

Management of alcohol-associated ACLF: How to improve the survival of our patients?

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DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIP(S) WITH INELIGIBLE COMPANIES

REFERENCES TO OFF-LABEL USAGE(S) OF PHARMACEUTICALS OR INSTRUMENTS

- Nothing to disclose

All relevant financial relationships have been mitigated.

LEARNING OBJECTIVES –

- 1) **Epidemiologic Trends**
- 2) **New Therapies and Advances**
- 3) **Liver Transplantation**

Epidemiologic Trends

From: **Alcohol-Related Deaths During the COVID-19 Pandemic**

JAMA. 2022;327(17):1704-1706. doi:10.1001/jama.2022.4308

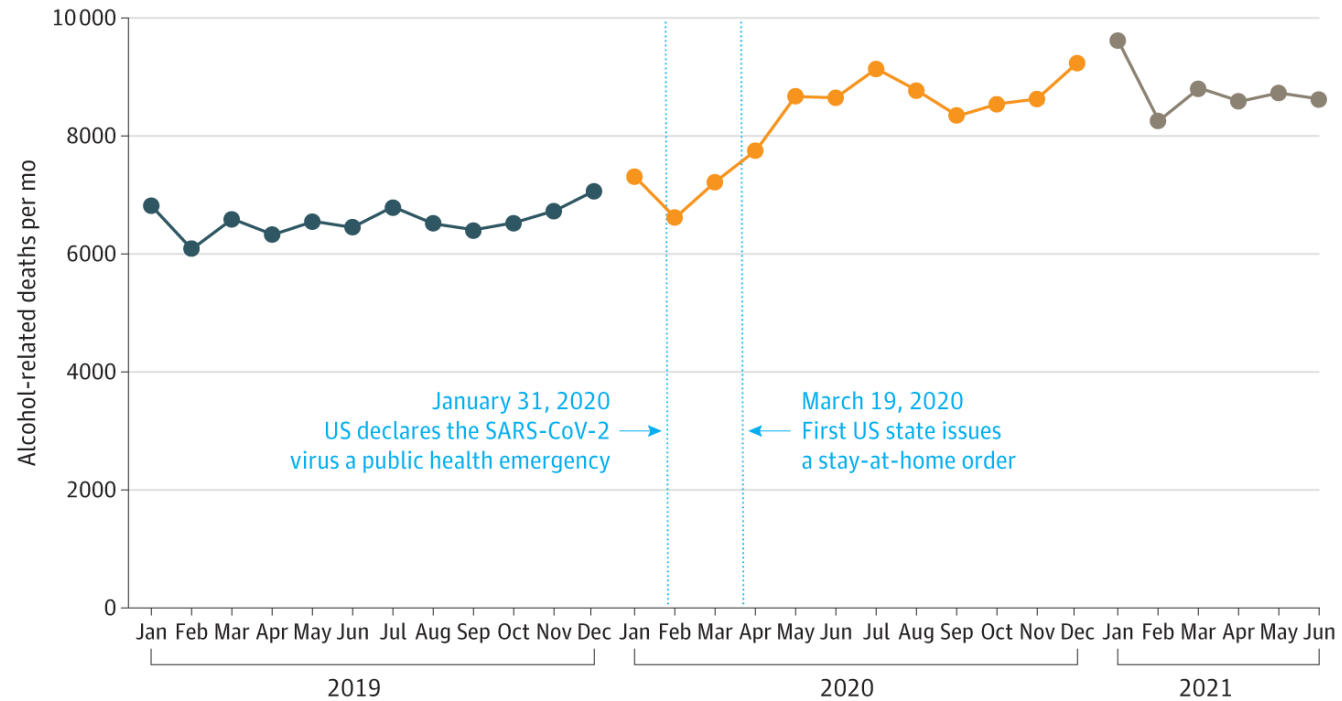
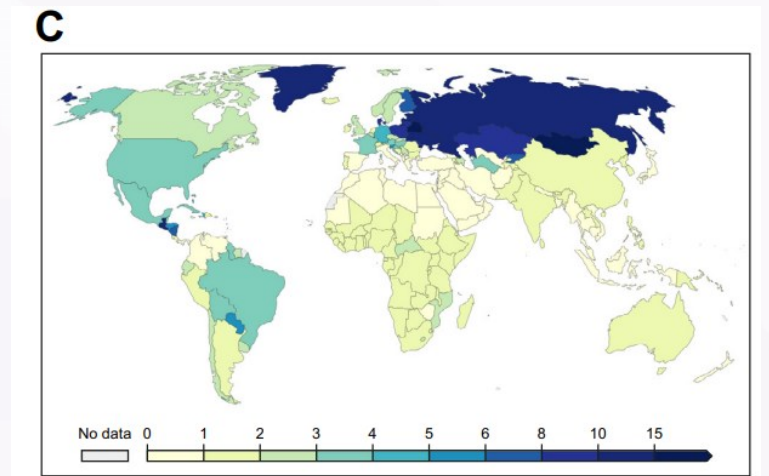
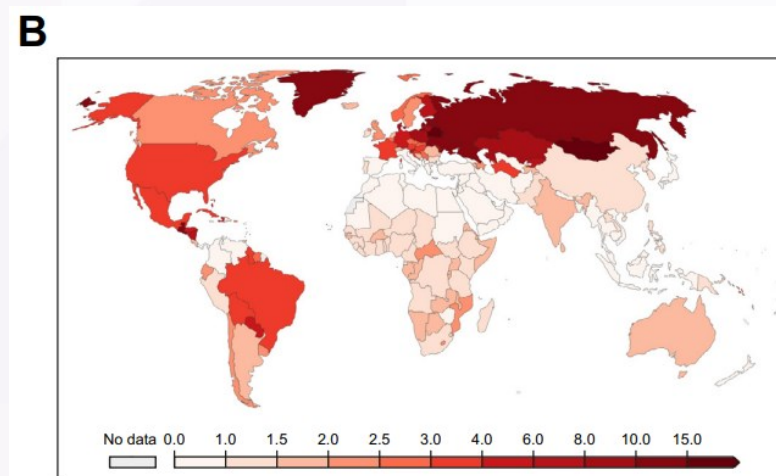
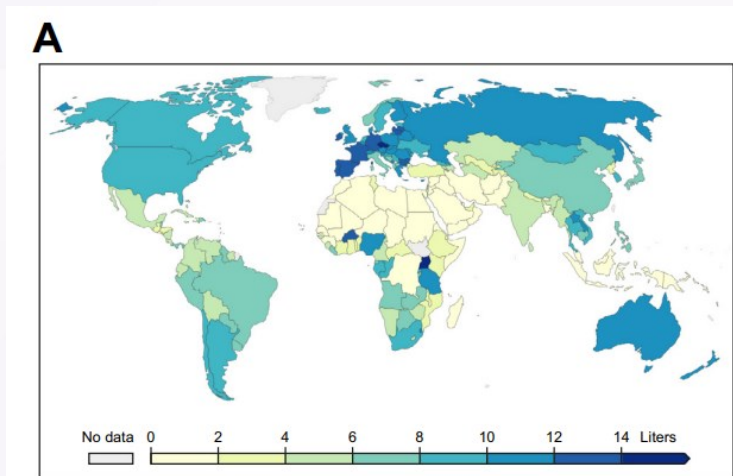


