

# Sesión de actualización en enfermedades infecciosas.

## Datos de CORIS del efecto del consumo de alcohol en la mortalidad

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9 de maig del 2024

Servei de Medicina Interna. Unitat d'Addiccions

Hospital Universitari Germans Trias i Pujol

## Guión de la sesión

- Introducción biográfica.
- *International URBAN Alcohol Research Collaboration on HIV/AIDS (ARCH) Center.*
- Alcohol:
  - Daño asociado al consumo de alcohol
  - ¿Cómo detectar el consumo de alcohol perjudicial?
- Presentación CROI 2024, Denver, USA.

## Biosketch

Attending Physician. Associate professor.

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Hospital Universitari Germans Trias i Pujol. Universitat Autònoma Barcelona. Spain.

1997-2002 *Resident in Internal Medicine*, Hospital Universitari Germans Trias i Pujol, Badalona.

2002-2006 *Clinical Investigator/Pre-doctoral Fellow*. HIV/AIDS Unit. Department of Internal Medicine. Hospital Universitari Germans Trias i Pujol. Badalona.

PhD dissertation thesis: “Treatment of Chronic Hepatitis C Virus infection in HIV and HCV co-infected patients”. July 2007. PhD Directors: B. Clotet, J. Tor, C. Tural.

2008-2020. *Member*. Red de Trastornos Adictivos (RTA)- Redes temáticas de Investigación Cooperativa en Salud (RETICS)-ISCIII

2021-present. *Member*. Red de Investigación en Atención Primaria de Adicciones (RIAPAD)- Redes de Investigación Cooperativa Orientadas a Resultados en Salud (RICORS) -ISCIII

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2012-present. *Member*. URBAN ARCH Study group [<http://sites.bu.edu/urbanarch/>]

2019-present. *Member*. CORIS cohort

Research interest: medical consequences of alcohol and substance use disorder. Alcohol-associated liver disease.



The **International URBAN Alcohol Research Collaboration on HIV/AIDS (ARCH) Center**, funded by the National Institute on Alcohol Abuse and Alcoholism, conducts and disseminates interdisciplinary research on the role of alcohol use among people with HIV



Alcohol Research Collaboration on HIV/AIDS

**Principal Investigator:**  
Jeffrey Samet MD MPH  
Boston University School of  
Medicine



<https://sites.bu.edu/urbanarch/>

# Prior publications on alcohol and HIV infection

AIDS RESEARCH AND HUMAN RETROVIRUSES  
Volume 29, Number 8, 2013  
© Mary Ann Liebert, Inc.  
DOI: 10.1089/aid.2012.0348

## Interleukin-6 Is Associated with Noninvasive Markers of Liver Fibrosis in HIV-Infected Patients with Alcohol Problems

Daniel Fuster<sup>1</sup>, Judith I. Tsui<sup>1</sup>, Debbie M. Cheng<sup>1,2</sup>, Emily K. Quinn<sup>3</sup>, Kaku A. Armah<sup>4</sup>, David Nunes<sup>5</sup>, Matthew S. Freiberg<sup>6</sup> and Jeffrey H. Samet<sup>1,7</sup>

## Inflammatory cytokines and mortality in a cohort of HIV-infected adults with alcohol problems

Daniel Fuster<sup>a</sup>, Debbie M. Cheng<sup>a,b</sup>, Emily K. Quinn<sup>c</sup>, Kaku A. Armah<sup>d</sup>, Richard Saitz<sup>a,f</sup>, Matthew S. Freiberg<sup>e</sup>, Jeffrey H. Samet<sup>a,g</sup> and Judith I. Tsui<sup>a</sup>

*AIDS* 2014, **28**:1059–1064



Article

## Alcohol Consumption and Hepatitis C Virus (HCV) RNA Levels in HIV/HCV Coinfected Patients

Daniel Fuster<sup>1,\*</sup>, David Nunes<sup>2</sup>, Debbie M. Cheng<sup>3,4</sup>, Richard Saitz<sup>3,5,6</sup> and Jeffrey H. Samet<sup>3,5,6</sup>

Published in final edited form as:

*Alcohol Clin Exp Res.* 2013 September ; 37(9): 1527–1535. doi:10.1111/acer.12129.

## Impact of lifetime alcohol use on liver fibrosis in a population of HIV-infected patients with and without hepatitis C coinfection

Daniel Fuster<sup>1</sup>, Judith I. Tsui<sup>1</sup>, Debbie M. Cheng<sup>1,2</sup>, Emily K Quinn<sup>3</sup>, Carly Bridden<sup>1</sup>, David Nunes<sup>4</sup>, Howard Libman<sup>5</sup>, Richard Saitz<sup>1,6</sup>, and Jeffrey H. Samet<sup>1,7</sup>

Published in final edited form as:

*Addiction.* 2014 January ; 109(1): 62–70. doi:10.1111/add.12367.

