

COMORBIDITATS EN EL PACIENT QUE VIU AMB EL VIH.

Anna Bonjoch

Disclosures



Lectures

Gilead

Janssen

MSD

COMORBIDITATS.



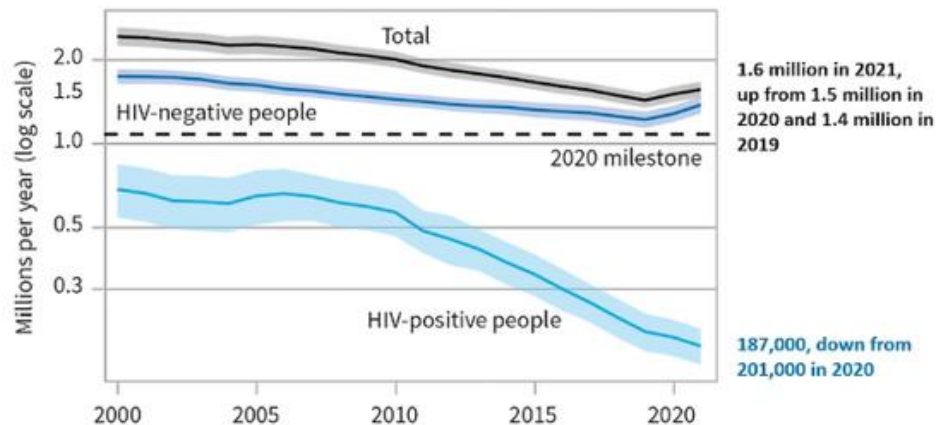
Resultats CROI 2023

Leading causes of HIV-related mortality



Tuberculosis:

- Continued increase in tuberculosis related deaths in 2020 (1.5 million) and 2021 (1.6 million), the first such increase since 2006 - trend has been reversed
- 187,000 deaths among HIV-positive people in 2021, down from 201,000 deaths in 2020.



Source: Global tuberculosis report, Geneva: WHO, 2022.

Cryptococcal Disease

- Cryptococcal meningitis accounts for 15% of all people dying from AIDS-related causes globally, three quarters of whom are in sub-Saharan Africa

Severe Bacterial Infections

- Limited diagnostic capability
- Estimated to cause more than one third of hospitalizations among adults and children living with HIV worldwide
- Burden of mortality and morbidity attributable to severe bacterial infections is not defined



Other causes of mortality

- Non-communicable diseases: Compared with the general population, people living with HIV have increased risk of developing a range of chronic non-communicable diseases, including cardiovascular disease, hypertension, diabetes, chronic obstructive pulmonary disease, kidney disease and cancer.
 - Cardiovascular disease is now one of the leading causes of non-AIDS-related morbidity and mortality among people living with HIV¹
 - Cervical cancer: The most common cancer among women living with HIV globally and the leading cause of cancer death for women in sub-Saharan Africa. Of the roughly 110,000 women diagnosed annually with cervical cancer, approximately 66% die from the disease²
- Mental health conditions: A recent systematic review showed that the risk of death by suicide is 100 times higher among PLHIV than in the general population³
- Natural, climate-induced and/or conflict humanitarian emergencies

1- Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO.
2- IN DANGER: UNAIDS Global AIDS Update 2022. Geneva: Joint United Nations Programme on HIV/AIDS; 2022. Licence: CC BY-NC-SA 3.0 IGO.
3- IN DANGER: UNAIDS Global AIDS Update 2022. Geneva: Joint United Nations Programme on HIV/AIDS; 2022. Licence: CC BY-NC-SA 3.0 IGO.

Conclusion



- Plateau of the global trends in mortality reduction is of concern
- Need for improved global and regional **understanding of causes of HIV-related mortality**
 - Systems to determine and document causes of HIV-related mortality
 - Summative data systems at global, regional and national-levels to understand predictors and causes of mortality
 - Attention to PLHIV at increased risk of death, e.g. late diagnosis, advanced HIV disease
- Development and scale-up of **context-specific interventions** to mitigate the causes of mortality considering age, gender and regional-specific causes of mortality are needed
- A global monitoring and evaluation framework to **track causes of death at country level** is critical to further understand trends in HIV-related mortality and tailor interventions to address these



THEMED DISCUSSION: TD-04

Monday, February 20, 2023



TRENDS IN MORTALITY IN PEOPLE LIVING WITH HIV IN AN INTERNATIONAL COHORT (RESPOND)

Erich Tusch

University of Copenhagen, Copenhagen, Denmark

— 30th —
CROI 2023

Disclosure(s): No financial relationships to disclose.



Background & Methods

- Mortality rates in people living with HIV have declined due to effective antiretroviral treatment (ART) (1).
- Aging, coinfections, and comorbidities may also drive changes in mortality (2).
- We investigated recent patterns in mortality to **identify opportunities to reduce mortality.**
- The RESPOND cohort consortium was initiated in 2017 and includes over 33,000 people living with HIV from 17 cohorts across Europe and Australia.
- Prospective follow up from 2012 to 2019. Participants before 2017 enrolled retrospectively.
- Age-standardized mortality rates were compared over time.
- Risk factors for all-cause mortality investigated with multivariable Poisson regression.