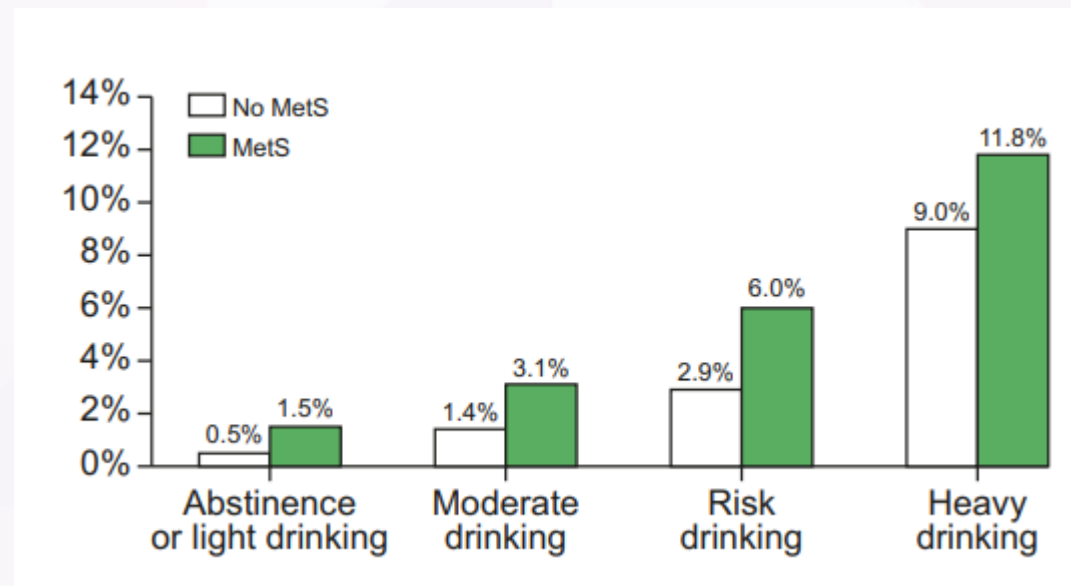
Figure Legend:

Monthly Alcohol-Related Deaths Among People 16 Years and Older The dotted vertical lines indicate important dates in the US at the beginning of the COVID-19 pandemic. Deaths increased in the spring of 2020 as the pandemic unfolded, and the number of deaths remained elevated in the first half of 2021.