## Chronic Hepatitis C Virus Infection is Associated with All-Cause and Liver-Related Mortality in a Cohort of HIV-Infected Patients with Alcohol Problems

Daniel Fuster<sup>1</sup>, Debbie M. Cheng<sup>1,2</sup>, Emily K. Quinn<sup>3</sup>, David Nunes<sup>4</sup>, Richard Saitz<sup>1,5</sup>, Jeffrey H. Samet<sup>1,6</sup>, and Judith I. Tsui<sup>1</sup>

Published in final edited form as:

*Curr HIV Res.* 2021 ; 19(4): 324–331. doi:10.2174/1570162X19666210519151320.

## Lack of association between recent cannabis use and advanced liver fibrosis among HIV-positive heavy drinkers

Daniel Fuster<sup>1</sup>, Kaku So-Armah<sup>2</sup>, Debbie M. Cheng<sup>3</sup>, Sharon M. Coleman<sup>4</sup>, Natalia Gnatienco<sup>5</sup>, Dmitry Lioznov<sup>6,7</sup>, Evgeny M. Krupitsky<sup>8,9</sup>, Matthew S. Freiberg<sup>10</sup>, Jeffrey H. Samet<sup>2,11</sup>

## Review papers



Submit a Manuscript: <http://www.wjgnet.com/esps/>  
Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>  
DOI: 10.4254/wjh.v8.i31.1295

*World J Hepatol* 2016 November 8; 8(31): 1295-1308  
ISSN 1948-5182 (online)  
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REVIEW

### **Alcohol use disorder and its impact on chronic hepatitis C virus and human immunodeficiency virus infections**

Daniel Fuster, Arantza Sanvisens, Ferran Bolao, Inmaculada Rivas, Jordi Tor, Robert Muga

*The NEW ENGLAND JOURNAL of MEDICINE*

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

### **Alcohol Use in Patients with Chronic Liver Disease**

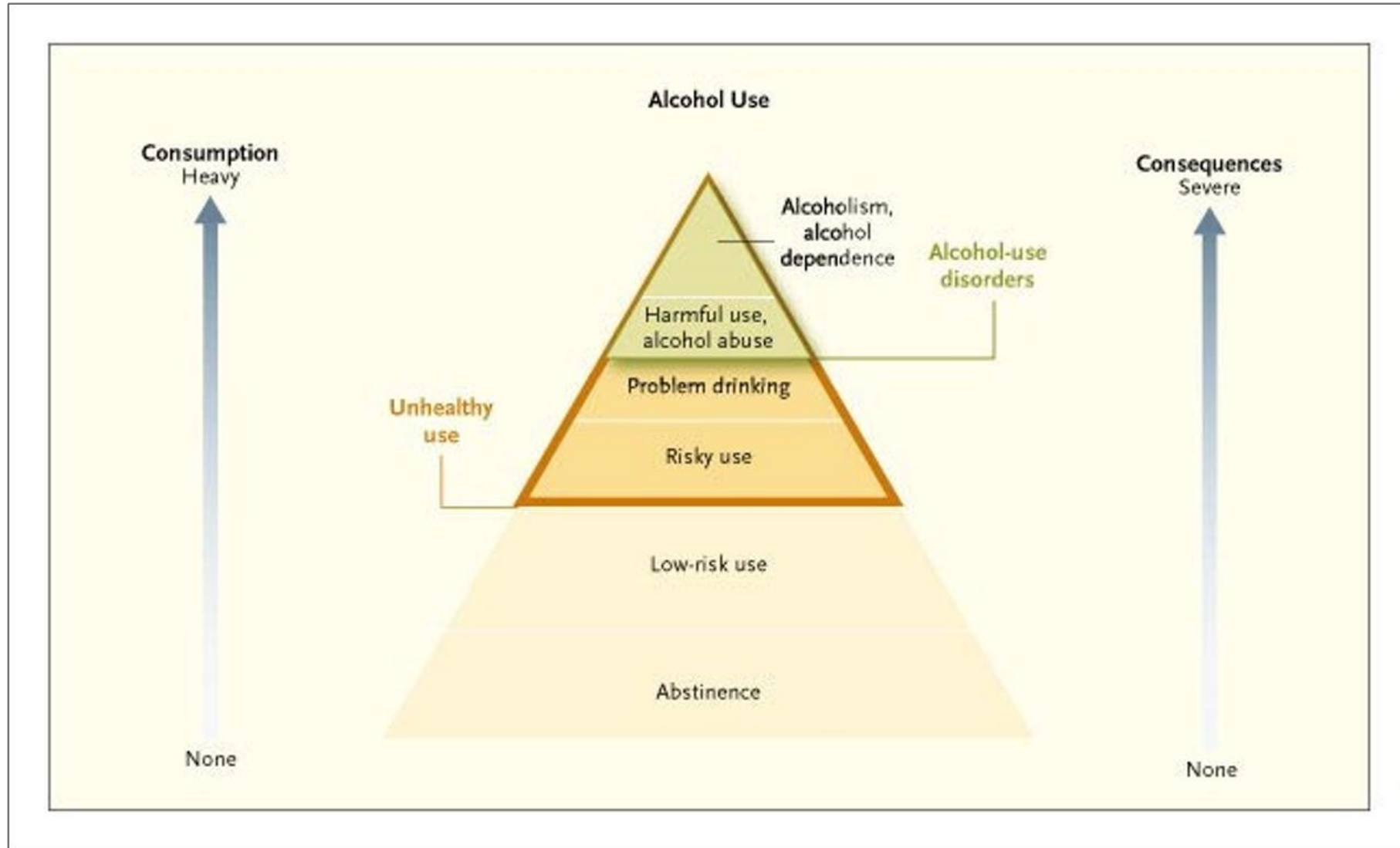
Daniel Fuster, M.D., Ph.D., and Jeffrey H. Samet, M.D., M.P.H.

