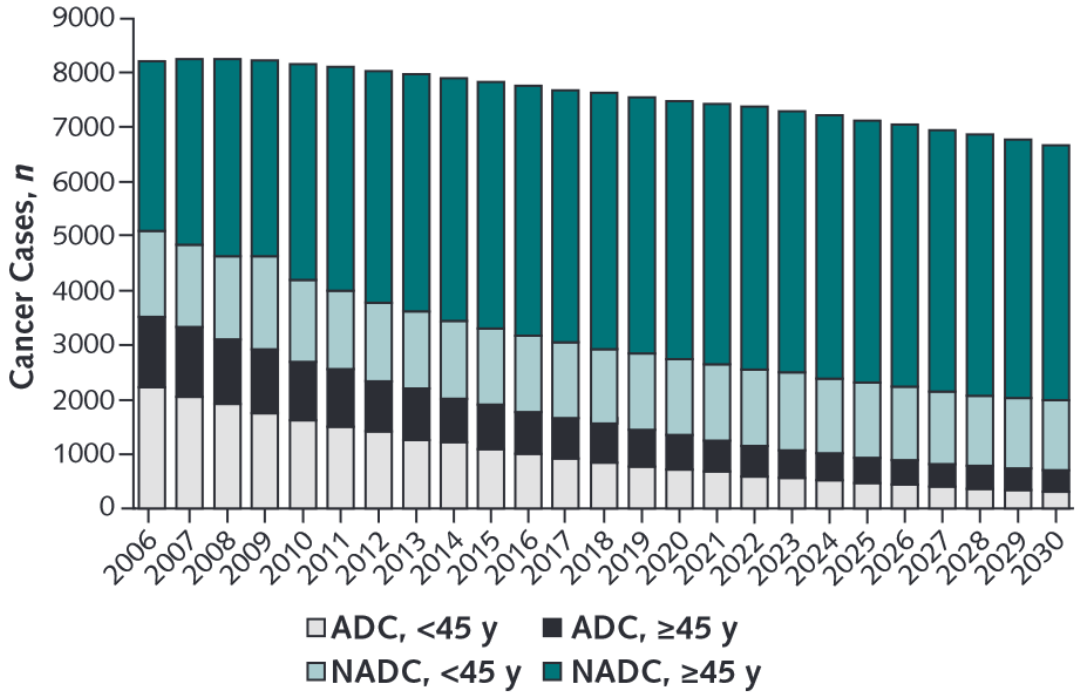
NÚMERO DE CÁNCERES EN PVVIH en EEUU en 2006 -2030

Figure 1. Age-standardized cancer rates for U.S. adults with HIV.



Rates were standardized to the 2010 U.S. HIV population by age group and by risk group (for Kaposi sarcoma, anal cancer, and liver cancer only).

Estimated number of incident diagnoses of ADC and NADC in adults living with HIV in the United States during 2006–2030, stratified by age. Black segments represent ADC, green segments represent NADC, dark bars represent cancer cases among persons aged ≥45 y, and light bars represent cancer cases among those aged <45 y. ADC = AIDS-defining cancer; NADC = non–AIDS-defining cancer

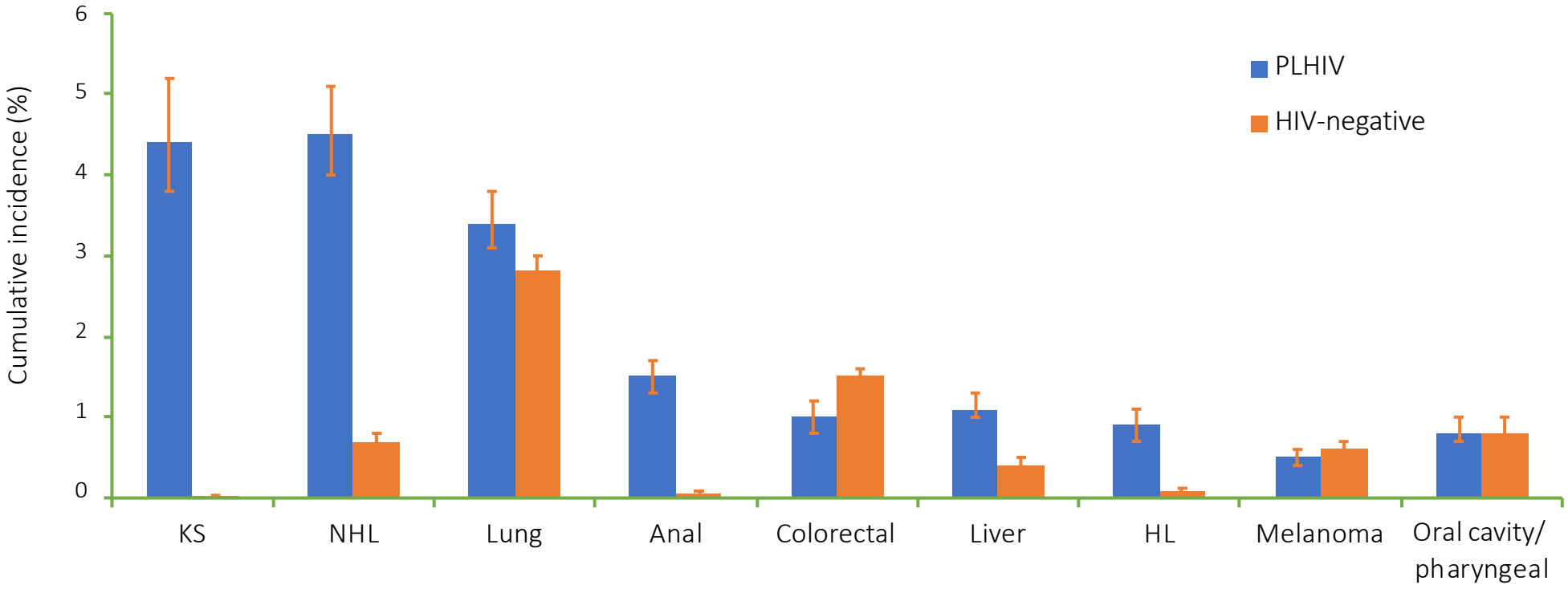


cáncer no SIDA 90% in 2030

Shiels et al. 'Projected Cancer Incidence Rates and Burden of Incident Cancer Cases in HIV-Infected Adults in the United States Through 2030'. Annals of Internal Medicine 2018

Cohorte NA-ACCORD: PVVIH tienen mayor riesgo de tumores que la población general en >75 años

Study of 86,620 PLHIV and 196,987 HIV-negative age-, sex- and race/ethnicity-matched adults, 1996–2009



*AIDS-related cancers.

KS, Kaposi sarcoma; HL, Hodgkin lymphoma; NHL, non-Hodgkin lymphoma; PLHIV, people living with HIV.

Silverberg MJ, et al. *Ann Intern Med* 2015;163:507–18.

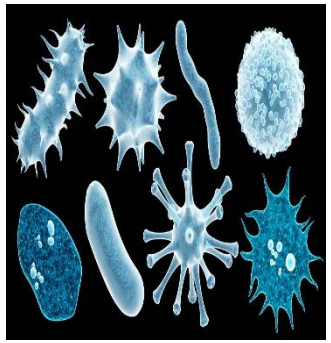
FACTORES Y MECANISMO ASOCIADOS A MORBI/MORTALIDAD POR CÁNCER NO SIDA

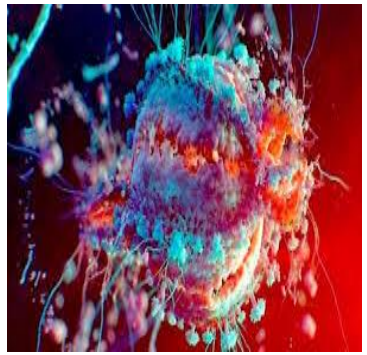
FACTORES DE RIESGO TRADICIONALES

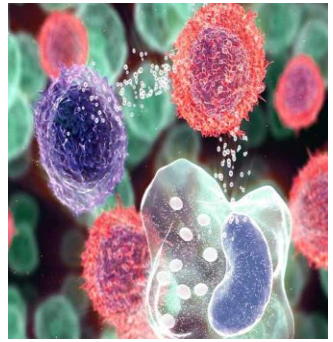
- Envejecimiento
- Consumo de tabaco y alcohol
- Coinfecciones con virus oncogénicos (VPH, VHB y VHC)

FACTORES DE RIESGO ASOCIADOS AL VIH

- Inmunodeficiencia
- Viremia no controlada
- Activación inmune crónica / inflamación
- (TAR)

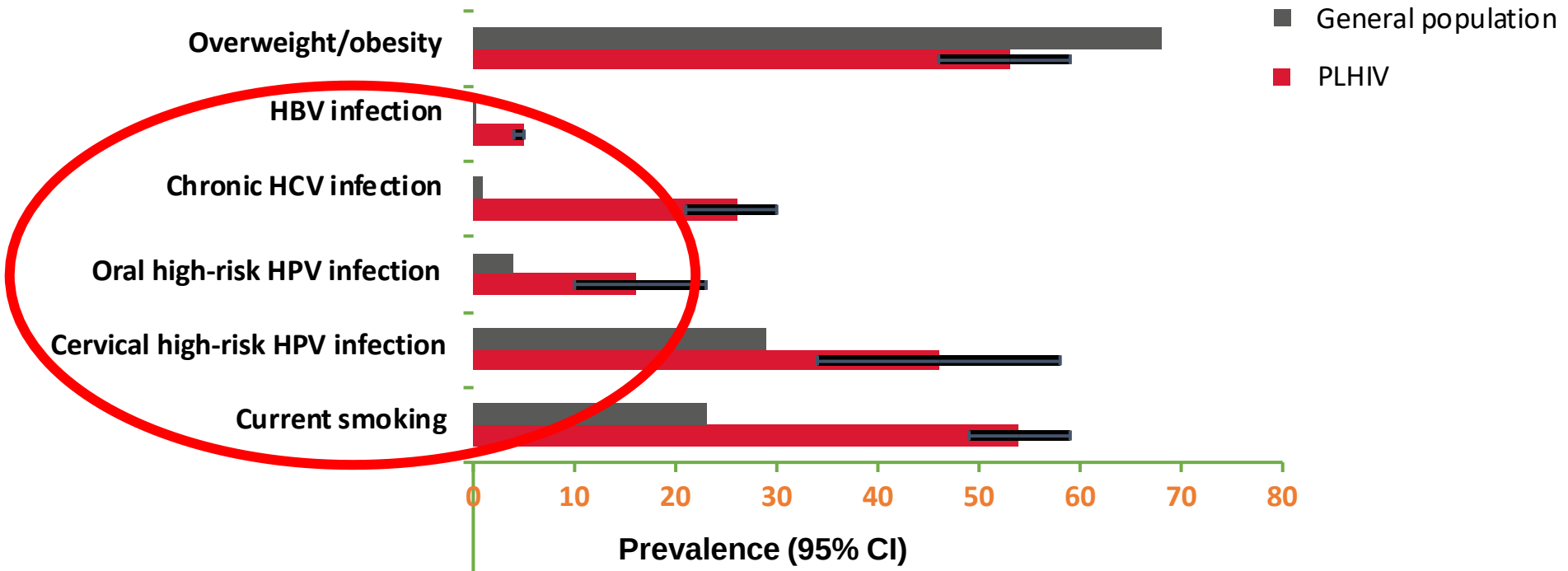






FACTORES DE RIESGO ASOCIADOS

Random effects **meta-analyses of 113 publications** investigating prevalence of modifiable cancer risk factors in people living with HIV/AIDS versus published prevalence estimates in US adults, **2011–2013**[1]



- ART exposure was generally not associated with non–AIDS-defining cancer risk[2]
- The prevalence of **smoking** and **oncogenic viral infections** were significantly **higher among PLHIV** than the general population[1]

ART, antiretroviral therapy; CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus; HPV, human papillomavirus; PLHIV, people living with HIV.