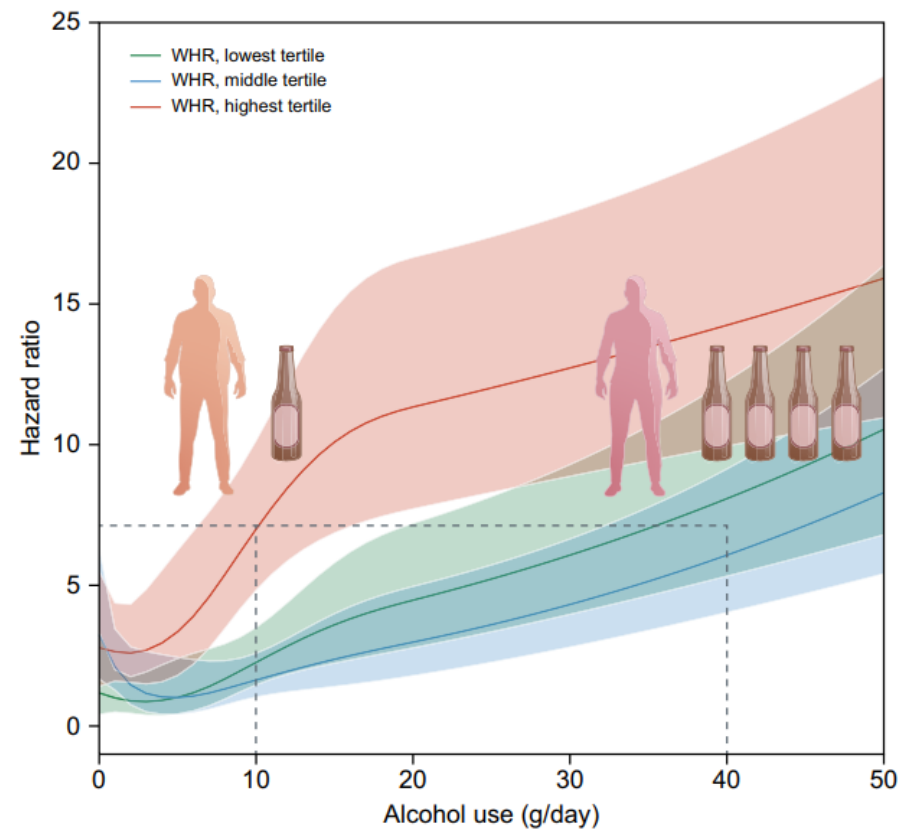
Global trends: alcohol-related epidemiology and mortality/disability statistics: Consumption, death, and disease burden



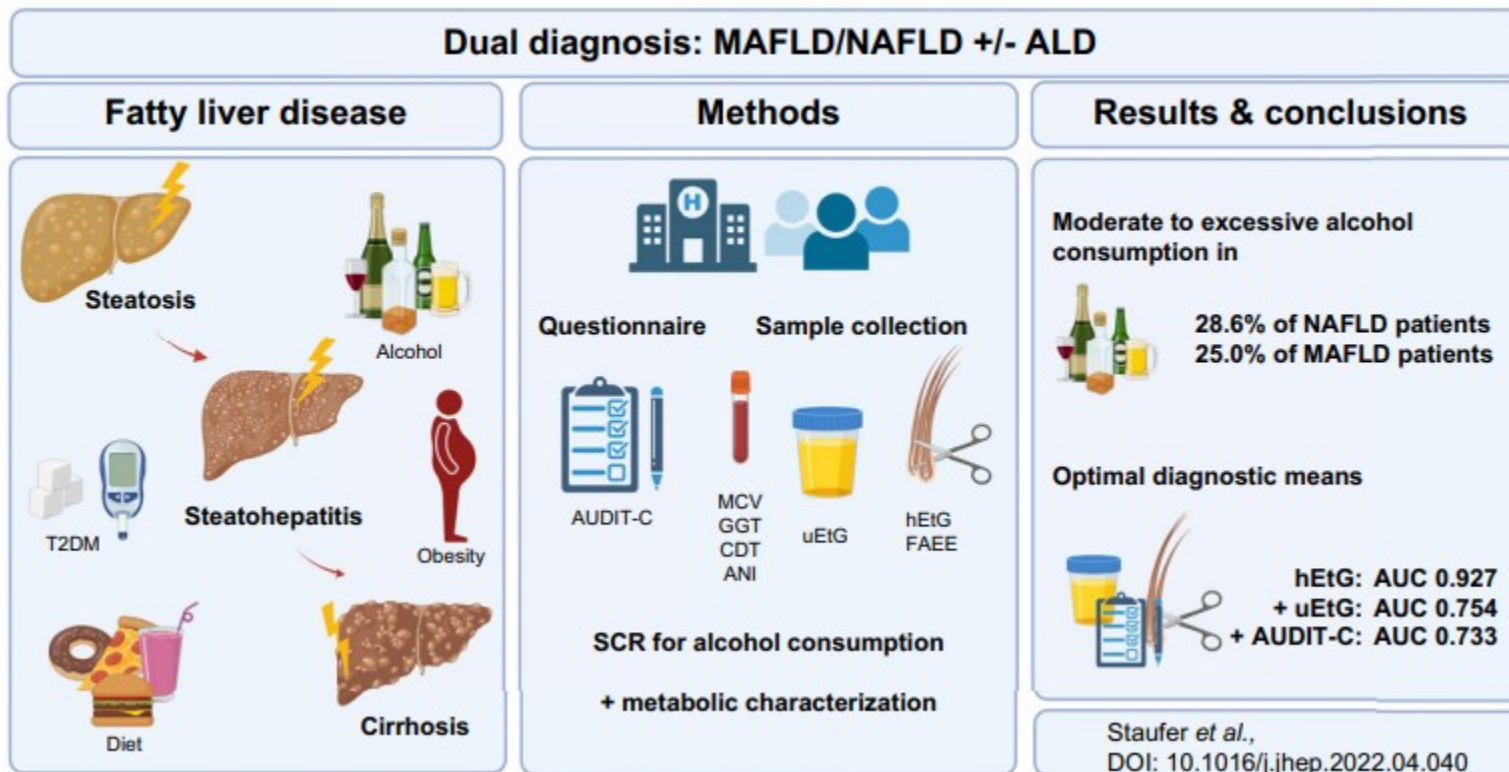
Combined effects of alcohol and metabolic syndrome on liver-related outcomes