## Alcohol-associated harm

- Alcohol is the seventh risk factor for both death and the burden of disease and injury.
- Alcohol use accounts for 6.8% of age-standardized deaths in men and 2.2% in women, with a disproportionate effect on young people (1 in 4 deaths occur in people 20-24 years of age).
- Except for tobacco, alcohol accounts for a higher burden of disease than any other drug.
- Alcohol is responsible of >140,000 deaths per year in the US and 1 million deaths in Europe.
- In the US, 10.2% of the population have an Alcohol Use Disorder.
- Europe is the world region with higher alcohol intake per capita (11.3 liters)
- In Spain, 77% of the population drink and 5.2% have an AUDIT score equal or greater than 8 (6.7% in males and 3.7% in females). Alcohol responsible of 4% of all deaths.

Global Burden of Disease Study 2016. *Lancet* 2018; 392: 1015-1035. Rehm J et al. *Lancet* 2009; 373: 2223-33; Fuster D, Samet JH. *N Engl J Med.* 2018;379:1251-1261; Donroe JH, Edelman EJ. *Ann Intern Med.* 2022;175(10):ITC145-ITC158; EDADES 2022 *Plan Nacional sobre Drogas, Spain*; Donat M et al. *Plan Nacional Sobre Drogas, 2020*

# Spectrum of unhealthy alcohol use





# ACUTE ALCOHOL-RELATED HARM

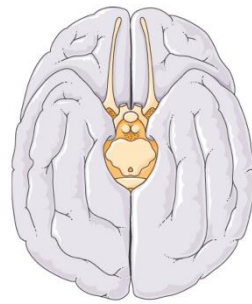
# CHRONIC ALCOHOL-RELATED HARM

Fuster D et al. In *Drogodependencias. Panamericana*, 2023

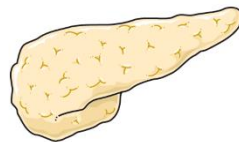
## ALCOHOL INTOXICACION

- Speech impairment
- Motor coordination loss
- Memory loss
- Loss of consciousness
- Respiratory depression
- Nausea/vomiting (aspiration pneumonia)

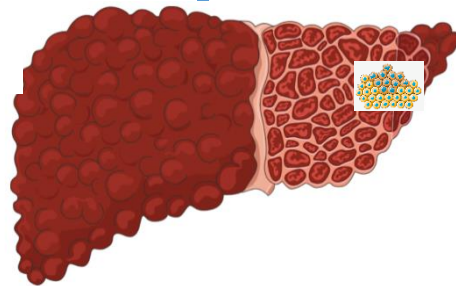
- ↑ lactic acid
- ↓ glycemia
- ↓ calcium
- ↓ magnesium
- ↓ phosphate



Alcohol withdrawal (*delirium tremens*)  
Wernicke's encephalopathy  
Cerebellar degeneration  
Marchiafava- Bignami syndrome  
Alcohol-associated dementia  
Stroke



pancreatitis

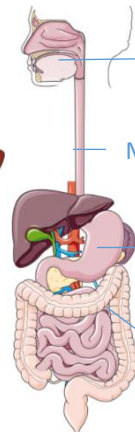


Steatohepatitis

Fibrosis

Cirrhosis

Hepatocarcinoma



Oral leucoplakia

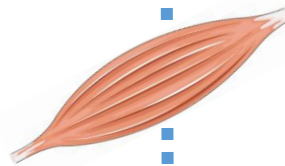
Mallory Weiss syndrome

EGR  
Peptic Ulcer  
Portal hypertension  
Gastropathy

Colon cancer

Rabdomiolysis

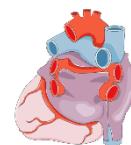
Myopathy



HBP



Cancers



Atrial fibrillation  
Alcohol cardiomyopathy



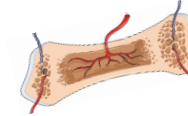
Fetal alcohol spectrum disorder



Polyneuropathy



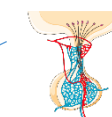
Macrocytic anemia  
Iron deficiency



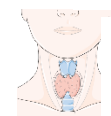
↓ Bone mineral density  
↑ fracture risk



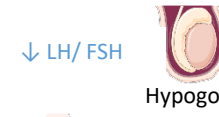
Low platelet count



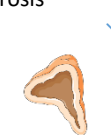
↓ GH  
Insulin resistance  
Growth impairment