1. Park LS, et al. *AIDS* 2016;30:273–91; 2. Chao C, et al. *AIDS* 2012:26:2223–31.

Incidencia de cáncer no SIDA en PVVIH vs población general

PVVIH tienen entre un **70% y un 100% más de riesgo** de desarrollar un **cáncer no SIDA** que la población general

Rubinstein PG, Aboulafia DM, Zloza A. Malignancies in HIV/AIDS. AIDS [Internet] 2014;28:453–65.

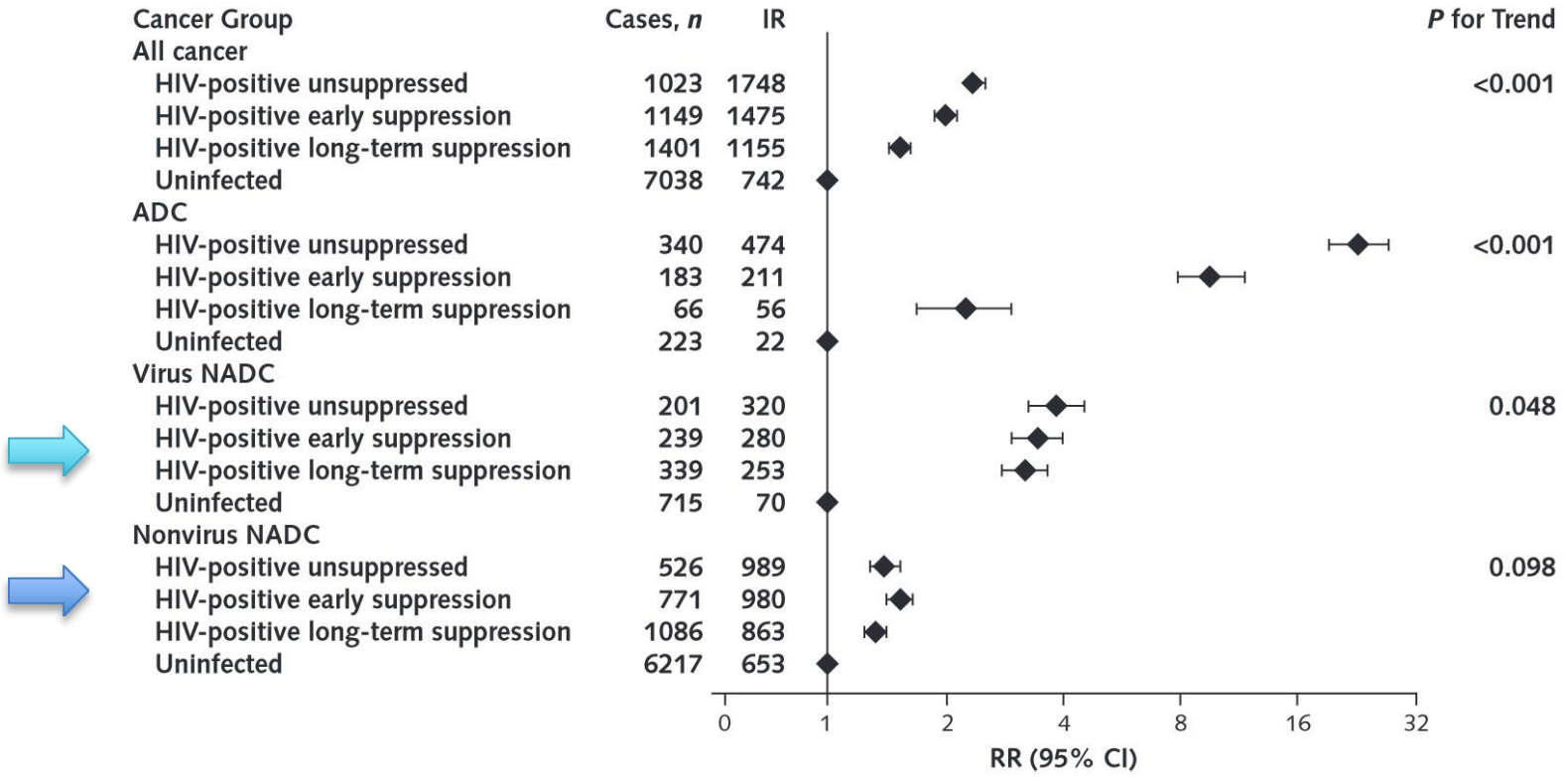
Incidencia de cáncer no SIDA de origen viral en PVVIH vs población general

El **riesgo de desarrollar un cáncer no sida en las PVVIH** puede ser **hasta 4 veces más elevado** que en personas sin VIH [revisión sistemática, 1996 – 2015]

Chiao EY et al. The effect of non-AIDS-defining cancers on people living with HIV. Lancet Oncol 2021

RIESGO DE CÁNCER EN VIH- y VIH+ SEGÚN EL ESTADO DE SUPRESIÓN VIRAL EN EL ESTUDIO VETERANS AGING COHORT STUDY

Figure 1. Numbers of cancer cases, IRs (per 100 000 person-years), multivariate Poisson regression RRs with 95% CIs by HIV viral suppression status, and *P* values for HIV-positive IR viral suppression trend, for cancer groups.



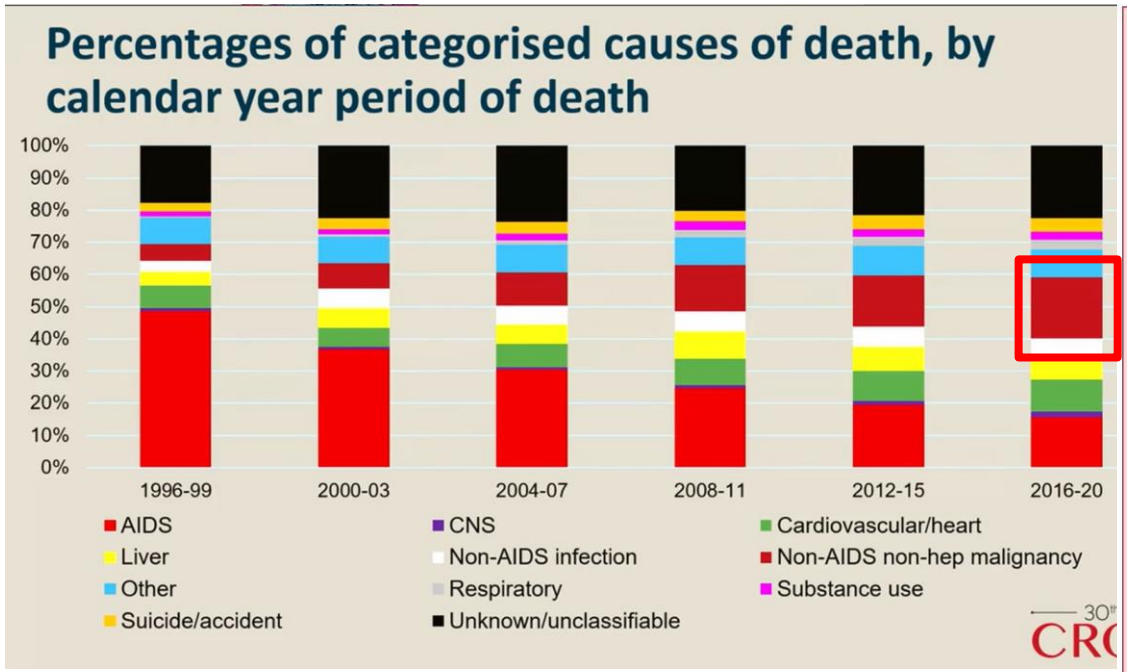
Participantes: VIH+ (N = 42,441) y VIH- (N = 104,712) de 1999–2015

El uso de **TAR temprano** y la consecuente supresión viral puede contribuir a la **prevención del cáncer**, con una marcada reducción del riesgo de ADC, una reducción mucho más leve para NADC viral y posibles reducciones para ciertos tipos de NADC no viral.

Park LS, et al. Association of Viral Suppression With Lower AIDS-Defining and Non-AIDS-Defining Cancer Incidence in HIV-Infected Veterans: A Prospective Cohort Study. Ann Intern Med. 2018 Jul 17

MORTALIDAD

Las neoplasias no SIDA son la **principal causa de mortalidad** en PVVIH



	Mortality rate per 10 000 person-years (95% CI)	Observed deaths	Expected deaths*	Standardised mortality ratio (95% CI)
People diagnosed with HIV	448 839 person-years			
All-cause mortality	118 (115–121)	5302	938	5·7 (5·5–5·8)
Non-AIDS deaths	44·9 (43·0–46·9)	2017	923	2·2 (2·1–2·3)
Non-AIDS infections	8·0 (7·2–8·9)	358	33	10·8 (9·8–12·0)
Non-AIDS cancers	8·6 (7·8–9·5)	388	300	1·3 (1·2–1·4)
Cardiovascular disease and stroke	8·4 (7·6–9·3)	378	223	1·7 (1·5–1·9)
Liver disease	5·2 (4·6–5·9)	234	63	3·7 (3·3–4·2)
Accident	2·1 (1·7–2·6)	94	68	1·4 (1·2–1·7)
Suicide	2·1 (1·8–2·6)	96	48	2·0 (1·6–2·4)
Substance misuse	2·7 (2·3–3·2)	121	47	2·6 (2·1–3·1)
Other causes	7·8 (7·0–8·6)	348	141	2·5 (2·2–2·7)

Rates of Key Death Causes With HIV Falling in Europe/America. Deaths Due to Comorbidities 30th CROI, Conference on Retroviruses and Opportunistic Infections, February 19-22, 2023, Seattle Mark Mascolini

Croxford S, Kitching A, Desai S, et al. Mortality and causes of death in people diagnosed with HIV in the era of highly active antiretroviral therapy compared with the general population: an analysis of a national observational cohort. Lancet Public Health. 2017 Jan;2(1):e35-e46. doi: 10.1016/S2468-2667(16)30020-2. Epub 2016 Dec 15. PMID: 29249478.