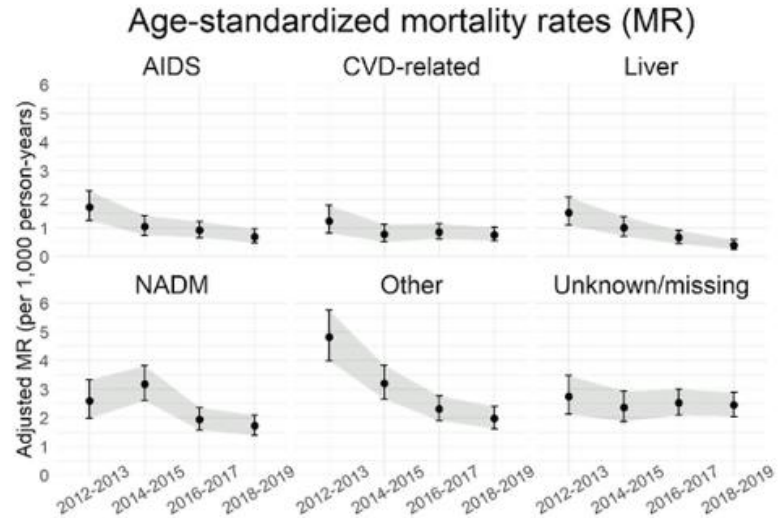
(1) Smith CJ, et al. The Lancet. 2014

(2) Pelchen-Matthews A, et al. AIDS. 2018



Results

- 33,598 participants
- 167,930 PYFU
(median 4.8; IQR 3.1–8.0)
- 1,700 (5.1%) died
- Age-adjusted cause-specific mortality **decreased** for all causes except unknown/missing

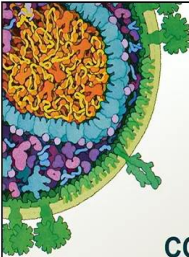


NADM: Non-AIDS-Defining Malignancy



Conclusions

- **Cause-specific age-adjusted mortality** (AIDS, CVD, liver, NADM, and other) **declined from 2012–13 to 2018–19**
- Mortality due to **NADM** was greater than **AIDS-, CVD-, or liver-related**.
- **All-cause mortality** was strongly associated with **modifiable risk factors**, especially **immunologic/virologic status** and **chronic conditions**, indicating areas for improvement.
- Limitations:
 - Many unknown/missing causes of death.
 - Retrospective enrollment may lead to selection bias.



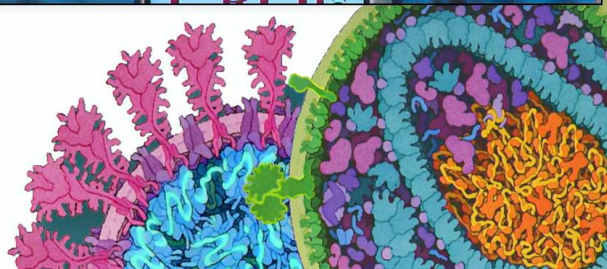
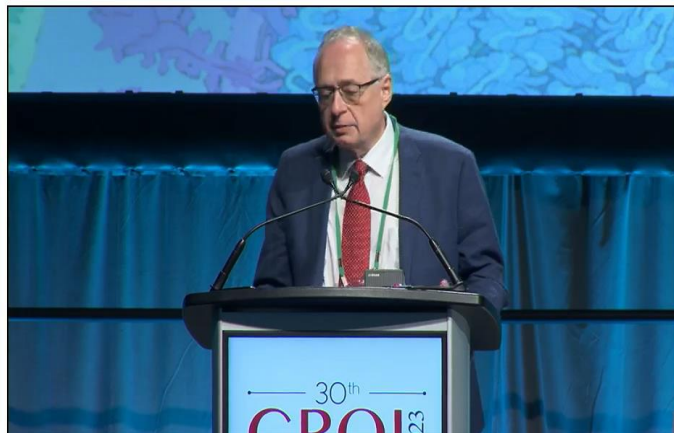
PLENARY: PL-3
Wednesday, February 22, 2023