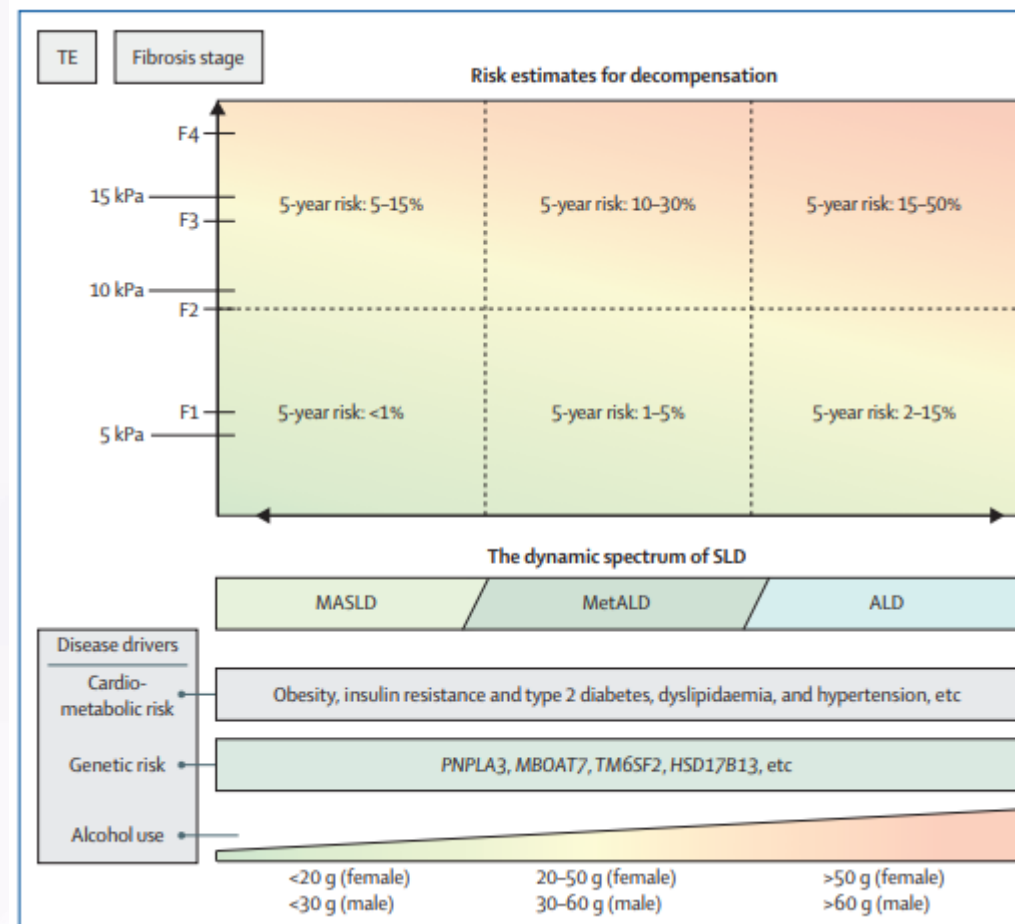
Abdominal obesity increases alcohol-related liver toxicity by fourfold



PETH testing and overlap of ASH from NASH



The Dynamic Spectrum of Steatotic Liver Disease



Bariatric Surgery and Female Sex

- 28% of participants in a survey endorsed problems with alcohol control after bariatric surgery in comparison to only 5% before surgery
- Bariatric surgery is more common in women than men
- Patients after gastric bypass surgery drank significantly more alcoholic beverages per day as compared to before surgery.
- Potential mechanisms that may account for this include neurohumoral consequences of gastric secretion, the concept of addiction transfer, and changes in alcohol metabolism