CÁNCER ANAL

Es la tercera, tras pulmón e hígado, con **mayor mortalidad.** Es la primera con **más años de vida perdidos**

Table 2. Cancer-attributable Mortality Among People Living With Human Immunodeficiency Virus from 10 States, 2001–2015, by Cancer Site

Cancer Site	Number of Cancers	Proportion of Deaths Preceded by Cancer, p_c (95% CI)	Adjusted Hazard Ratio (95% CI)	Population-attributable Fraction (95% CI)	Cancer-attributable Mortality Rate
All sites combined	31 611	17.5% (17.3%–17.8%)	5.79 (5.69–5.89)	14.5% (13.6%–15.4%)	386.9
AIDS-defining cancers	12 315	6.5% (6.4%–6.7%)	4.28 (4.17–4.40)	5.0% (4.4%–5.6%)	134.1
Kaposi sarcoma	4485	1.9% (1.8%–2.0%)	2.99 (2.86–3.14)	1.3% (.9%–1.6%)	34.0
Non-Hodgkin lymphoma	7072	4.3% (4.1%–4.4%)	5.35 (5.18–5.52)	3.5% (3.0%–3.9%)	92.6
Cervical	758	.4% (.3%–.4%)	2.56 (2.31–2.85)	.2% (.1%–.4%)	5.9
Non–AIDS-defining cancers	19 296	11.0% (10.8%–11.2%)	6.21 (6.08–6.34)	9.2% (8.5%–9.9%)	245.7
Anus	1729	.8% (.7%–.9%)	4.02 (3.74–4.31)	.6% (.4%–.8%)	16.1
Liver	1331	1.1% (1.1%–1.2%)	19.0 (17.9–20.2)	1.1% (.8%–1.3%)	28.4
Hodgkin lymphoma	1420	.6% (.5%–.6%)	3.47 (3.20–3.77)	.4% (.2%–.6%)	11.3
Breast	1110	.4% (.4%–.5%)	2.97 (2.70–3.27)	.3% (.1%–.4%)	7.8
Prostate	2252	.5% (.5%–.6%)	1.21 (1.11–1.32)	.1% (–.1%–.2%)	2.3
Lung	2878	2.5% (2.4%–2.6%)	16.3 (15.7–17.0)	2.4% (2.0%–2.7%)	63.0
Colorectal	1272	.6% (.6%–.7%)	4.00 (3.69–4.34)	.5% (.3%–.7%)	12.6
Other	7304	4.3% (4.2%–4.5%)	6.25 (6.06–6.45)	3.6% (3.2%–4.1%)	97.4

Table 2. Total years of life lost to cancer by subgroups, and by cancer types in the total United States population of people with HIV between 2006 and 2015.

Subgroup	TYLL to cancer	Percentage of TYLL to any cancer
Overall	135 000	100.0
Age		
20–39	23 400	17.3
40–59	91 200	67.5
60+	20 400	15.1
Race		
Non-Hispanic white	37 200	27.5
Non-Hispanic black	72 600	53.8
Hispanic	21 700	16.1
Risk group		
MSM, non-PWID	73 400	54.4
PWID	14 600	10.8
All other	46 900	34.7
Cancer type		
AIDS-defined cancer		
Non-Hodgkin lymphoma	27 800	20.5
Kaposi sarcoma	12 800	9.5
Cervix Uteri	2600	1.9
Non-AIDS-defined cancer		
Anal	9700	7.2
Lung and bronchus	9000	6.6
Colon and rectum	6000	4.4
Hodgkin Lymphoma	5000	3.7
Liver	4500	3.3
Breast	3800	2.8
Prostate	2600	1.9
Other	35 000	25.9

PWID, persons who inject drugs; TYLL, total years of life lost.

Horner MJ, Shiels MS, Pfeiffer RM, Engels EA. Deaths attributable to cancer in the US HIV population during 2001-2015 J Acquir Immune Defic Syndr 2022;90(2):184-192. doi: 10.1097/QAI.0000000000002930.

Luo Q, Pfeiffer RM, Noone AM, et al. Years of life lost to cancer among the United States HIV population, 2006-2015. *AIDS.* 2022;36(9):1279-1286. doi: 10.1097/QAD.0000000000003249.

CÁNCER ANAL, ESTUDIO ANCHOR

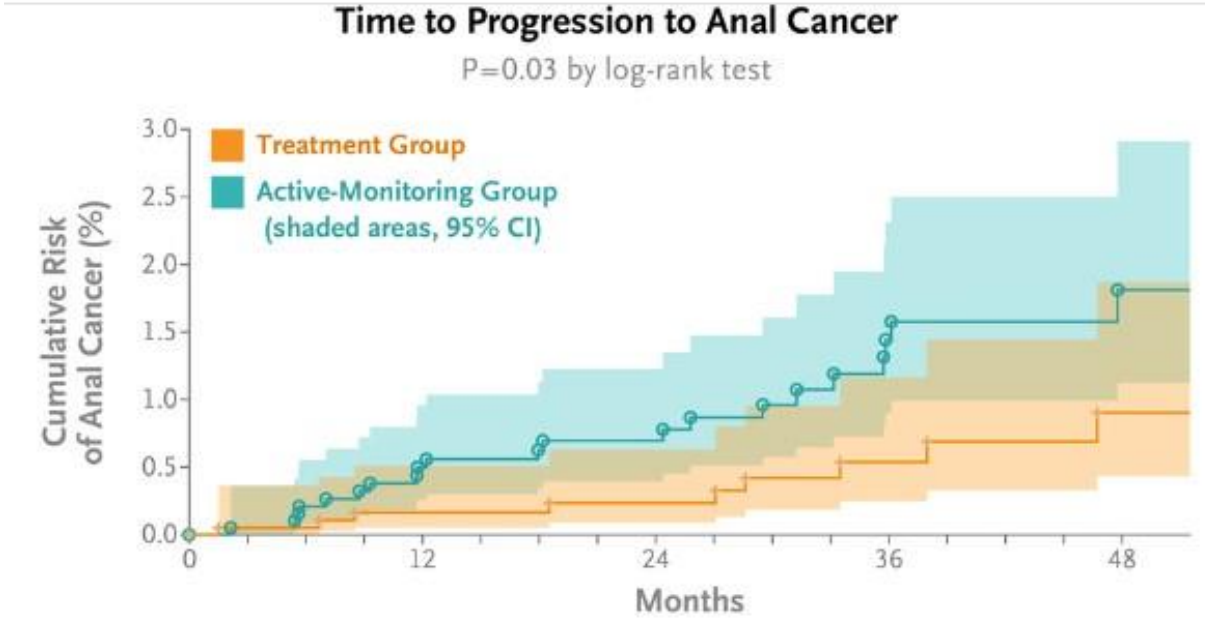
Tto HSIL: Reducción del riesgo de progresión a cáncer del 57%

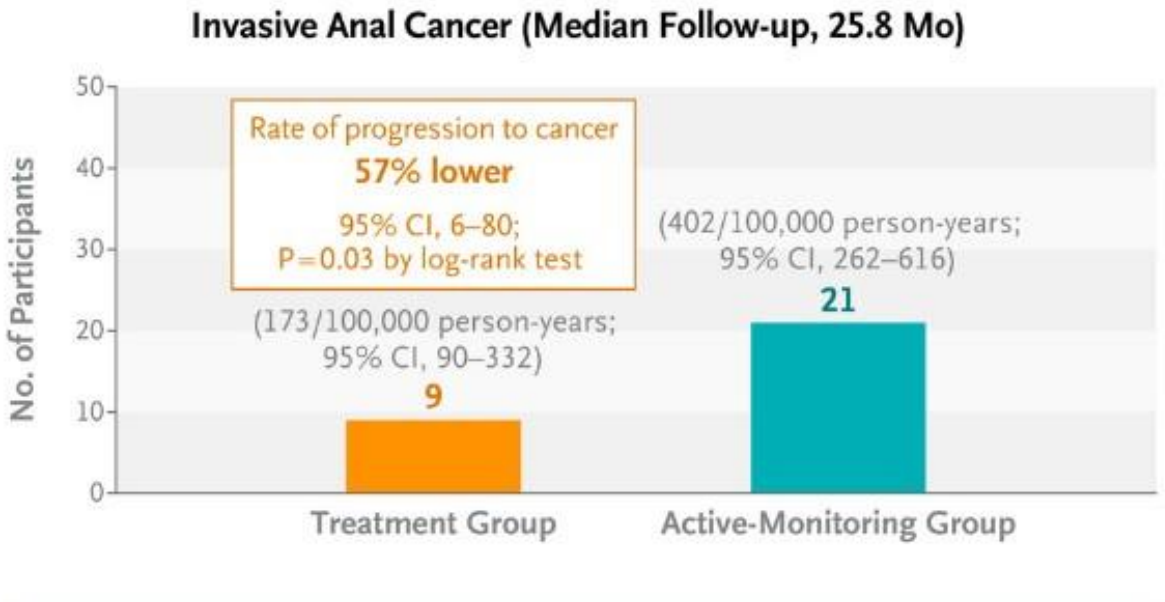
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Treatment of Anal High-Grade Squamous Intraepithelial Lesions to Prevent Anal Cancer

J.M. Palefsky, J.Y. Lee, N. Jay, S.E. Goldstone, T.M. Darragh, H.A. Dunlevy,



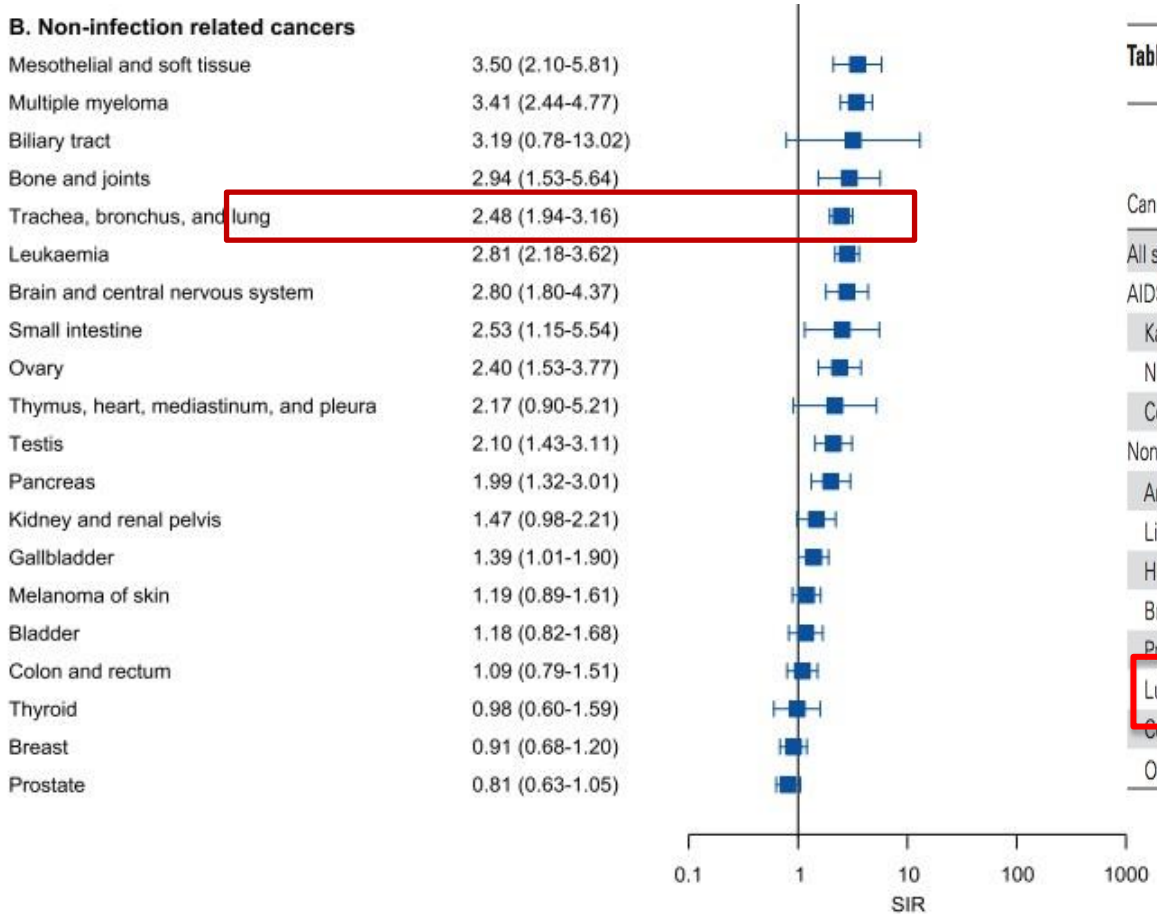


Palefsky JM, Lee JY, Jay N, et al; ANCHOR Investigators Group. Treatment of Anal High-Grade Squamous Intraepithelial Lesions to Prevent Anal Cancer. N Engl J Med. 2022 Jun 16;386(24):2273-2282. doi: 10.1056/NEJMoa2201048. PMID: 35704479; PMCID: PMC9717677.