**THE SCIENCE OF AGING: LESSONS
FOR HIV AT THE INTERFACE OF
COMMONALITY AND HETEROGENEITY**

George A. Kuchel
University of Connecticut, Farmington, CT, United States

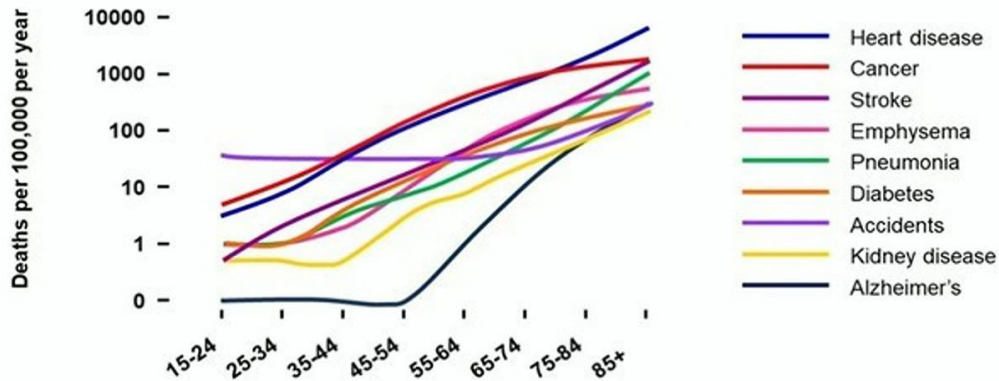
30th
CROI
2023

Disclosure(s): No financial relationships to disclose.





Biological Age as Modifiable Risk Factor for Lifespan & Healthspan



Espinoza, Justice, Newman, Pignolo and Kuchel; Chapter 40 Applied Clinical Geroscience, Hazzard's Geriatric Medicine and Gerontology, 8th edition

nature Vol 460 | 16 July 2009 | doi:10.1038/nature08221

LETTERS

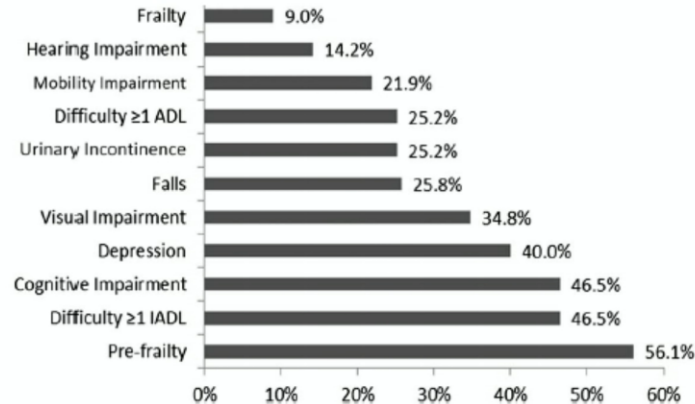
Rapamycin fed late in life extends lifespan in genetically heterogeneous mice

David E. Harrison^{1*}, Randy Strong^{2*}, Zelton Dave Sharp³, James F. Nelson⁴, Clinton M. Astle¹, Kevin Flurkey¹, Nancy L. Nadon⁵, J. Erby Wilkinson⁶, Krystyna Frenkel⁷, Christy S. Carter⁸, Marco Pahor⁹, Martin A. Javors¹⁰, Elizabeth Fernandez⁷ & Richard A. Miller^{10*}