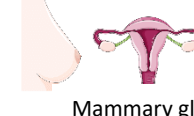
↓ TSH  
↓ T3 y T4  
↓ volume  
↑ fibrosis



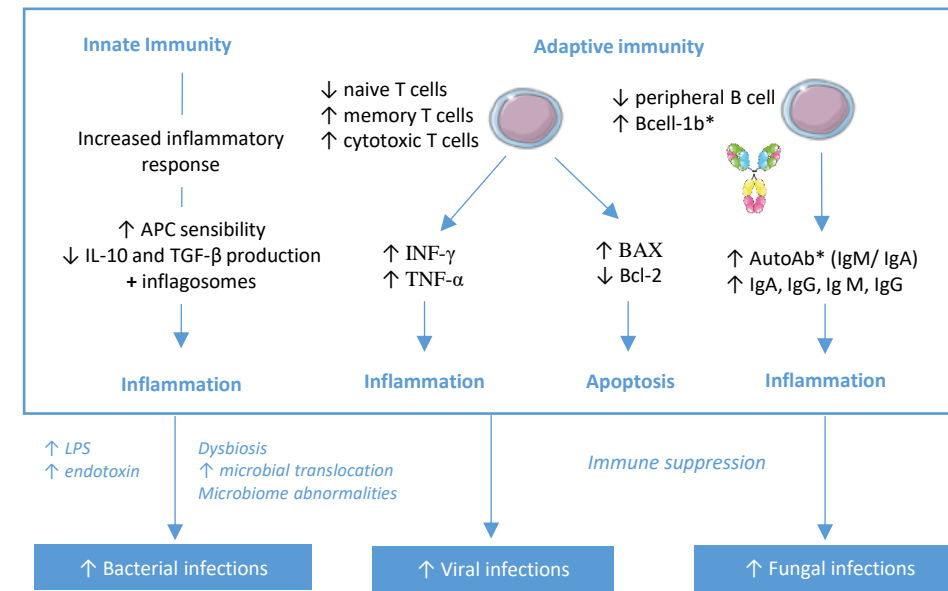
↓ LH/ FSH  
Hypogonadism



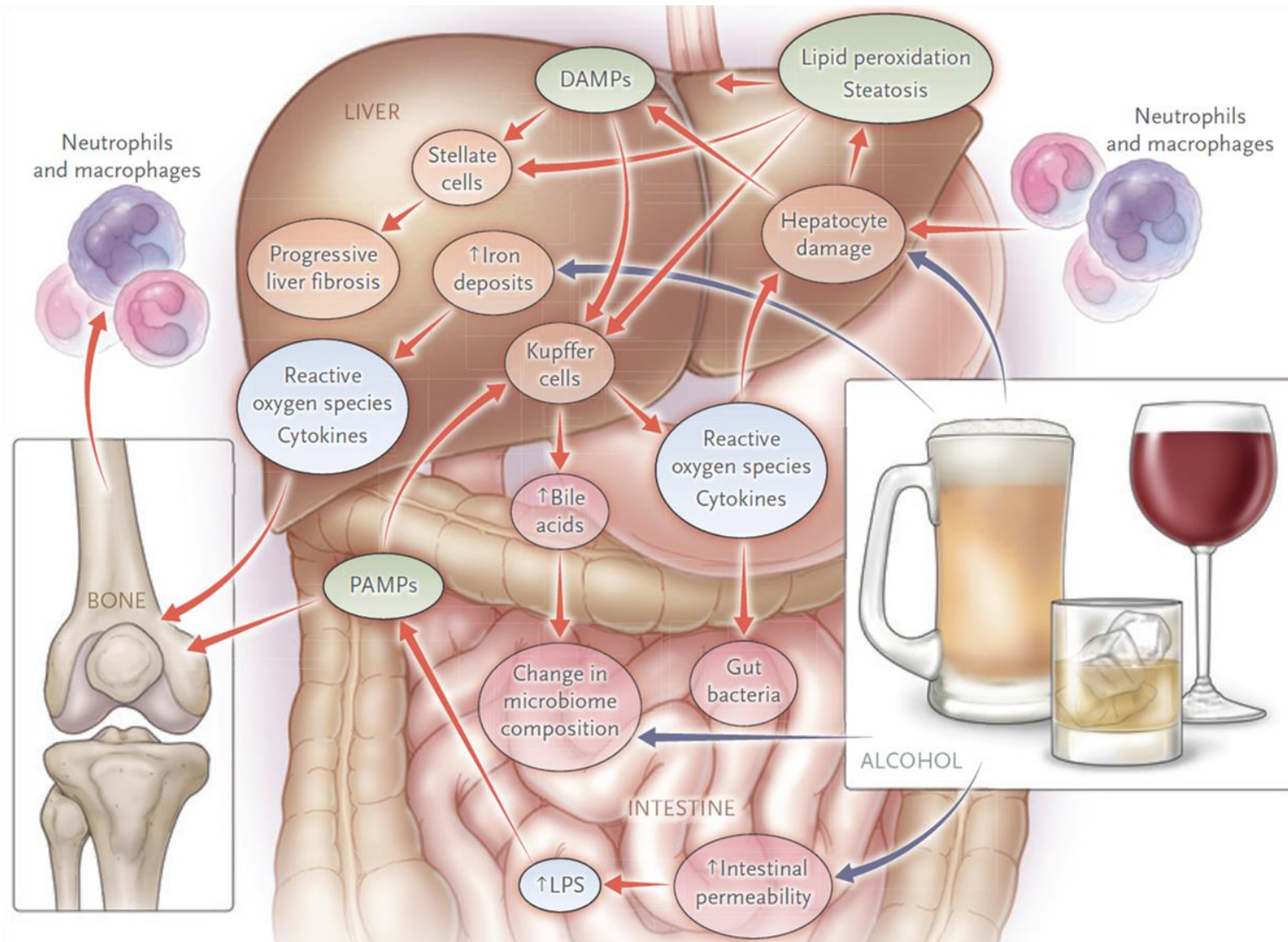
↓ ACTH  
↓ cortisol



Mammary gland atrophy  
Menstrual abnormalities



# Diagram of alcohol-associated liver damage



## NIAAA recommended screening opportunities

- During routine examinations
- Before prescribing a medication with potential interactions with alcohol
- In the emergency department or urgent care center
- When seeing patient who:
  - Is pregnant or planning conception
  - Has risk factors for unhealthy alcohol use
  - Has potentially alcohol-related health problems
  - Has a chronic condition resistance to usual treatment

# NIAAA Single Alcohol Screening Question

## NIAAA Single Alcohol Screening Question

**Question:** How many times in the past year have you had x or more drinks in a day? (where x is 5 for men and 4 for women)

**Scoring:**  $\geq 1$  episode is considered a positive screening result, which should be followed by administration of the AUDIT-C or another measure to categorize level of risk

AUDIT-C*					
Questions	Points				
	0	1	2	3	4
1. How often did you have a drink containing alcohol in the past year?	Never	Monthly or less	2–4 times a month	2–3 times a week	$\geq 4$ times a week
2. How many drinks did you have on a typical day when you were drinking in the past year?	0–2	3–4	5–6	7–9	$\geq 10$
3. How often did you have $\geq 6$ drinks on 1 occasion in the past year?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily

**Scoring:** Points for each of the 3 items are summed. Total score of  $\geq 4$  for men and  $\geq 3$  for women is considered positive for unhealthy alcohol use. Cutoffs may vary depending on purpose and population of interest. For the USAUDIT-C, the response scale, the drinking threshold in question 3, and the scoring cutoffs differ from those in the AUDIT-C.

# AUDIT

Alcohol Use Disorders Identification Test

1-7= low-risk consumption

8 –14 = hazardous or harmful alcohol consumption

15 or more= likelihood of alcohol dependence (moderate-severe AUD)

Item no.	The AUDIT question	AUDIT domain*	Established AUDIT Variations				
			AUDIT-10	AUDIT- C	AUDIT-3	FAST	AUDIT-4
1	How often do you have a drink containing alcohol?	C	*	*			*
2	How many drinks containing alcohol do you have on a typical day when you are drinking?	C	*	*			*