CÁNCER DE PULMÓN

2,5 veces mayor incidencia que en población general

Es la neoplasia no SIDA con mayor mortalidad



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1Yuan T, Hu Y, Zhou X, Yang L, Wang H, Li L, Wang J, Qian HZ, Clifford GM, Zou H. Incidence and mortality of non-AIDS-defining cancers among people living with HIV: A systematic review and meta-analysis. EClinicalMedicine. 2022 Aug 11;52:101613. doi: 10.1016/j.eclinm.2022.101613. PMID: 35990580; PMCID: PMC9386399.

RIESGO DE CÁNCER DE PULMÓN EN VIH- y VIH+ EN EL ESTUDIO VETERANS AGING COHORT STUDY

Characteristic	IRR	p-value	95% CI
HIV infection	1.7	<0.001	1.5–1.9
Age *	2.3	<0.001	2.2–2.5
Female Gender	0.8	0.5	0.5–1.5
Race/Ethnicity			
Non-Hispanic white	–	–	–
Non-Hispanic black	1.0	0.4	0.8–1.1
Hispanic	0.6	<0.001	0.4–0.8
Other race	0.2	<0.001	0.1–0.4
Smoking exposure			
Never smoker	–	–	–
Former smoker	3.0	<0.001	2.2–4.1
Current smoker	6.3	<0.001	4.7–8.4
Chronic obstructive pulmonary disease	1.9	<0.001	1.5–2.3
Previous bacterial pneumonia	1.5	0.007	1.1–2.0

* 10 year increments

Participantes: VIH+ (N = 37,294, **457**x100,000 persona-años canceres de pulmon) y VIH- (N = 75,750, **204**x100,000 persona-años)

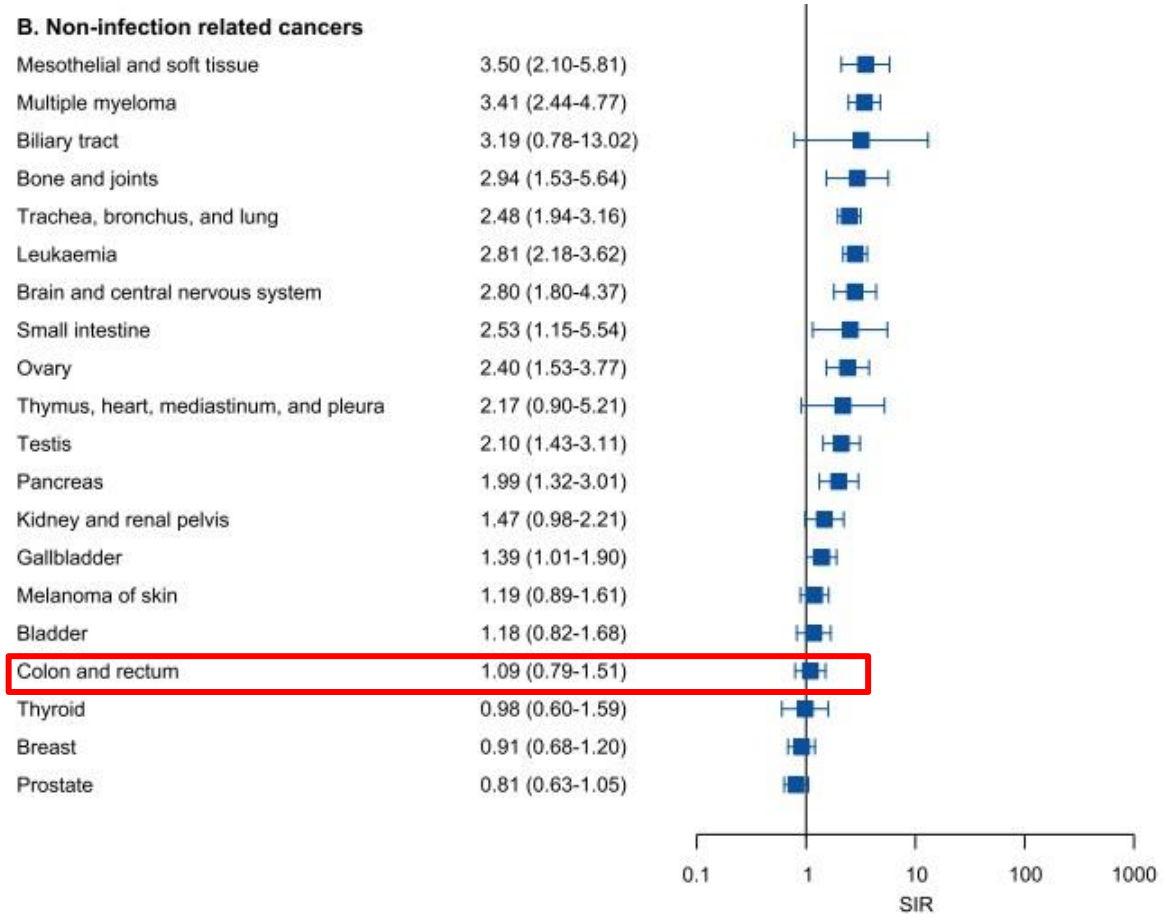
La infección por **VIH** es un **factor de riesgo independiente** para el cáncer de pulmón

Tabla: Razones de tasas de incidencia ajustadas por cáncer de pulmón

Sigel et al, 'HIV as an Independent Risk Factor for Incident Lung Cancer'. AIDS 2012

CÁNCER DE COLON

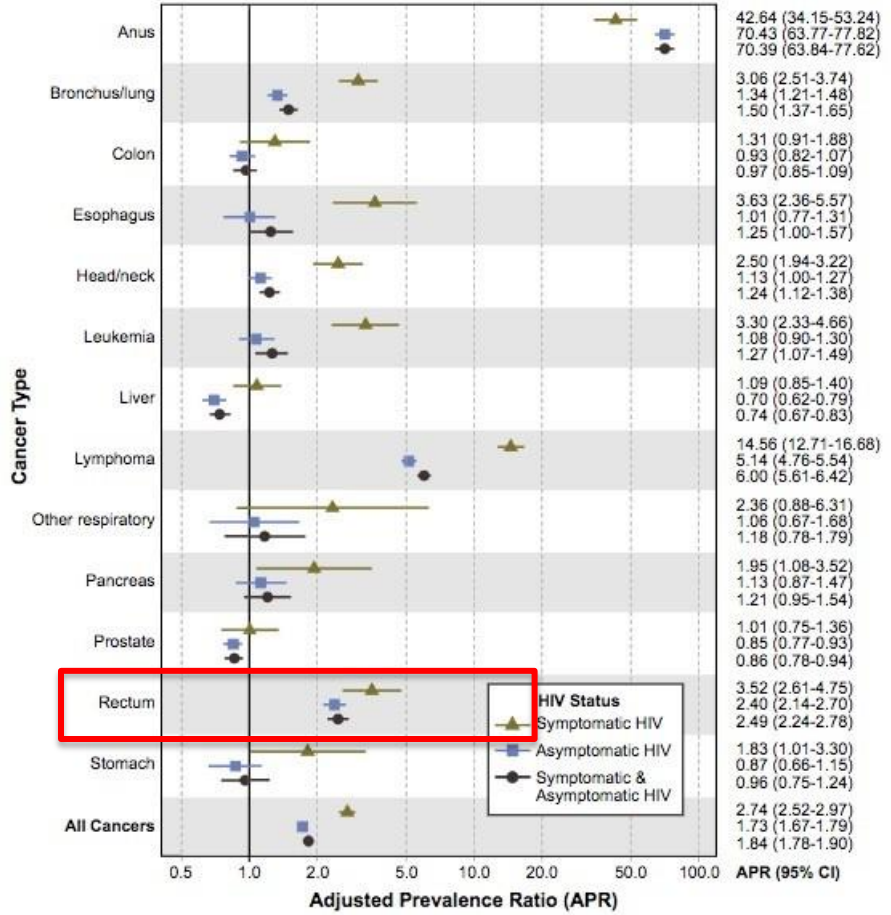
Incidencia similar a población general



Yuan T, Hu Y, Zhou X, Yang L, Wang H, Li L, Wang J, Qian HZ, Clifford GM, Zou H. Incidence and mortality of non-AIDS-defining cancers among people living with HIV: A systematic review and meta-analysis. EClinicalMedicine. 2022 Aug 11;52:101613. doi: 10.1016/j.eclinm.2022.101613. PMID: 35990580; PMCID: PMC9386399.

CÁNCER RECTAL

Mayor prevalencia de cáncer rectal, sobre todo el **escamoso relacionado con VPH**



Koroukian SM, Zhou G, Navale SM, Schiltz NK, Kim U, Rose J, Cooper GS, Moore SE, Mintz LJ, Avery AK, Mukherjee S, Markt SC. Excess cancer prevalence in men with HIV: A nationwide analysis of Medicaid data. Cancer. 2022 May 15;128(10):1987-1995. doi: 10.1002/cncr.34166. Epub 2022 Mar 14. PMID: 35285515.

CÁNCER DE CÉRVIX

Estimates of the global burden of cervical cancer associated with HIV

Dominik Stelzle, Luana F Tanaka*, Kuan Ken Lee, Ahmadaye Ibrahim Khalil, Iacopo Baussano, Anoop S V Shah, David A McAllister, Sami L Gottlieb, Stefanie J Klug, Andrea S Winkler, Freddie Bray, Rachel Baggaley, Gary M Clifford, Nathalie Broutet, Shona Dalal*

6 veces más frecuente en mujeres con VIH

Stelzle D, Tanaka LF, Lee KK, et al. Estimates of the global burden of cervical cancer associated with HIV. *Lancet Glob Health.* 2021;9(2):e161-e169. doi: 10.1016/S2214-109X(20)30459-9.