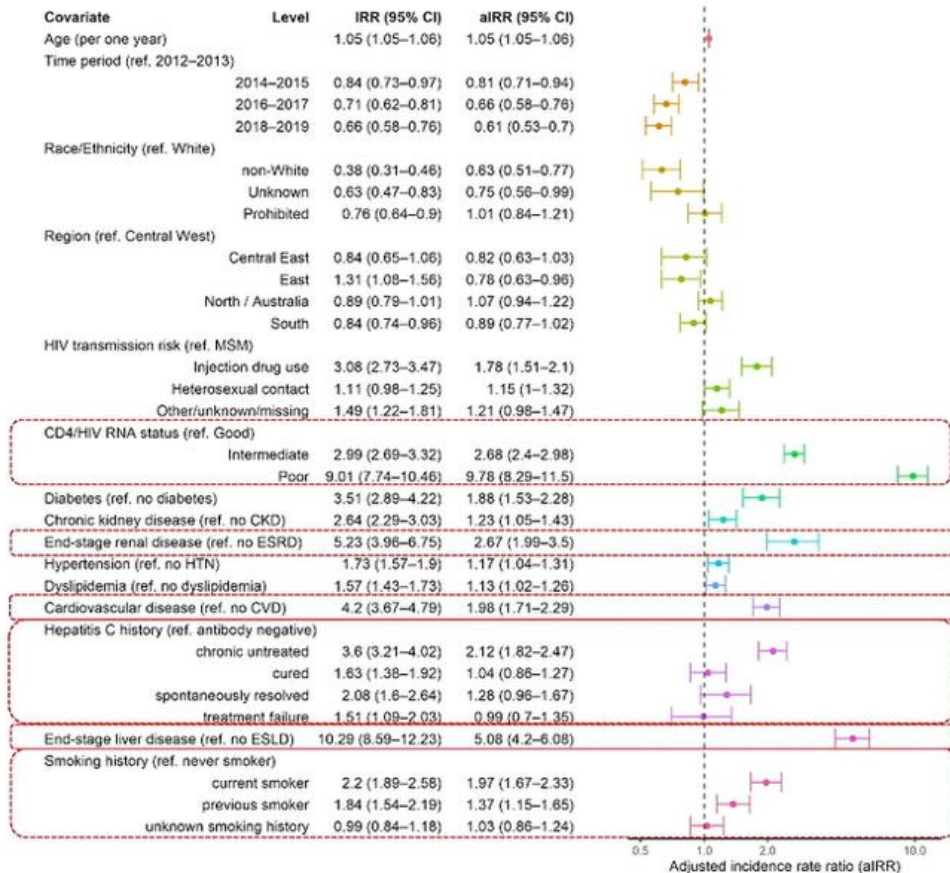
HIV as accelerated (accentuated) aging

Geriatric Syndromes in Older HIV-Infected Adults



Nearly two-thirds
of these individuals
were still 60 years
or younger

All-cause mortality univariable and multivariable time-updated Poisson regressions



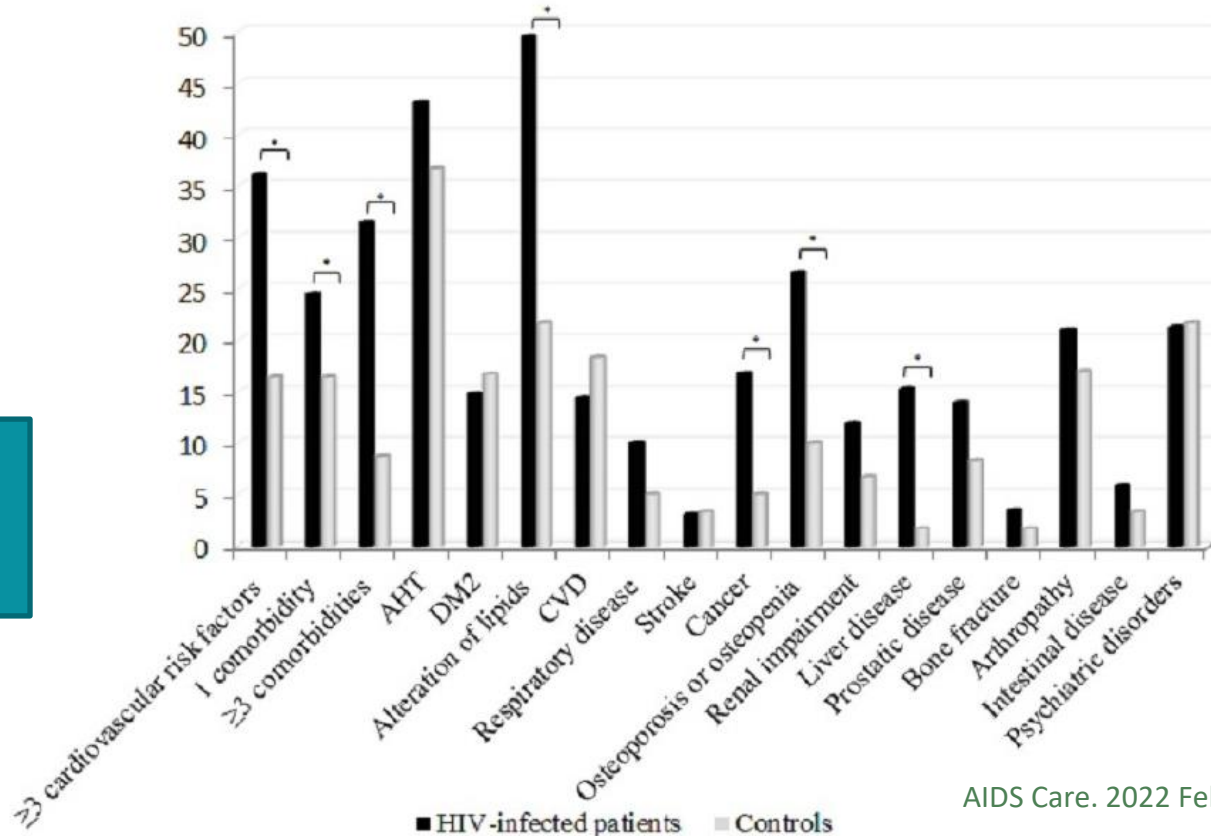
Multivariable analysis also adjusted by Gender, Hepatitis B; aIRR n.s.