3	How often do you have six or more drinks on one occasion?	C	*	*	*	*	*
4	How often during the last year have you found that you were not able to stop drinking once you had started?	D	*				
5	How often during the last year have you failed to do what was expected of you because of alcohol?	D	*			*	
6	How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?	D	*				
7	How often during the last year have you had a feeling of guilt and remorse after drinking?	H	*				
8	How often during the last year have you been unable to remember what happened the night before because of your drinking?	H	*			*	
9	Have you or someone else been injured because of your drinking?	H	*				
10	Has a relative, friend, doctor or other healthcare worker been concerned about your drinking or suggested you cut down?	H	*			*	*
Score range:			0–40	1–12	0–4	0–16	1–16

\*AUDIT domains are: C, alcohol consumption; D, alcohol dependence; H, harmful alcohol use.<sup>5</sup>

## CAGE questionnaire

**Table 1. CAGE questionnaire<sup>12</sup>**

C	Have you felt the need to <b>C</b> ut down?
A	Have you felt <b>A</b> nnoyed at the suggestion that you might have an alcohol problem?
G	Have you felt <b>G</b> uilty about excessive drinking?
E	Do you need an <b>E</b> ye opener in the morning?
Score 1 for each positive response; scores of 2 or more suggest an alcohol problem	

## DSM-5 Alcohol Use Disorder Diagnostic Criteria (APA, 2013).

1. Alcohol is often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control alcohol use.
3. A great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects.
4. Craving, or a strong desire or urge to use alcohol.
5. Recurrent alcohol use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol.
7. Important social, occupational, or recreational activities are given up or reduced because of alcohol use.
8. Recurrent alcohol use in situations in which it is physically hazardous.
9. Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol.
10. Tolerance, as defined by either of the following:
  - a. A need for markedly increased amounts of alcohol to achieve intoxication or desired effect
  - b. A markedly diminished effect with continued use of the same amount of alcohol
11. Withdrawal, as manifested by either of the following:
  - a. The characteristic withdrawal syndrome for alcohol
  - b. Alcohol (or a closely related substance, such as a benzodiazepine) is taken to relieve or avoid withdrawal symptoms.