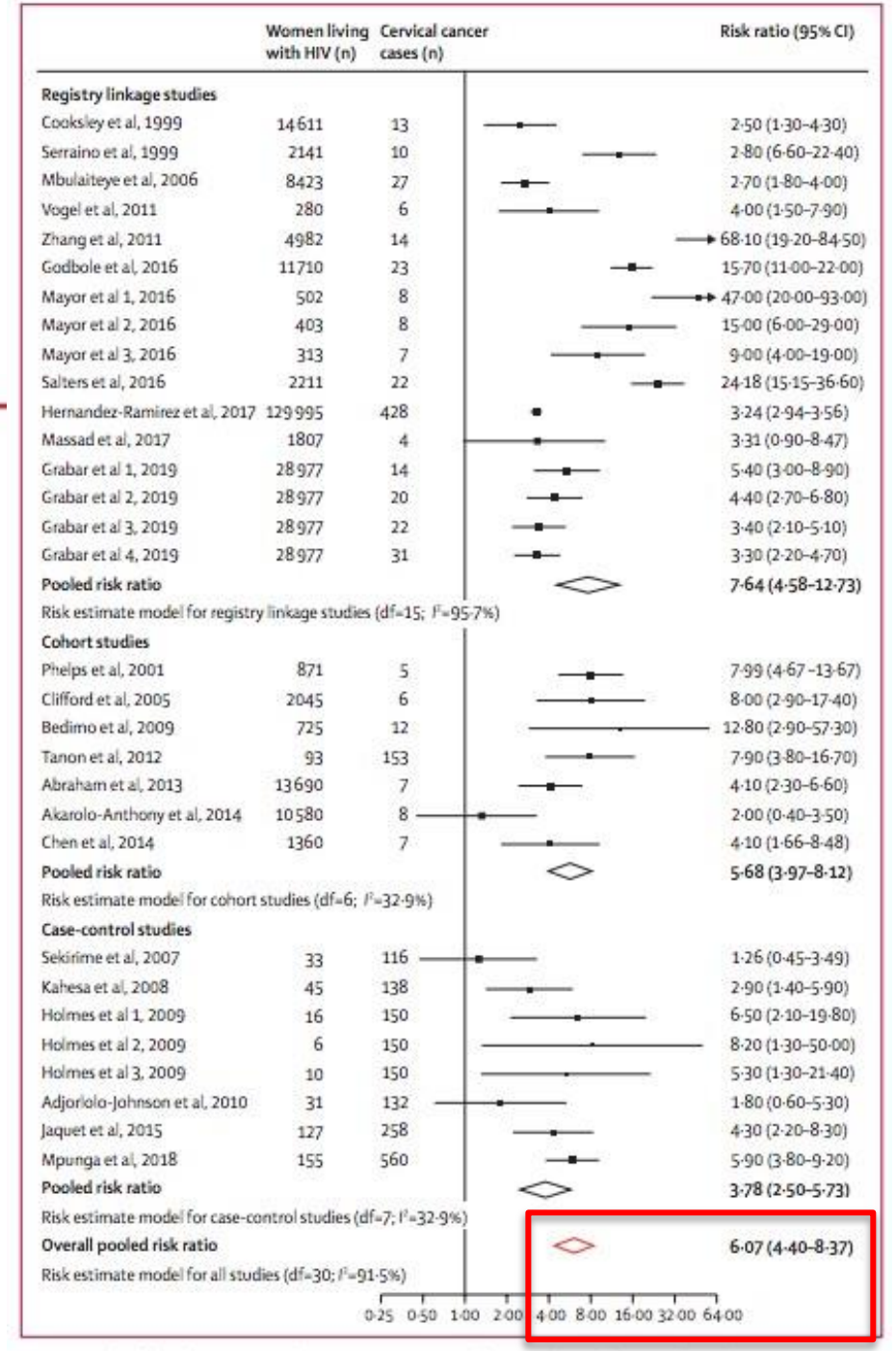


Figure 1: Risk of developing cervical cancer among women living with HIV, by type of study

EACS GUIDELINES 2022 / GESIDA 2019

Cancer: Screening Methods[i]

Problem	Persons	Procedure	Evidence of benefit	Screening interval	Additional comments
Anal cancer	MSM and persons with HPV-associated dysplasia[ii]	Digital rectal exam ± anal cytology	Unknown; advocated by some experts	1-3 years	If anal cytology abnormal, anoscopy
Breast cancer	Women 50-74 years[iii]	Mammography	↓ Breast cancer mortality	1-3 years	
Cervical cancer	Women > 21 years	PAP smear or liquid based cervical cytology test	↓ Cervical cancer mortality	1-3 years	HPV genotype testing may aid PAP/liquid based cervical screening
Colorectal cancer	Persons 50-75 years or with a life expectancy > 10 years	According to local screening programme practice. Colonoscopy every 10 years if willing/able. If unable, annual faecal immunochemistry test (FIT) for occult blood, or multitarget stool DNA (MT-sDNA) testing every 3 years, or computed tomography colonography (CTC) every 5 years	↓ Colorectal cancer mortality	Depending on screening method used	
HepatoCellular Carcinoma (HCC)	HCC screening should follow current EASL guidelines* see pages 8, 81 and 115[iv]	Ultrasound (and alpha-foetoprotein)	Earlier diagnosis allowing for improved ability for surgical eradication	Every 6 months	* Risk factors for HCC in this population include family history of HCC, ethnicity (Asians, Africans), HDV and age > 45 years. EASL guidelines propose using the PAGE-B score in Caucasians to assess the HCC risk, however this score has not been validated in persons with HIV
Prostate cancer	Men > 50 years with a life expectancy >10 years	PSA[v]	Use of PSA is controversial	1-2 years	Pros: ↑ early diagnosis and modest ↓ prostate cancer specific mortality. Cons: overtreatment, adverse effects of treatment on quality of life
Lung Cancer	Age 50-80 years old who are at high risk of lung cancer (at least a 20 pack-year smoking history, and are either current smokers or former smokers having quit within the past 15 years)	Low-dose helical CT (where local screening programs are available)	↓ Lung cancer related mortality	Every year	Evidence confirmed in large RCT, but persons with HIV not included and there may be a higher false positive rate among people with HIV

GUÍA DE PRÁCTICA CLÍNICA SOBRE LOS TUMORES NO DEFINITORIOS DE SIDA E INFECCIÓN POR EL VIH

(ACTUALIZACIÓN MARZO 2019)

PANEL DE EXPERTOS DE GeSIDA

Hígado

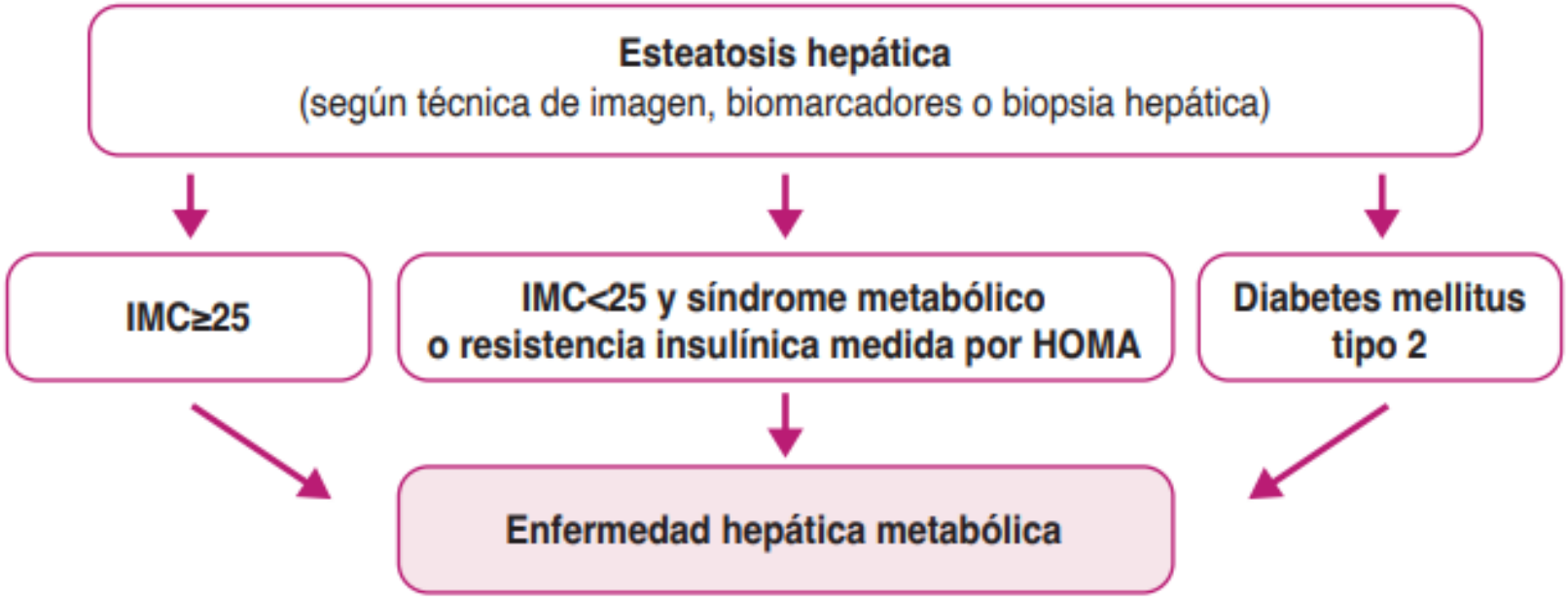
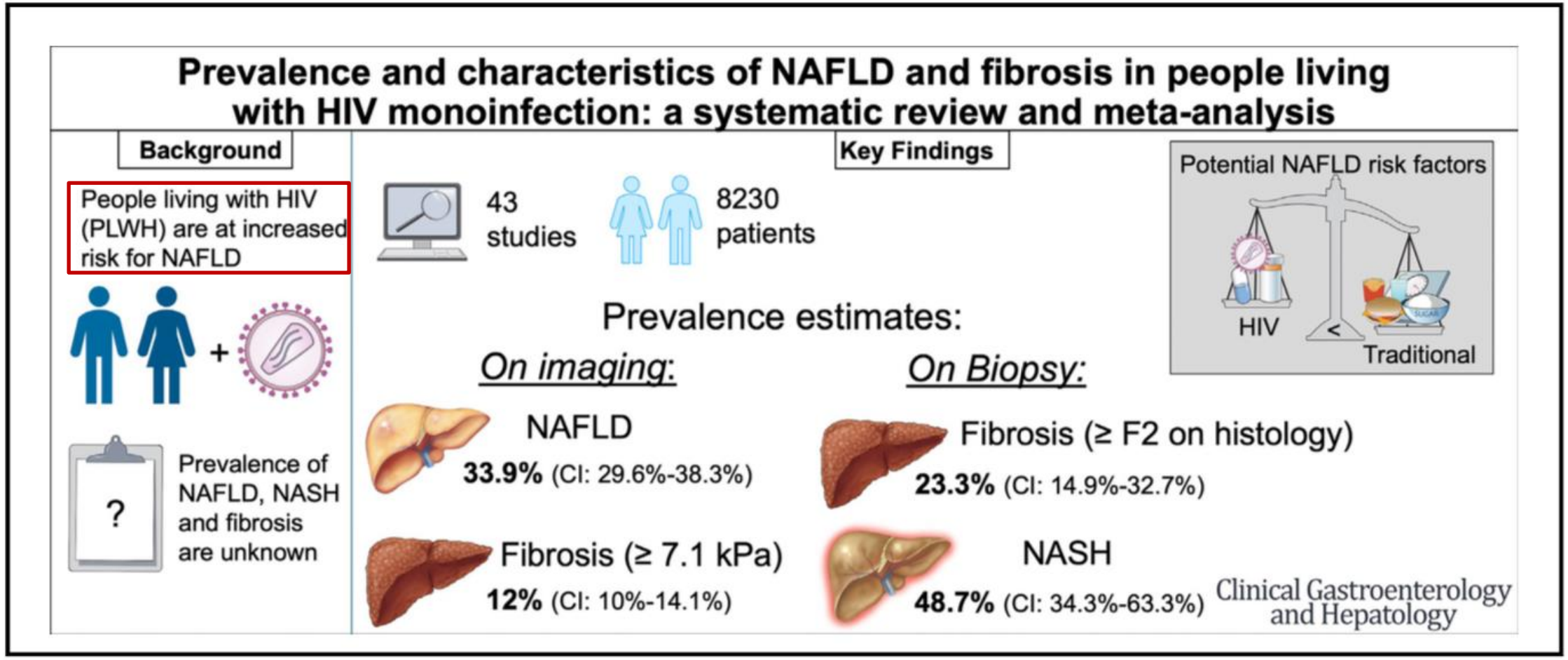


Figura 1. Criterios diagnósticos de la enfermedad hepática metabólica (Adaptado de Eslam M et al. J Hepatol. 2020).