Accentuated aging associated with HIV in a Mediterranean setting occurs mainly in persons aged >70 years: a comparative cohort study (Over50 cohort)



208 HIV+ 104
MATCHED
CONTROLS





Malaltia renal



Tabla 1. Principales factores de riesgo para el desarrollo de nefropatía en los pacientes con infección por el VIH

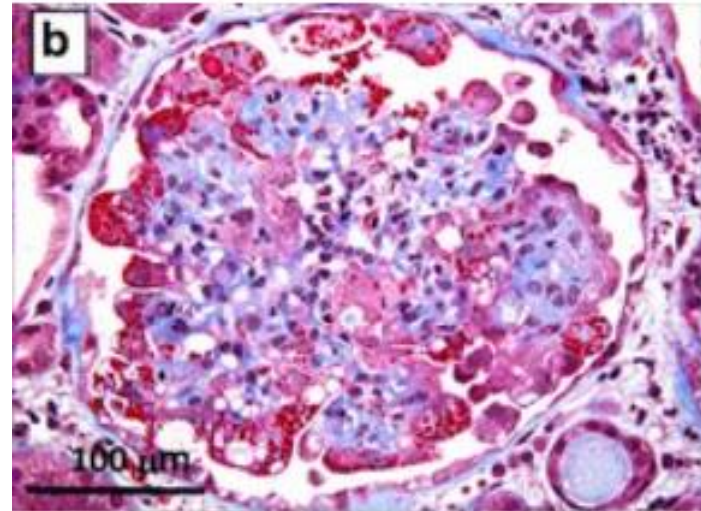
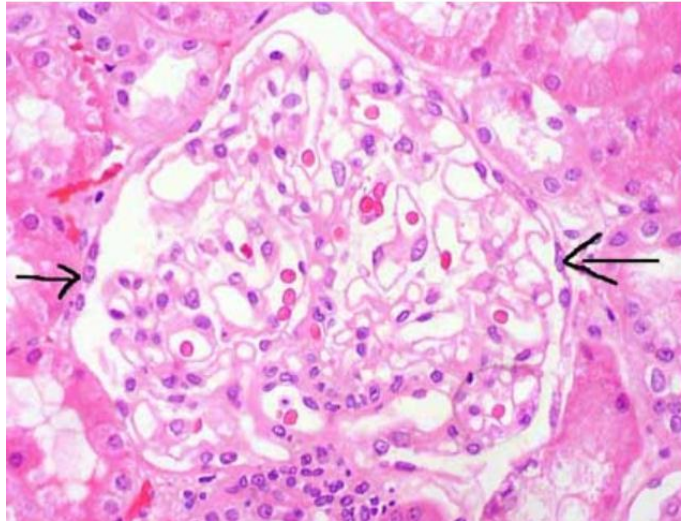
Factores demográficos y genéticos
Edad avanzada
Raza negra
Genotipos de alto riesgo de APOL1
Peso corporal bajo
Factores asociados con la infección por el VIH
Replicación vírica
Cifra nadir de linfocitos CD4+ <200 células/ μ L
Diagnóstico previo de SIDA por eventos clínicos de categoría C
Enfermedades concomitantes
Hipertensión arterial
Diabetes mellitus
Enfermedad cardiovascular
Hepatitis crónica por VHC o VHB
Uso de fármacos potencialmente nefrotóxicos
Antirretrovirales: tenofovir ^a , indinavir ^{a,b} , atazanavir ^{a,b} , lopinavir/ritonavir ^{a,b} .
Otros: anti-inflamatorios no esteroideos ^c , aminoglucósidos ^a , anfotericina B ^a , colistina ^a , Vancomicina ^a , cotrimoxazol ^b , sulfadiazina ^b , aciclovir ^a , foscarnet ^{a,b} , cidofovir ^a , IECA/ARA-II ^c , contrastes iodados



Evolució de les alteracions renals relacionades amb VIH

HIVAN

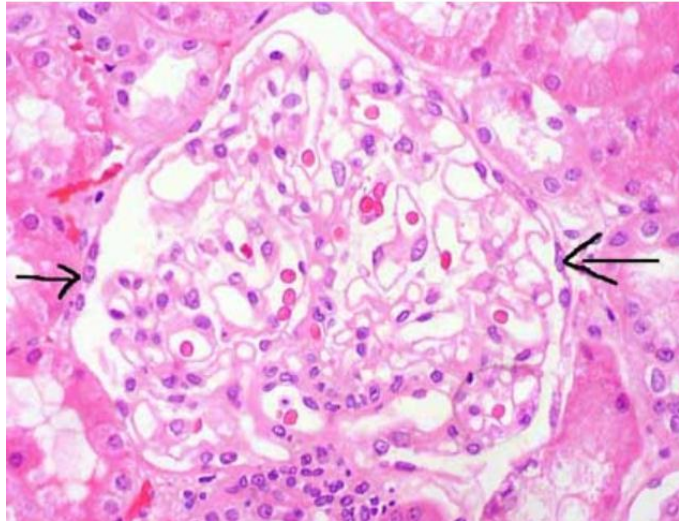
- Glomèrul normal





Evolució de les alteracions renals relacionades amb VIH

- Glomèrul normal



HIVAN

Col.lapse glomerular
Quadre: proteinúria,
sd nefròtic, fracàs
renal agut.