Mild: 2–3 symptoms; Moderate: 4–5 symptoms; Severe: ≥6 symptoms

2024 Conference on Retroviruses and Opportunistic Infections, Denver (Colorado)

# Associations of alcohol consumption with long-term mortality of ART-naïve persons seeking HIV care.

**Daniel Fuster**<sup>1</sup>, Paola Zuluaga<sup>1</sup>, Enric Abellí-Deulofeu<sup>1</sup>, Laura Bermejo<sup>2</sup>, Santiago Moreno<sup>3</sup> Lucio Jesús García Fraile Fraile<sup>4</sup>, Jose Antonio Iribarren<sup>5</sup>, Cristina Moreno<sup>6</sup>, Inés Suarez-García<sup>7</sup>, David Vinuesa García<sup>8</sup>, Vicente Estrada<sup>9</sup>, Julián Olalla Sierra<sup>10</sup>, Juan Macias Sanchez<sup>11</sup>, Inma Jarrin<sup>6</sup>, Robert Muga<sup>1</sup>.

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## Background: Alcohol and HIV

- Between 8% and 42% of persons living with HIV (PLWH) report unhealthy drinking.
- Alcohol use is an independent risk factor for HIV acquisition.
- Experimental studies: alcohol administered to macaques before and after infection with simian immunodeficiency virus (SIV) increases levels of SIV viremia and mortality. Thus alcohol use might be an important factor in HIV disease progression.
- Chronic alcohol use and HIV independently damage the intestinal mucosa, increase microbial translocation and inflammation.
- Chronic alcohol use impacts both innate and adaptive immunity.
- Among PLWH, alcohol blood levels are higher than in the general population, an effect that is mitigated once ART is started.
- Alcohol use is associated with decreased retention in care and worse ART adherence (dose-response relationship).
- The effect on adherence is less apparent with newer ART regimens.
- Faster CD4 recovery after ART initiation among PLWH with low alcohol consumption compared with PLWH with moderate and high alcohol consumption.
- Alcohol consumption among PLWH is also associated poorer clinical outcomes and increased mortality.
- HCV infection (more common among PLWH who use alcohol) also increases mortality.

## Study aim

- We aimed to examine the associations and prognosis of excessive alcohol consumption in HIV+, ART-naïve individuals admitted to HIV care.

## Methods

- Longitudinal study in the Spanish network on HIV/AIDS (CoRIS Cohort Study)
- Individuals enrolled between 2004 and 2021 in 47 HIV/AIDS units in Spain.
- Excessive alcohol consumption at first visit was defined as a  $\geq 40$  grams/ day.
- We calculated crude and adjusted mortality rates stratified by excessive alcohol consumption.
- We performed Survival analysis curves (Kaplan-Meier) stratified by excessive alcohol use
- We performed Cox regression models to assess the association between excessive alcohol consumption and overall mortality.



- CoRIS is an open, prospective multicenter cohort of persons with confirmed HIV infection, naïve to ART at study entry, recruited in 48 centers from 14 Autonomous Regions in Spain from 2004-onwards.
- Summarily, CoRIS collects a minimum dataset that encompasses baseline and follow-up sociodemographic, immunological and clinical data, including data on antiretroviral medications. Data are highly standardized and submitted to periodic quality control procedures.

# Baseline characteristics

	Study population N= 8,378
Women [n (%)]	1257 (15)
Age (years) Median [Interquartile range (IQR)]	36.1 (29.2-44.2)
CD4 count (cell/mm <sup>3</sup> ) Median (IQR) (n=8,301)	398 (219-596)
HIV viral load (log <sub>10</sub> UI/mL) Median (IQR) (n= 8,238)	4.54 (3.67-5.13)
HCV infection (EIA +) [n (%)]	740 (8.8)
Mode of HIV acquisition [n (%)]:	
• Men who have sex with men (MSM)	5,122 (61)
• Heterosexual transmission	2,379 (28)
• Injection drug use (IDU)	524 (6.3)
• Other/unknown	353 (4.2)
No alcohol consumption [n (%)]	5,194 (62.0)
Alcohol consumption <40 grams/ day [n (%)]	2,823 (33.7)
Alcohol consumption ≥40 grams/ day [n (%)]	361 (4.3)