¿Hígado como "órgano diana" del RCV, sd metabólico?

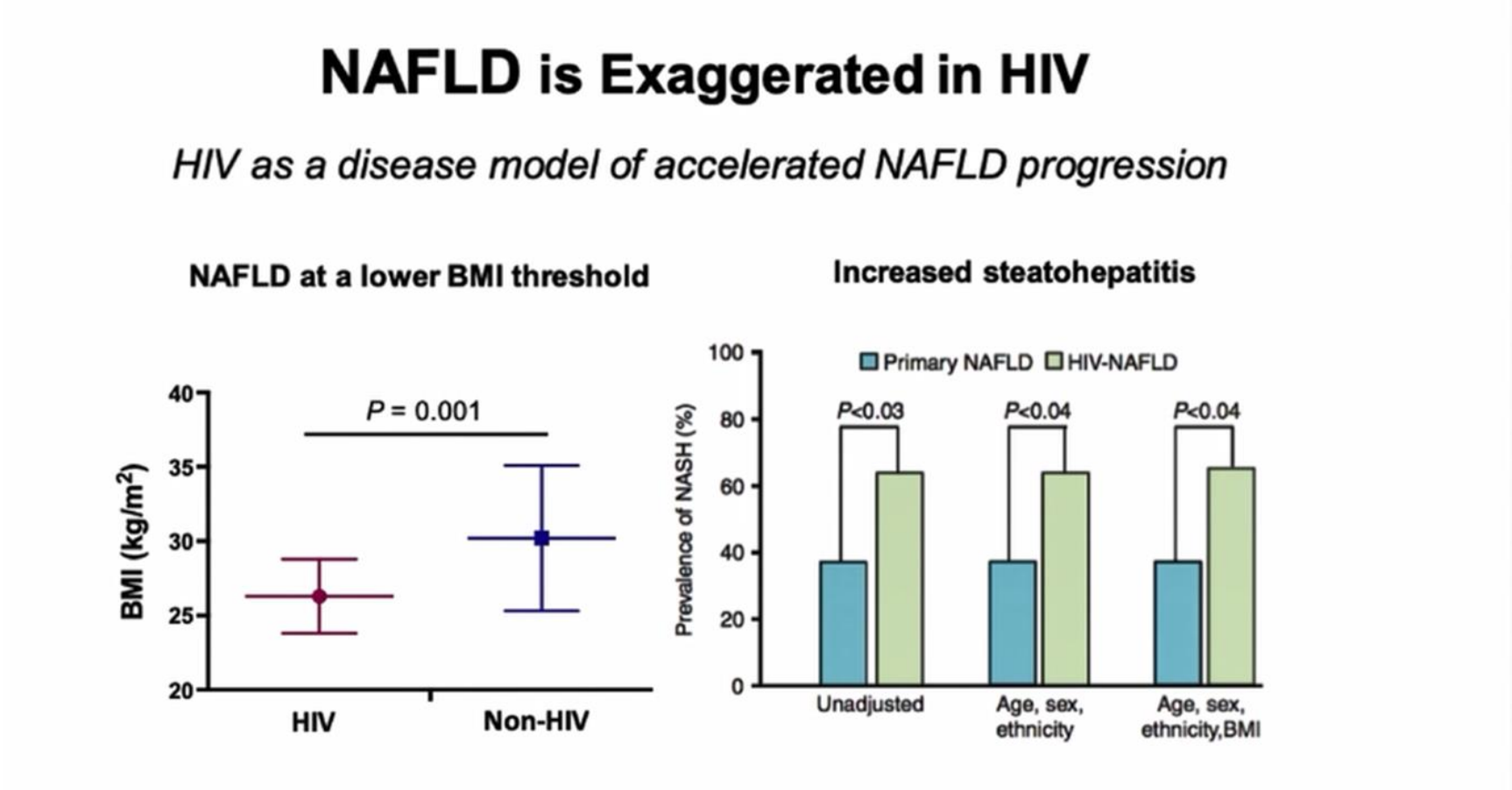
Opinión del ponente

NAFLD y VIH



Kalligeros M et al, 2023

NAFLD en PVVIH se presenta con un IMC menor



Vodkin, I., Valasek, M.A., Bettencourt, R., Cachay, E. and Loomba, R. (2015), Clinical, biochemical and histological differences between HIV-associated NAFLD and primary NAFLD: a case–control study. Aliment Pharmacol Ther, 41: 368-378. https://doi.org/10.1111/apt.13052

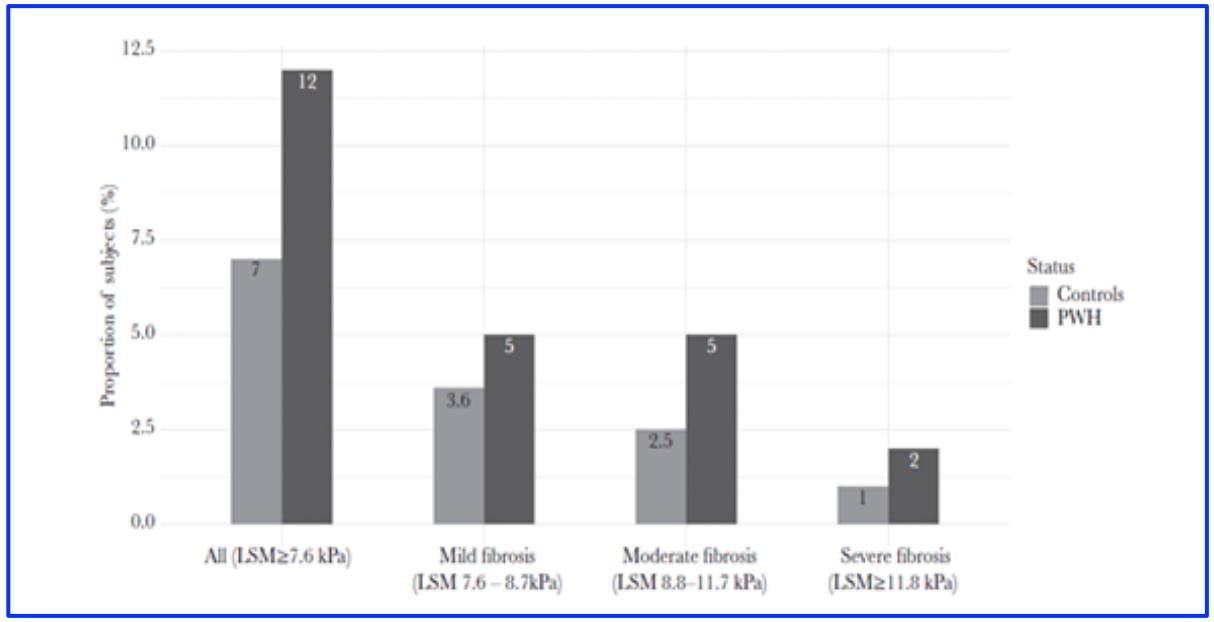
Progresión de la fibrosis en PVVIH

The Journal of Infectious Diseases

MAJOR ARTICLE

Increased Prevalence of Liver Fibrosis in People Living With Human Immunodeficiency Virus Without Viral Hepatitis Compared to Population Controls

Ditte Marie Kirkegaard-Klitbo,[1] Flemming Bendtsen,[2,3] Jens Lundgren,[3,4,©] Robert J. de Knegt,[5] Klaus Fuglsang Kofoed,[6,7] Susanne Dam Nielsen,[3,8] and Thomas Benfield[1,3]; for the Copenhagen Co-Morbidity in HIV Infection (COCOMO) Study Group

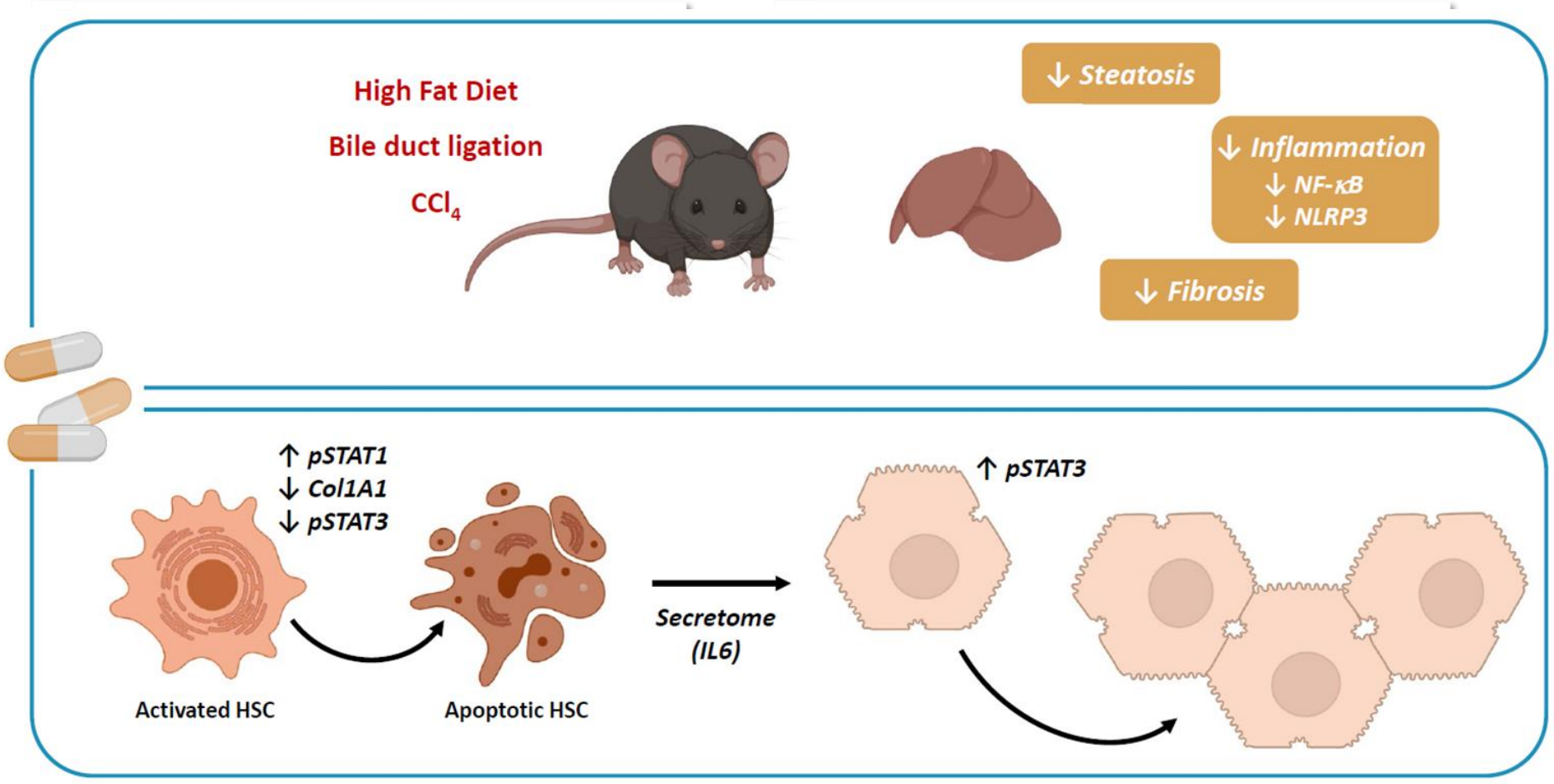


Mayor prevalencia y progresión de **fibrosis** en VIH

Kirkegaard-Klitbo, Ditte Marie et al. The Journal of infectious diseases 224,3 (2021): 443-452

¿Papel del TAR?