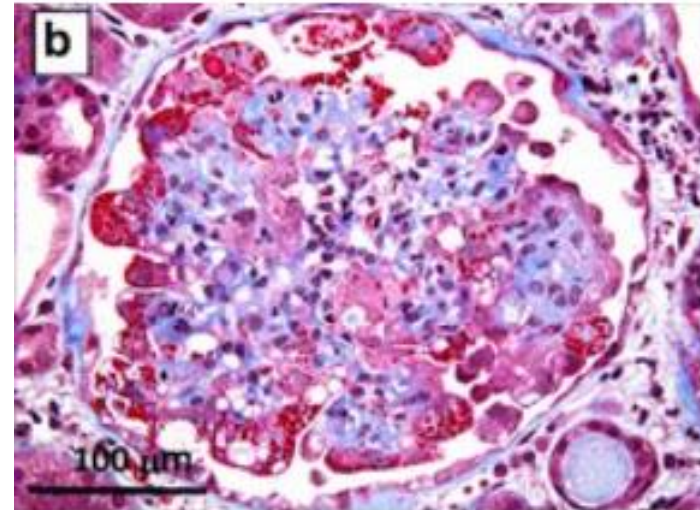




Tabla 3. Presentaciones clínicas más frecuentes y marcadores analíticos en las enfermedades glomerulares de los pacientes con infección por el VIH

	NAVIH	GNMP	IgA	GSF	GNM	GNA	Lupus - Like
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	-	++++	+	+	++	-	++

Nota:

NAVIH, nefropatía asociada al VIH; GNMP, glomerulonefritis membranoproliferativa; IgA, nefropatía IgA; GSF, glomeruloesclerosis segmentaria y focal no colapsante; GNM, glomerulonefritis membranosa; GNA, glomerulonefritis agudas postinfecciosas. VHC, virus de la hepatitis C; VHB, virus de la hepatitis B ; (+), la característica o marcador se presenta generalmente en la nefropatía con mayor o menor intensidad; (-), la característica no se presenta generalmente en esa nefropatía

> Dtsch Med Wochenschr. 1997 Jun 13;122(24):803.

[Crystalluria and nephrolithiasis during therapy with the protease inhibitor indinavir]

> J Antimicrob Chemother. 2013 Aug;68(8):1850-6. doi: 10.1093/jac/dkt125. Epub 2013 Apr 18.

High levels of atazanavir and darunavir in urine and crystalluria in asymptomatic patients

Victoire de Lastours¹, Erika Ferrari Rafael De Silva, Michel Daudon, Raphaël Porcher, Benedicte Loze, Hélène Sauvageon, Jean-Michel Molina



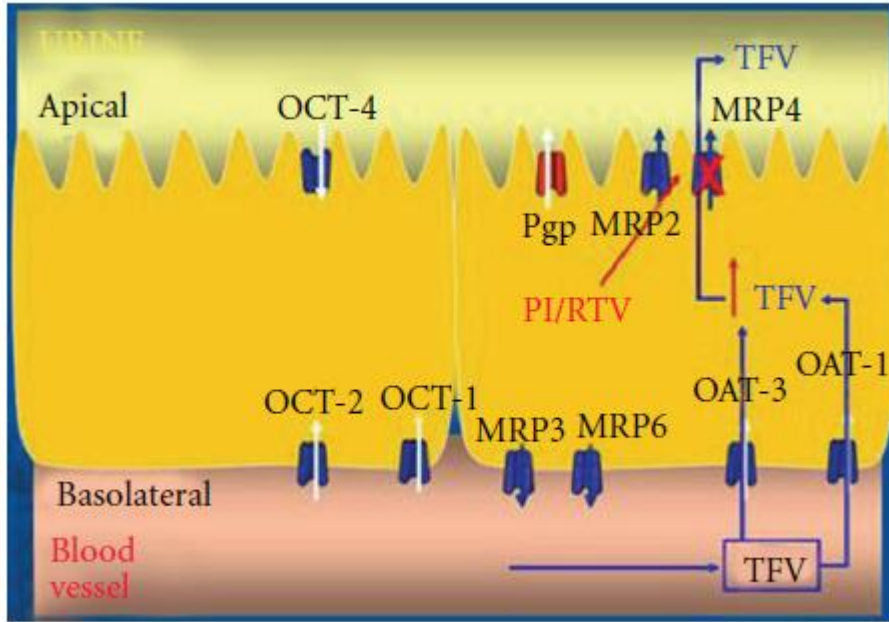
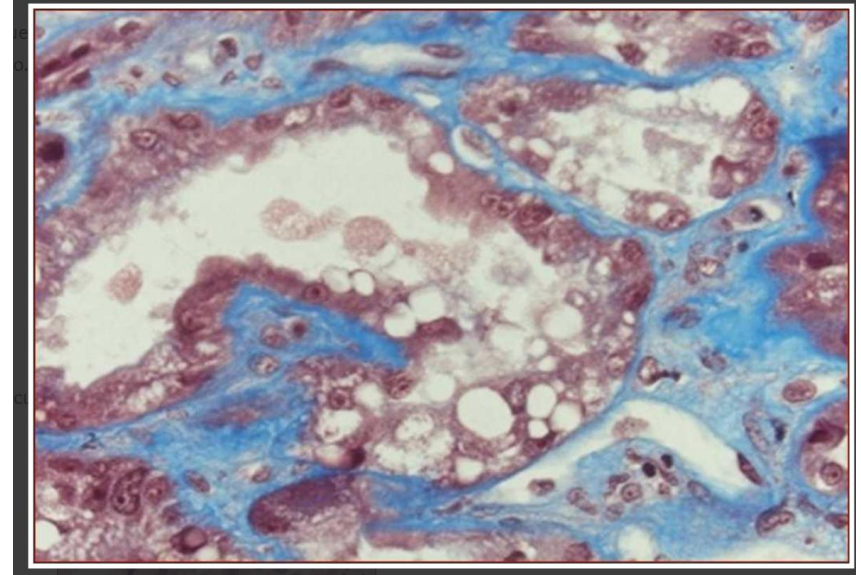