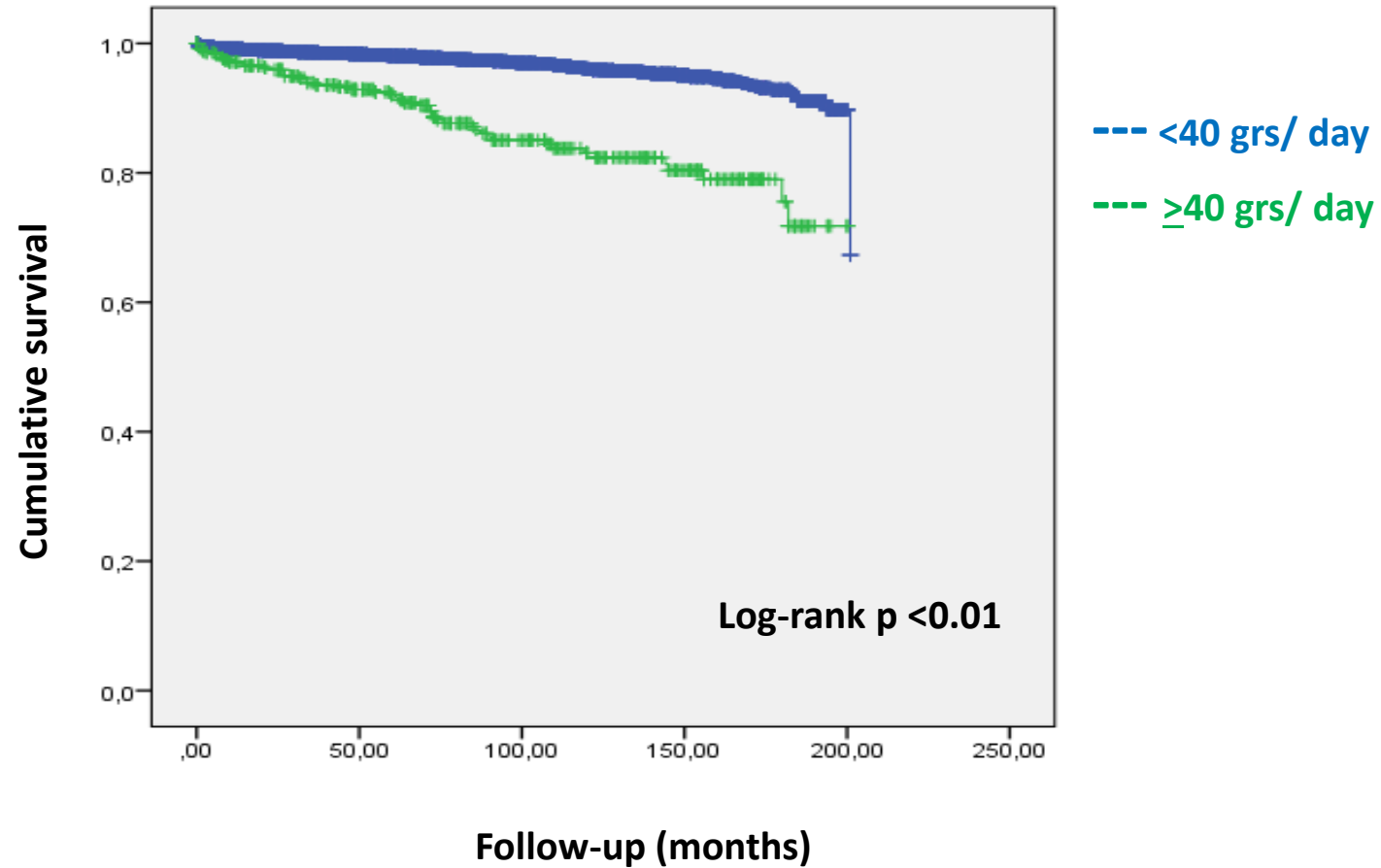
# ART-naïve patients by alcohol consumption at baseline

	<40 grs/day N= 8,017	≥40 grs/day N= 361	p-value
Women [n (%)]	1,214 (15.2)	43 (11.9)	0.93
Age (years) (IQR)	42.7 (34.8-51.4)	48.7 (41.5-55.9)	<b>&lt;0.01</b>
CD4 count (cell/mm <sup>3</sup> ) (IQR)	400 (418-617)	360 (198-588)	0.05
HIV viral load (log <sub>10</sub> UI/mL) (IQR)	4.58 (3.68-5.13)	4.53 (3.38-5.14)	0.67
HCV infection (EIA +) [n (%)]	617 (7.7)	123 (34)	<b>&lt;0.01</b>
Mode of HIV acquisition [n (%)]:			<b>&lt;0.01</b>
• MSM	5,002 (62.4)	120 (33.2)	
• Heterosexual	2,258 (28.2)	121 (33.5)	
• IDU	416 (5.2)	108 (29.9)	
• Other/ unknown	341 (4.3)	12 (3.3)	

# Follow-up, mortality rates

	Study population	Alcohol <40 grs/ day	Alcohol ≥40 grs/ day
Follow-up (p-y)	52,799	50,463.4	2,636
Median Follow-up (years)	5.6 (2.5-9.8)	5.6 (2.5-9.78)	6.5 (3.3-11.5)
Deaths [n (%)]	267 (3.1)	218 (2.8)	49 (13.6)
Mortality rate	0.51 x 100 p-y	0.43 x 100 p-y	1.86 x 100 p-y
Mortality rate ratio		1	<b>4.30 (95% CI: 3.15-5.87), p &lt;0.01</b>