Alcohol Use, Alcohol-Related Problems, and Treatment Before Bariatric Surgery and During First and Second Postoperative Years

	No. (%) of Participants ^a			P Value		
	Preoperative Assessment	1-y	2-y	Preoperative vs 1-y Postoperative Assessment	Preoperative vs 2-y Postoperative Assessment	1-y vs 2-y Postoperative Assessment
		Postoperative Assessment	Postoperative Assessment			
Select AUDIT items						
Frequency of alcohol consumption						
Never	578 (41.3)	628 (44.9)	580 (41.4)	.89	<.001	<.001
≤ Monthly	523 (37.4)	455 (32.5)	414 (29.6)			
2-4 times/mo	197 (14.1)	200 (14.3)	238 (17.0)			
2-3 times/wk	65 (4.6)	74 (5.3)	97 (6.9)			
≥4 times/wk	37 (2.6)	43 (3.1)	71 (5.1)			
Alcoholic drinks on a typical drinking day						
0	568 (41.8)	619 (45.5)	571 (42.0)	<.001	.22	.01
1-2	611 (44.9)	607 (44.6)	623 (45.8)			
3-4	134 (9.9)	106 (7.8)	129 (9.5)			
5-6	35 (2.6)	18 (1.3)	25 (1.8)			
7-9	8 (0.6)	8 (0.6)	11 (0.8)			
≥10	4 (0.2)	2 (0.2)	1 (0.1)			
AUDIT summary measures						
Consumption at hazardous level ^b	266 (19.6)	180 (13.3)	224 (16.5)	<.001	<.001	.02
AUDIT score ≥8 ^c	36 (2.6)	43 (3.1)	76 (5.5)	.36	<.001	<.001
Alcohol dependence symptoms ^d	39 (2.8)	44 (3.2)	77 (5.5)	.44	<.001	.01
Alcohol-related harm ^d	94 (6.8)	93 (6.7)	119 (8.6)	.65	.01	.02
Alcohol use disorder ^e	106 (7.6)	101 (7.3)	133 (9.6)	.98	.01	.01
Treatment for alcohol or drug abuse in past 12 mo						
Admitted to hospital for treatment ^f	1 (0.1)	3 (0.2)	2 (0.2)	.40	.52	.87
Outpatient treatment (ie, counseling) ^g	6 (0.5)	9 (0.7)	9 (0.7)	.29	.18	.74
In hospital or outpatient treatment ^h	6 (0.5)	10 (0.8)	9 (0.7)	.16	.25	.84

Abbreviation: AUDIT, Alcohol Use Disorders Identification Test.

^aLimited to participants with AUDIT data at all 3 time points (n=1400). The number of participants across categories may not sum to 1400 because of missing data. Differences by time point were determined with generalized linear mixed models using all available data (N=1945).

^bMissing data for 43 participants.

^cMissing data for 8 participants.

^dMissing data for 9 participants.

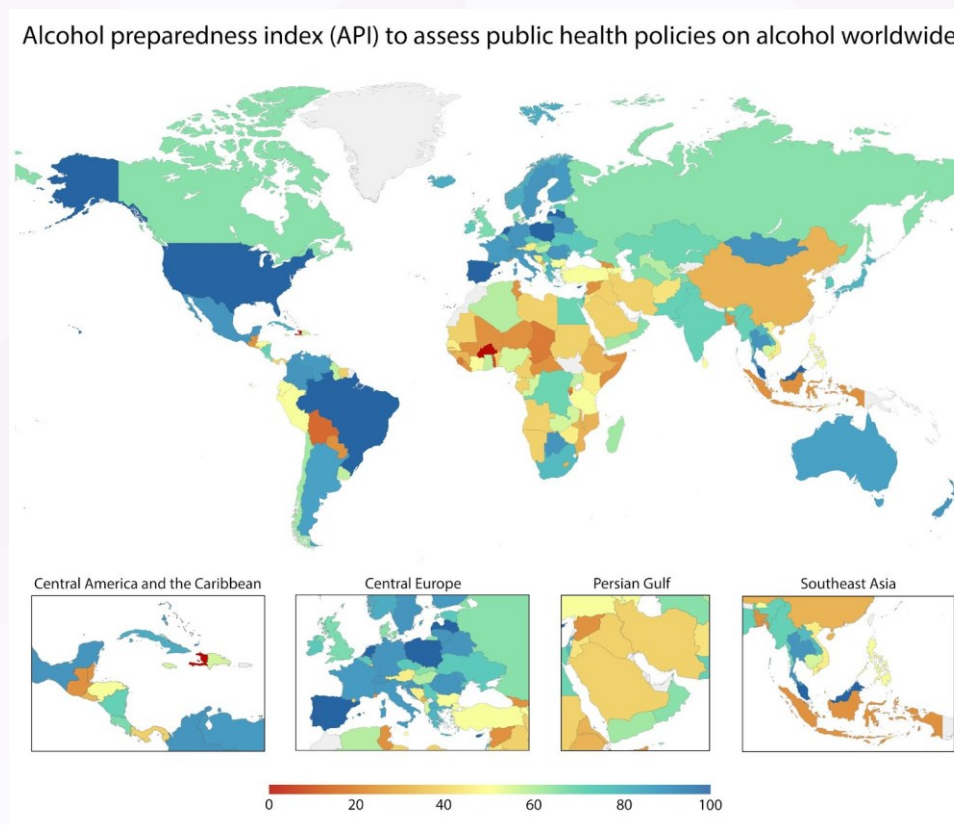
^eMissing data for 11 participants.