Rilpivirine attenuates liver fibrosis through selective STAT1-mediated apoptosis in hepatic stellate cells



Martí-Rodrigo, A. et al. Gut 2020;69:920-932. DOI: 10.1136/gutjnl-2019-318372

Comorbilidades Neuropsiquiátricas

Trastornos Psiquiátricos

En España, **el 32% de las PVVIH padecen trastornos psiquiátricos,** siendo los más comunes **insomnio, ansiedad, depresión y suicidio**[1-3]

ASOCIACIÓN:
- ✓ Discapacidad
- ✓ Peores resultados en el tto del VIH
- ✓ Peor QoL
- **- > SCREENING a todas las PVVIH**

En las PVIH la **prevalencia** comorbilidad neuropsiquiátrica **es muy superior a la población general**

Insomnio	Ansiedad	Depresión
4x	7x	10x
39%	47%	39%

1. Al-Dakkak I, et al. The impact of specific HIV treatment- related adverse events on adherence to antiretroviral therapy: a systematic review and meta-analysis. AIDS Care. 2013;25(4):400-14. doi: 10.1080/09540121.2012.712667

ART, antiretroviral therapy; CD4, cluster of differentiation 4; CNS, central nervous system; CSF, cerebrospinal fluid; HCV, hepatitis C virus; OI, opportunistic infection.

GeSIDA
GRUPO DE ESTUDIO DEL SIDA-SEIMC

DOCUMENTO DE CONSENSO SOBRE EL MANEJO CLÍNICO DE LA COMORBILIDAD NEUROPSIQUIÁTRICA Y COGNITIVA ASOCIADA A LA INFECCIÓN POR VIH-1

PANEL DE EXPERTOS DEL GRUPO DE ESTUDIO DE SIDA (GeSIDA)

PRINCIPALES SÍNDROMES PSICOPATOLÓGICOS

La infección por VIH puede incrementar el riesgo de la enfermedad psiquiátricos y, a su vez, la enfermedad psiquiátrica es un factor de riesgo para la adquisición del VIH[17,18]. Diferentes estudios han demostrado un aumento de la prevalencia de trastornos psicopatológicos en las personas con VIH en comparación con la población general[19–25]. El abordaje de estos trastornos requiere un abordaje multidisciplinar (medicina interna, psicología, psiquiatría, asistentes sociales, enfermería…) implicando, cuando sea posible a enfermería, como profesional de enlace. La valoración inicial y el seguimiento de los trastornos psicopatológicos en las personas con VIH deberá incluir[27]:

- Antecedentes familiares y personales de enfermedad mental y personales de consumo de tóxicos-drogas.
- Evaluación de la apariencia, del comportamiento, del pensamiento, del lenguaje, del juicio crítico, del estado de ansiedad y depresión, de la queja cognitiva (atención, memoria y funciones ejecutiva), de la motricidad y de la percepción sensorial.
- Evaluación de la situación laboral, familiar y social.

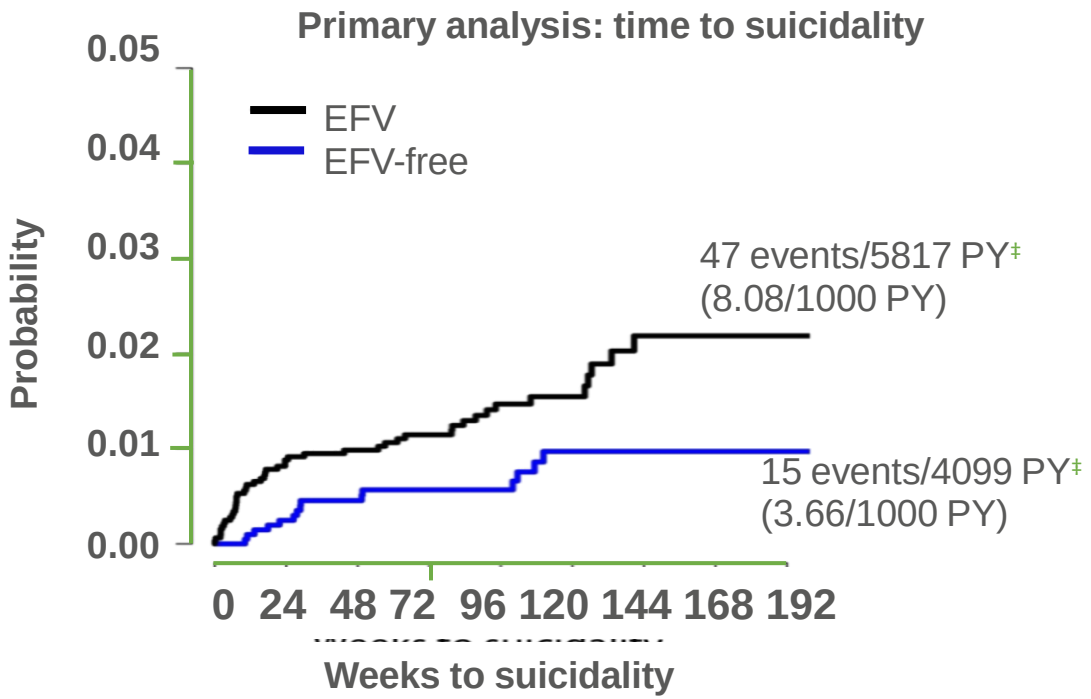
GeSIDA — Consenso de GeSIDA sobre comorbilidad neuropsiquiátrica – cognitiva y VIH
Versión 1.0. – junio de 2020.

VIH

Enfermedad psiquiátrica

Toxicidad de SNC del TAR

EFV y riesgo de suicidio



Initial treatment with EFV was associated with a 2-fold risk of suicidality compared with an EFV-free regimen

*ACTG A5095, A5142, A5175, A5202; †Protease inhibitor or 3-nucleoside based regimens; ‡Follow-up in A5095 and A5175 was censored at the time of the DSMB decisions.
ACTG, AIDS Clinical Trials Group; CI, confidence interval; DSMB, drug and safety monitoring board; EFV, efavirenz; HR, hazard ratio; ITT, intent-to-treat; PY, person-year.
Mollan K, et al. *Ann Intern Med* 2014;161:1–10.

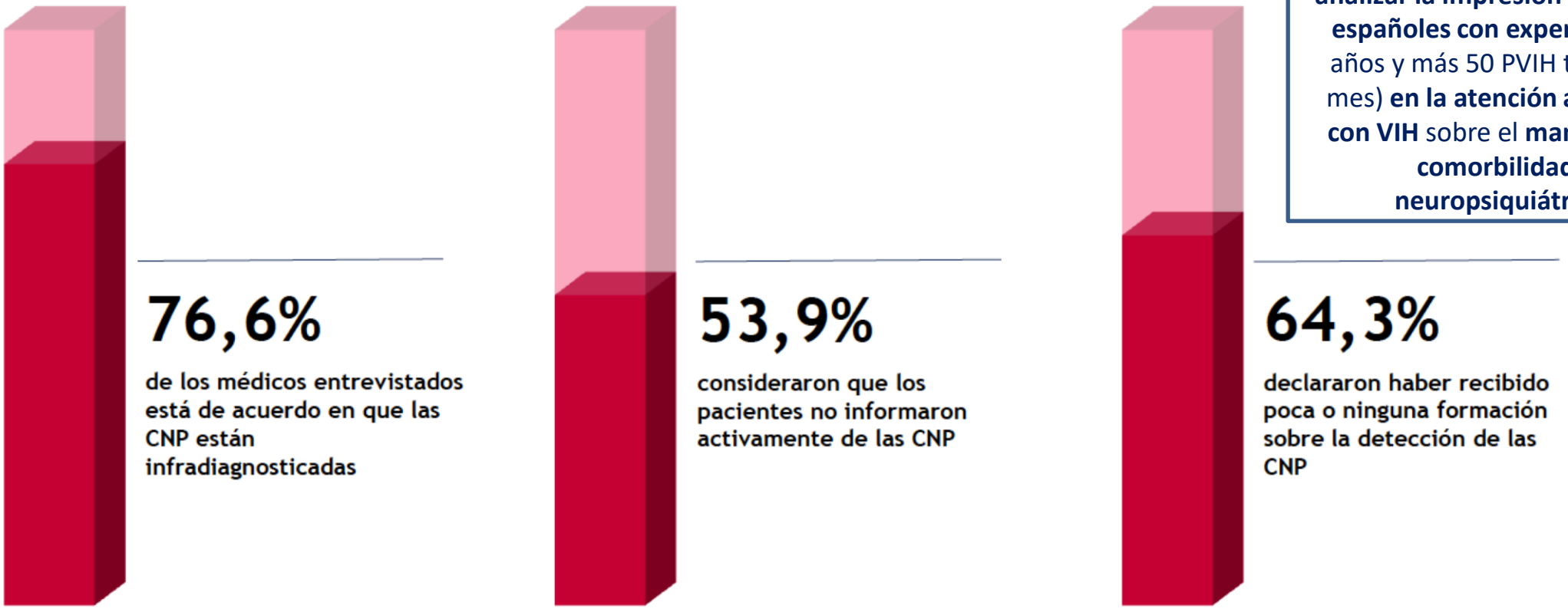
DTG y efectos adversos SNC

- Más frecuente en **estudios observacionales** que en ECA: 0.3- 5% vs. 0.7-3%. Asociado con:
  - Género **femenino**
  - Coadministración con **abacavir**
  - **Mayor edad**
- Posible asociación con **exposición mayor a DTG**
- Posible asociación con **alteraciones geneticas** (SNP genes codifican UGT1A1 y OCT2)

de Boer MG, et al. AIDS 2016; Hoffmann C et al. HIV Med 2017; Todd S et al. Int J STD AIDS 2017; Peñafiel J et al. JAC 2017; Cid-Silva P et al. BCPT 2017; Elzi L, et al. Aids 2017; Cuzin L, et al. JAC 2018; Fettiplace A, et al. JAIDS 2017; Bonfanti P, et al. AIDS 2017; Lepik KJ et al. AIDS 2018; Baldin G, et al. HIV Med 2019; Venter WDF, et al. NEJM, 2019; Yagura H, et al. BMC Infec Dis 2017; Borghetti A, et al. JAC 2019; Calcagno A, et al. Clin Pharm 2021; Hoffmann C, et al. Antiviral Therapy 2020; O'Halloran JA, et al. CROI 2020 #0438