FIGURE 1: Tenofovir is predominantly eliminated via a combination of glomerular filtration and active tubular secretion. It enters into the kidney cell from the basolateral side via organic anion transporters, OAT-1 and OAT-3 [44], and leaves either via P glycoprotein, MRP2, and/or MRP4 [45]. Inhibition of MRP4 by PI/RTV leads to increased intracellular tenofovir levels which may increase its nephrotoxic effects. OAT: organic anion transporter; MRP: multidrug resistant protein; PI/RTV: ritonavir-boosted protease inhibitor; TFV: tenofovir.

TUBULOOPATIA PROXIMAL
CLINICA SD FANCONI (glucosúria,
fosfatúria, proteinúria)



AIDS Research and Treatment
Volume 2011, Article ID 562790, 11 pages
doi:10.1155/2011/562790

Malaltia renal en la nostra cohort de pacients



Malaltia renal en la nostra cohort de pacients

- Proporció a l'any 2022 de GFR<60 o proteïnúria mantinguda: 7% de la població de 3500 pts.
- Diagnòstics més freqüents:
 - Nephropaty related to arterial hipertension and diabetis 31%
 - Renal disease by immune complex (mostly related to hepatitis C coinfection) 18%.



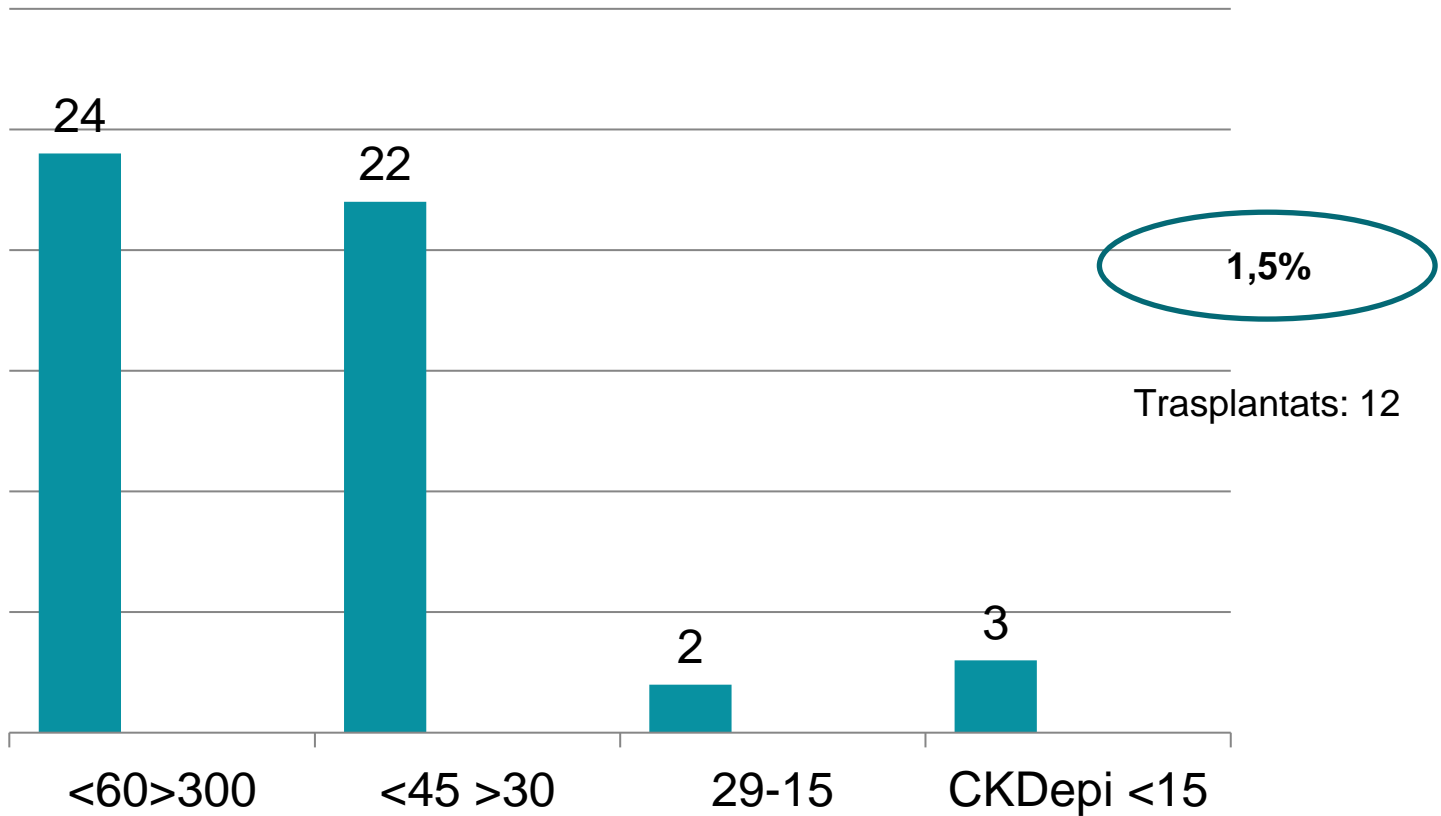
**Prognosis of CKD by GFR
and Albuminuria Categories:
KDIGO 2012**