^fMissing data for 34 participants.

^gMissing data for 101 participants.

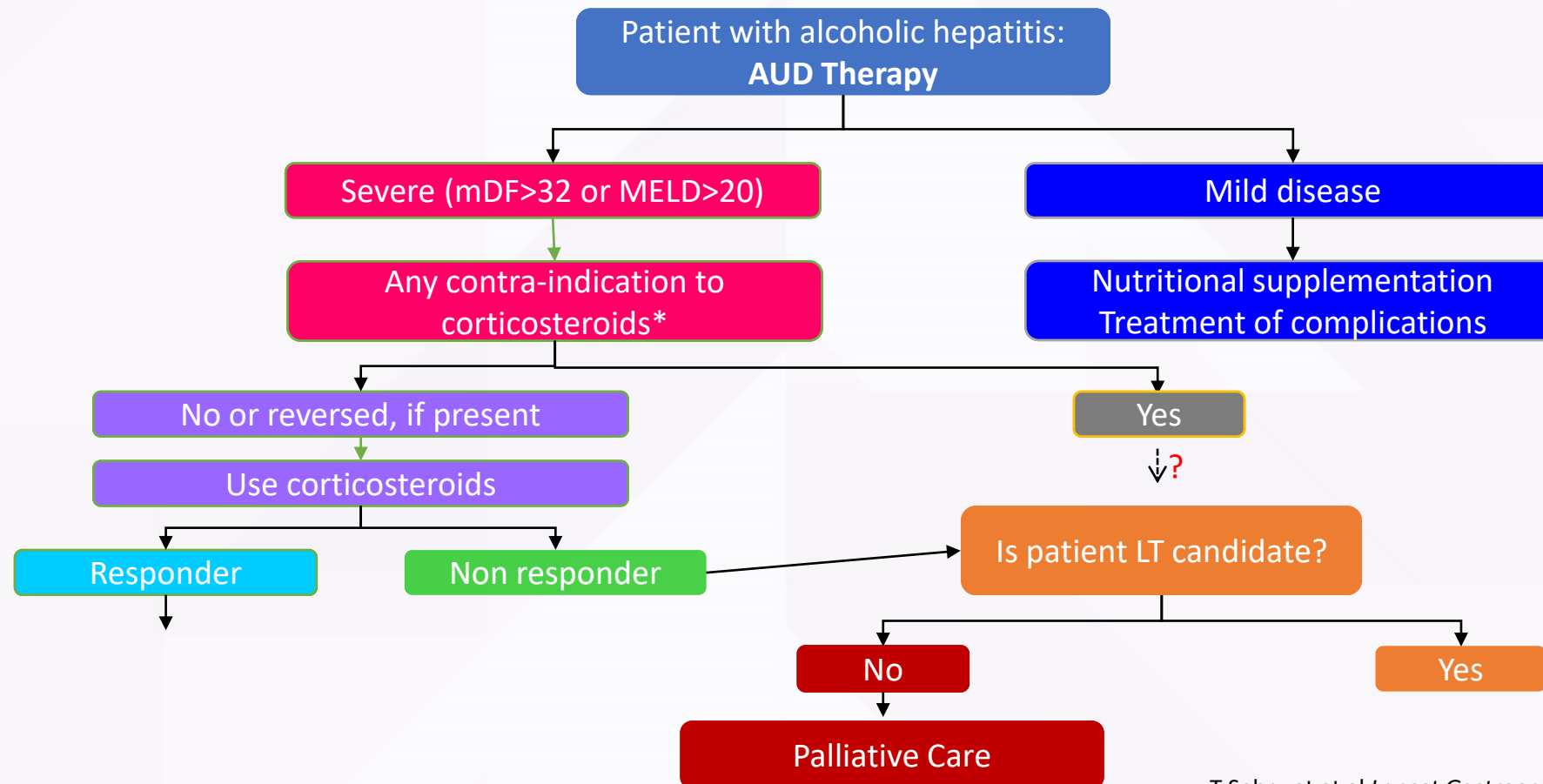
^hMissing data for 115 participants.