Estudio PERCEPTION-SNC: Las comorbilidades neuropsiquiátricas están infradiagnosticadas en PVVIH

La mayoría de los participantes consideraron que los médicos eran conscientes de la necesidad de detectar las comorbilidad neuropsiquiátrica (CNP)



76,6%

de los médicos entrevistados está de acuerdo en que las CNP están infradiagnosticadas

53,9%

consideraron que los pacientes no informaron activamente de las CNP

64,3%

declararon haber recibido poca o ninguna formación sobre la detección de las CNP

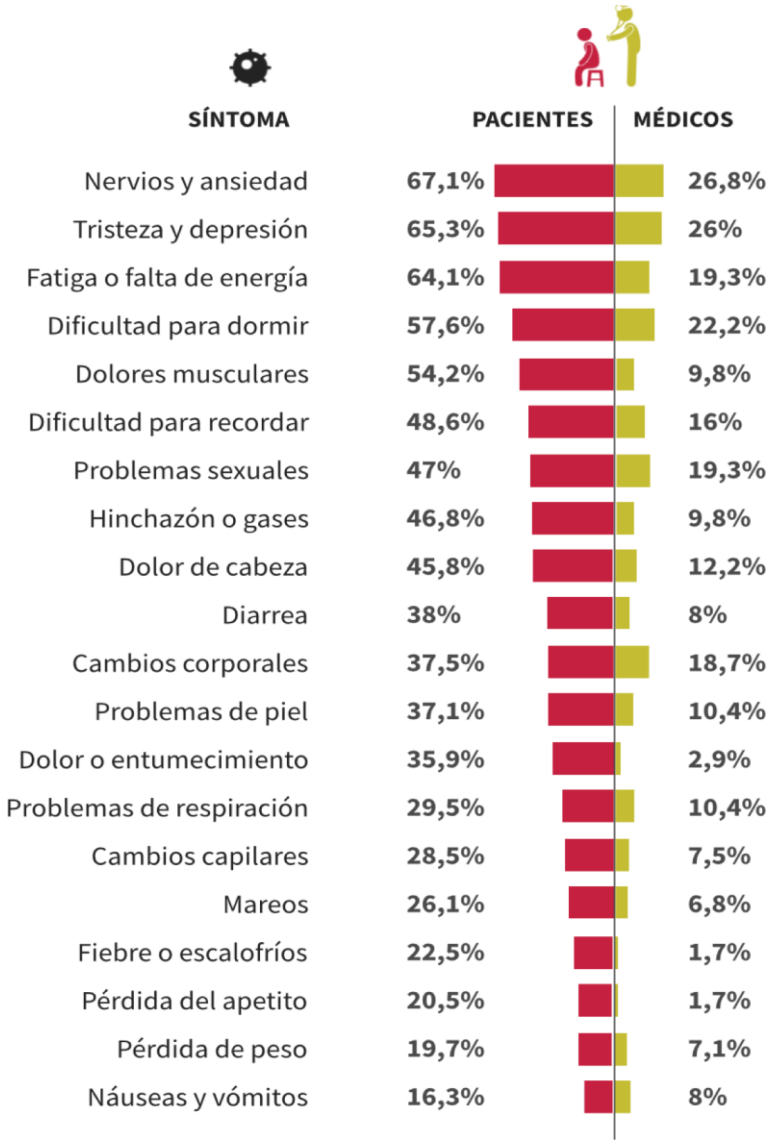
Estudio transversal diseñado para **analizar la impresión de médicos españoles con experiencia** (>4 años y más 50 PVIH tratados al mes) **en la atención a personas con VIH** sobre el **manejo de las comorbilidades neuropsiquiátricas.**

Pérez-Valero I, et al. Perception of HIV physicians in Spain towards diagnosis and management of neuropsychiatric comorbidities in people with HIV. HIV Medicine. 2022;00:1–9. doi: 10.1111/hiv.13296.

Estudio RET: La diferencia entre lo que paciente siente y lo que el médico percibe

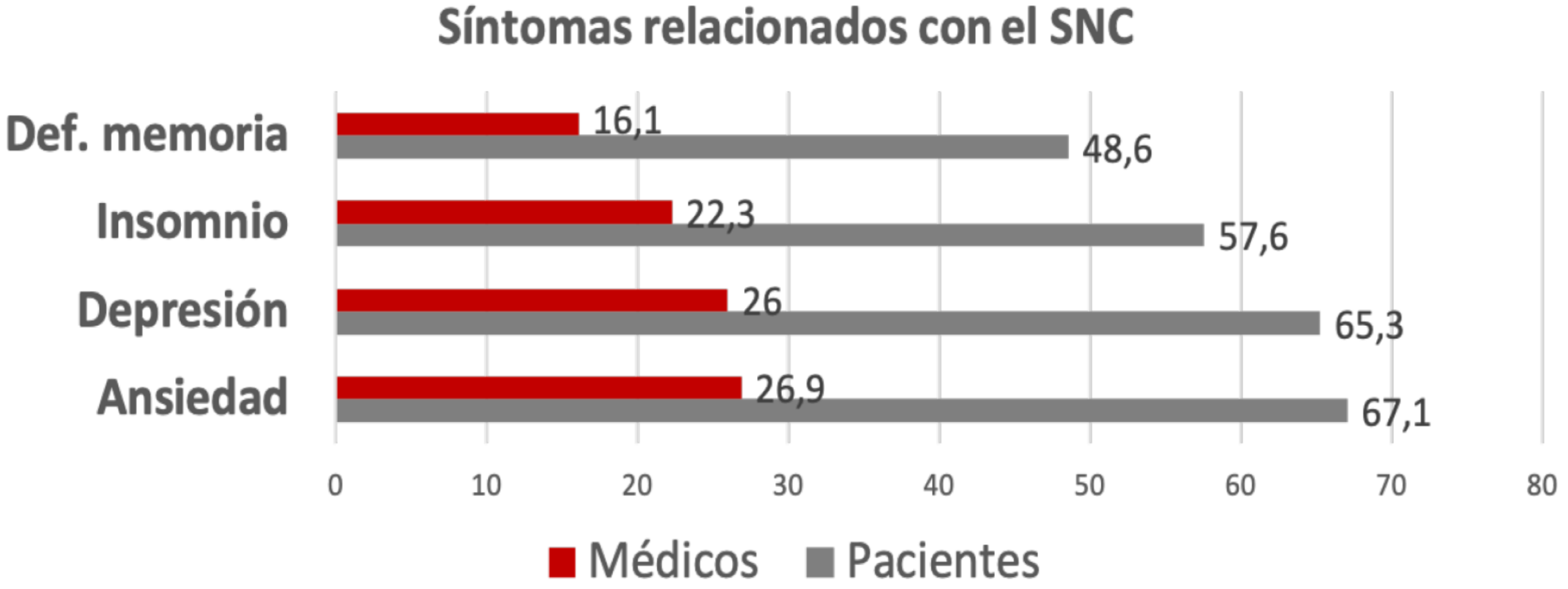
- ✓ Estudio observacional de 18 centros españoles en el 2020 (sanitarios y ONGs).
- ✓ Se incluyeron a 108 médicos de VIH y 502 PVVIH
- ✓ Se evaluaron: síntomas, percepción de TAR y CVRS referidos por los pacientes y estimados por los médicos.

Porcentaje de pacientes con VIH que reportan a su médico un síntoma determinado, comparado con el porcentaje de médicos que piensan que el paciente sufre ese síntoma



Amador C, et al. La percepción de los pacientes con VIH y de los médicos sobre las características del tratamiento antirretroviral, la satisfacción y el bienestar del paciente (estudio RET). Póster presentado en el XII Congreso Nacional GeSIDA. Málaga. 2021.

Estudio RET



Amador C, et al. La percepción de los pacientes con VIH y de los médicos sobre las características del tratamiento antirretroviral, la satisfacción y el bienestar del paciente (estudio RET). Póster presentado en el XII Congreso Nacional GeSIDA. Málaga. 2021.

Las comorbilidades neuropsiquiátricas en PVVIH se pueden identificar directamente en la consulta

- **CUESTIONARIOS Y ESCALAS**

- **PROs** (Patient Reported Outcomes): cualquier dato sobre el estado de salud de un paciente que proviene de este, sin la interpretación de la información por un médico.
  - Son una **medida**, basada en un informe que proviene **directamente del paciente**
  - Son una manera de **captar las perspectivas de los pacientes** sobre la salud, la enfermedad y los efectos de las intervenciones sanitarias
  - **Trasladan la voz del paciente a la práctica clínica**, proporcionando información que puede complementar otros resultados clínicos

Panel de expertos del grupo de estudio de SIDA (GeSIDA). Documento de consenso sobre el manejo clínico de la comorbilidad neuropsiquiátrica y cognitiva asociada a la infección por VIH-1. Versión 1.0 – junio de 2020.

1. Engler K, et al. A Review of HIV-Specific Patient-Reported Outcome Measures. Patient. 2017; 10:187-202. doi: 10.1007/s40271-016-0195-7
2. Wohl D,et al. Patient-reported symptoms over 48 weeks among participants in randomized, double-blind, phase III non-inferiority trials of adults with HIV on co-formulated bictegravir, emtricitabine, and tenofovir alafenamide versus co-formulated abacavir, dolutegravir, and lamivudine. Patient. 2018;11(5):561-573. doi:10.1007/s40271-018- 0322-8.

GILEAD

CONECTAR

COmorbilidad
NEuropsiquiátrica:
Clave en el
Tratamiento
Anti**R**etroviral

Avales

eimc

RAS

SEPSM

SOCIETAT CATALANA DE PSIQUIATRIA I SALUT MENTAL

sefh
Sociedad Española de Farmacia Hospitalaria

Consejo General de Colegios Oficiales de Enfermería de España

CONCLUSIONES

- ✓ **Aumento en la expectativa de vida PVVIH**, lo que conlleva un aumento del envejecimiento, la cronicidad, al fragilidad y las comorbilidades, y a su vez de la polifarmacia.

- ✓ Las **comorbilidades** suelen aparecer **antes** que en la población general (hasta 10 años), son **más prevalentes** y **se asocian** con más frecuencia.

- ✓ **Multifactorial**: FFRR “clásicos”, estilo de vida, VIH, toxicidad del TAR, inflamación crónica e inmunoactivación, coinfecciones, ...

- ✓ Importante detectarlas y tratarlas.

- ✓ **Elección del TAR** puede ser importante en el manejo de muchas comorbilidades.

- ✓ **PROs, modificaciones en el estilo de vida.**


Muchas
Gracias!