				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (ml/min/ 1.73 m ²) Description and range	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Advanced kidney disease corresponds to red boxes.



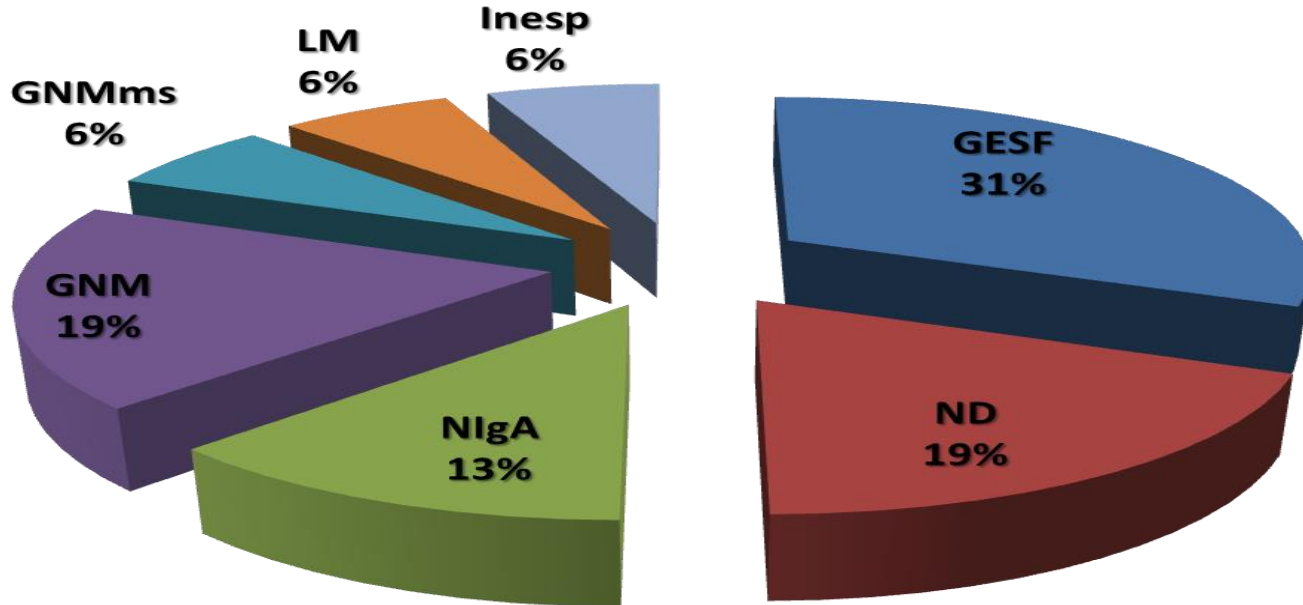
Malaltia renal avançada en la nostra població





- **BIOPSIAS RENALES DESDE 2008:**
 - **Diagnósticos predominantes:**
 - **Glomeruloesclerosis Segmentaria y focal,**
 - **Nefropatia Diabetica y**
 - **GN Membranosa**
 - **GNMms (gn mesangial) (LM: lesión mínima)**
 - **(N: 26)**

Biopsias renales en pacientes VIH+





CONCLUSIONS

- La mortalitat global de PVVIH ha disminuït en tots els àmbits
- Les morbiditats de la PVVIH en el nostre entorn que tenen més freqüència son les no relacionades amb el VIH
- L'envelliment és un factor important a l'hora de parlar de co morbiditats en aquest escenari
- La malaltia renal y la malaltia cardiovascular tenen un impacte important i creixent en la nostra població
- La malaltia renal predominant en PVVIH de la nostra cohort està vinculada amb comorbiditats no relacionades amb el VIH ni els tractaments antiretrovirals



Thanks

Any questions?