Heatmap of the Alcohol Preparedness Index (API) obtained for each country in 2010

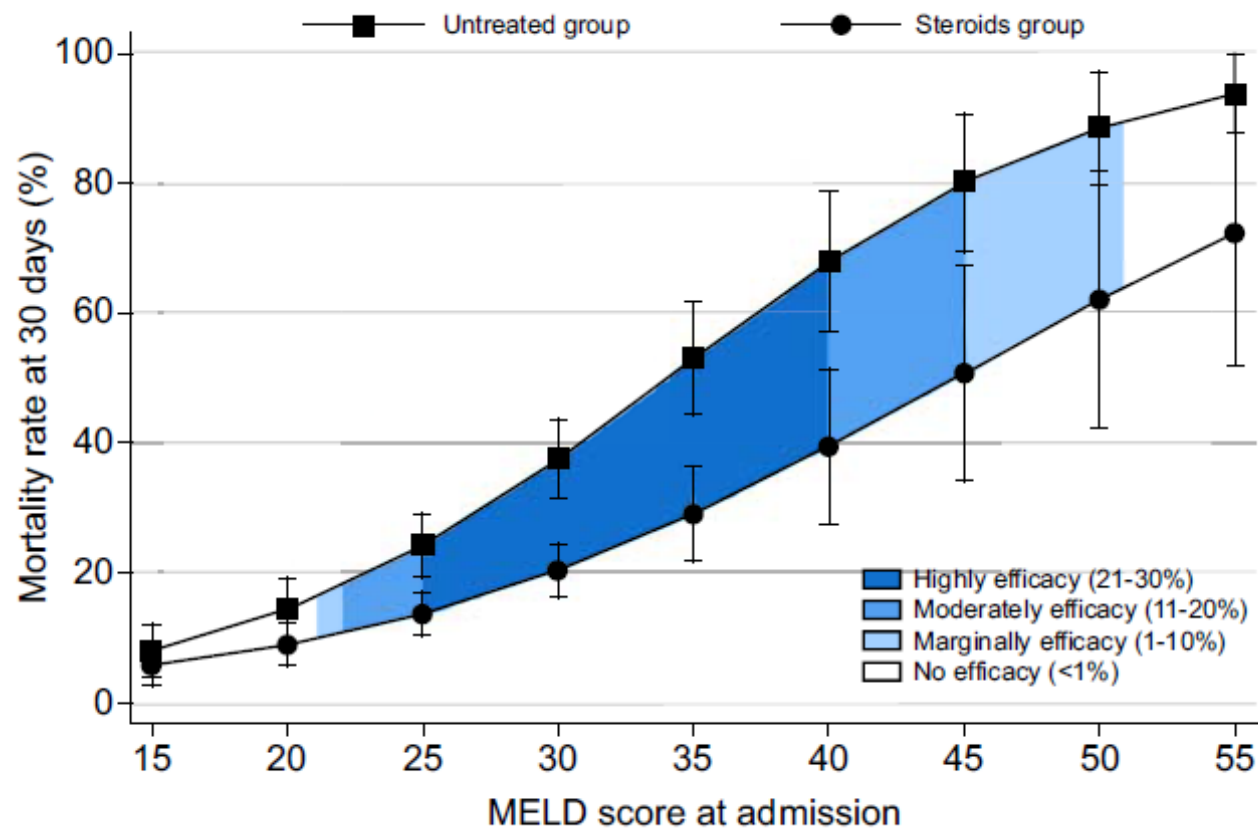


New Therapies and Advances

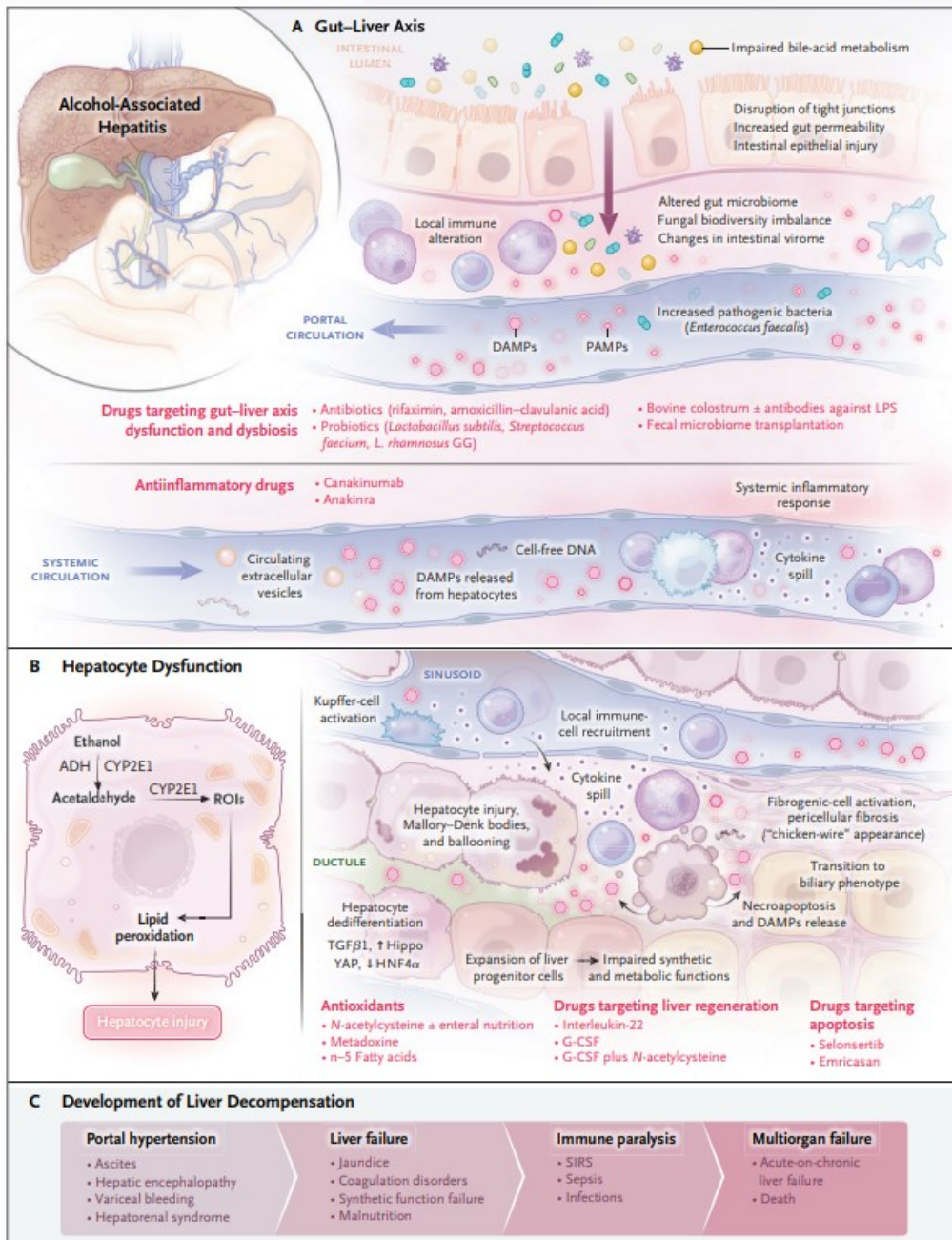
Practice Guideline of therapy in alcohol hepatitis