# Kaplan-Meier survival analysis





# Cox regression model

	Univariate HR (95% CI)	Multivariable HR (95% CI)
Alcohol $\geq$ 40 grs/ day	<b>4.28 (3.13-5.83)</b>	<b>2.39 (1.68-3.42)</b>
Sex	1.06 (0.47-1.06)	1.07 (0.75-1.51)
Age	1.00 (0.99-1.01)	1.21 (0.88-1.67)
HIV RNA (log)	1.04 (0.81-1.33)	1.01 (0.90-1.67)
CD4 cell count	<b>2.58 (1.96-3.40)</b>	<b>2.19 (1.65-2.93)</b>
HCV infection (EIA+)	<b>5.05 (3.94-6.48)</b>	<b>3.06 (2.02-4.63)</b>
IDU vs. other	<b>4.72 (3.64-6.17)</b>	<b>1.53 (1.0-2.41)</b>

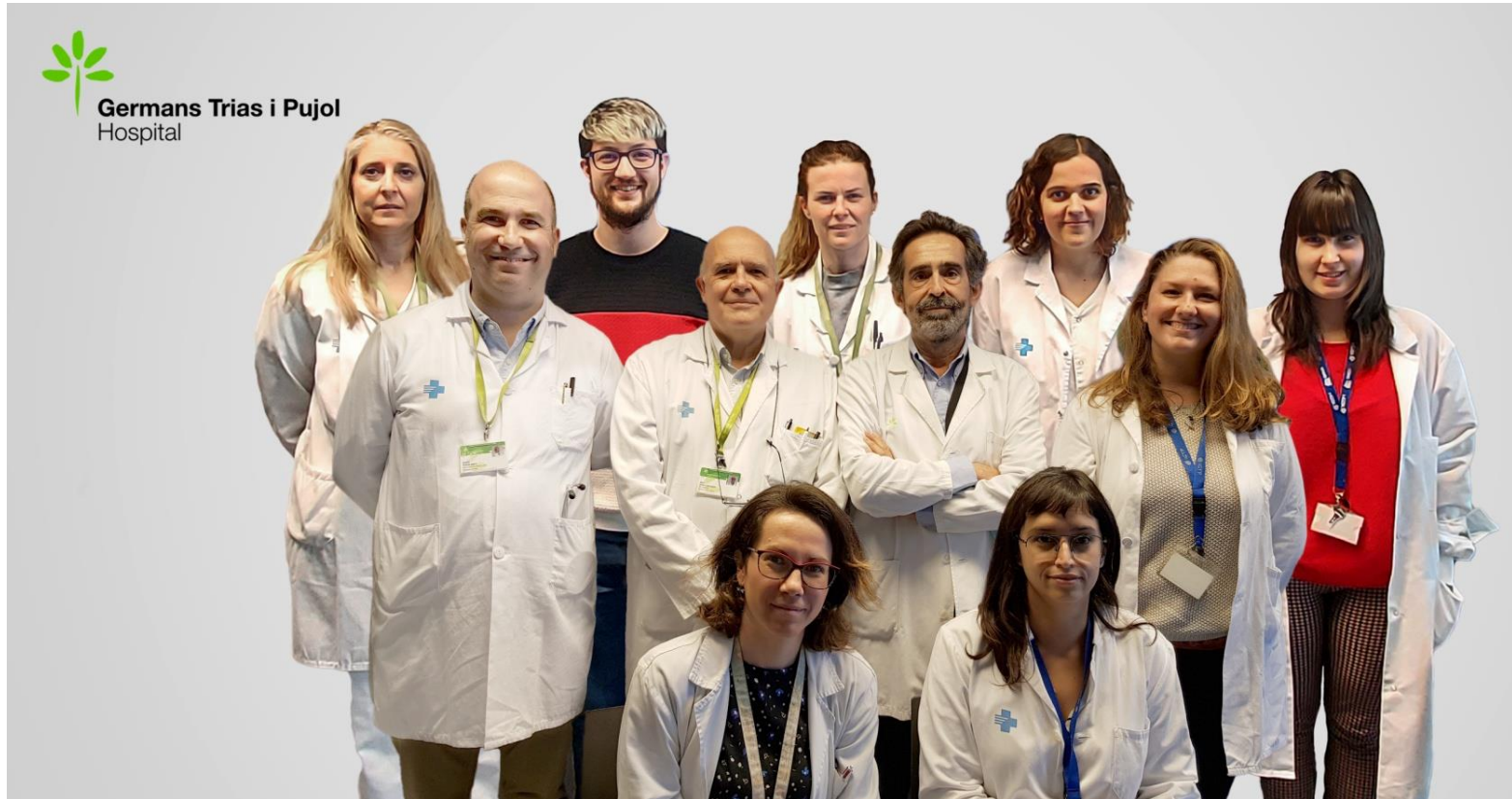
# Conclusions

- In this cohort of ART-naïve individuals entering HIV care, excessive alcohol use was associated with reduced survival.
- HCV infection, CD4 below the median and IDU were also independently associated with poorer survival
- These results underscore the importance of addressing alcohol use disorder in PLWHA.

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