Which patients respond best to steroids?

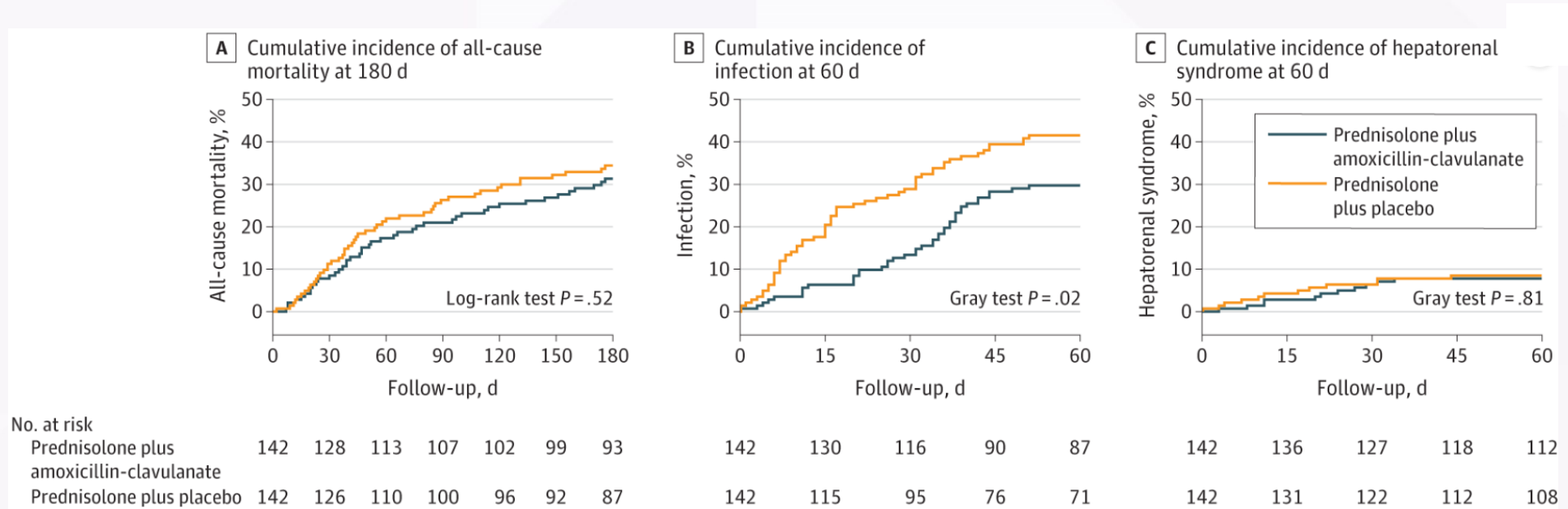


- MELD > 20
- Maximum benefit in MELD 25-39
- MELD > 50 defines futility
- Survival benefit at 30 d but not 90 or 180 d

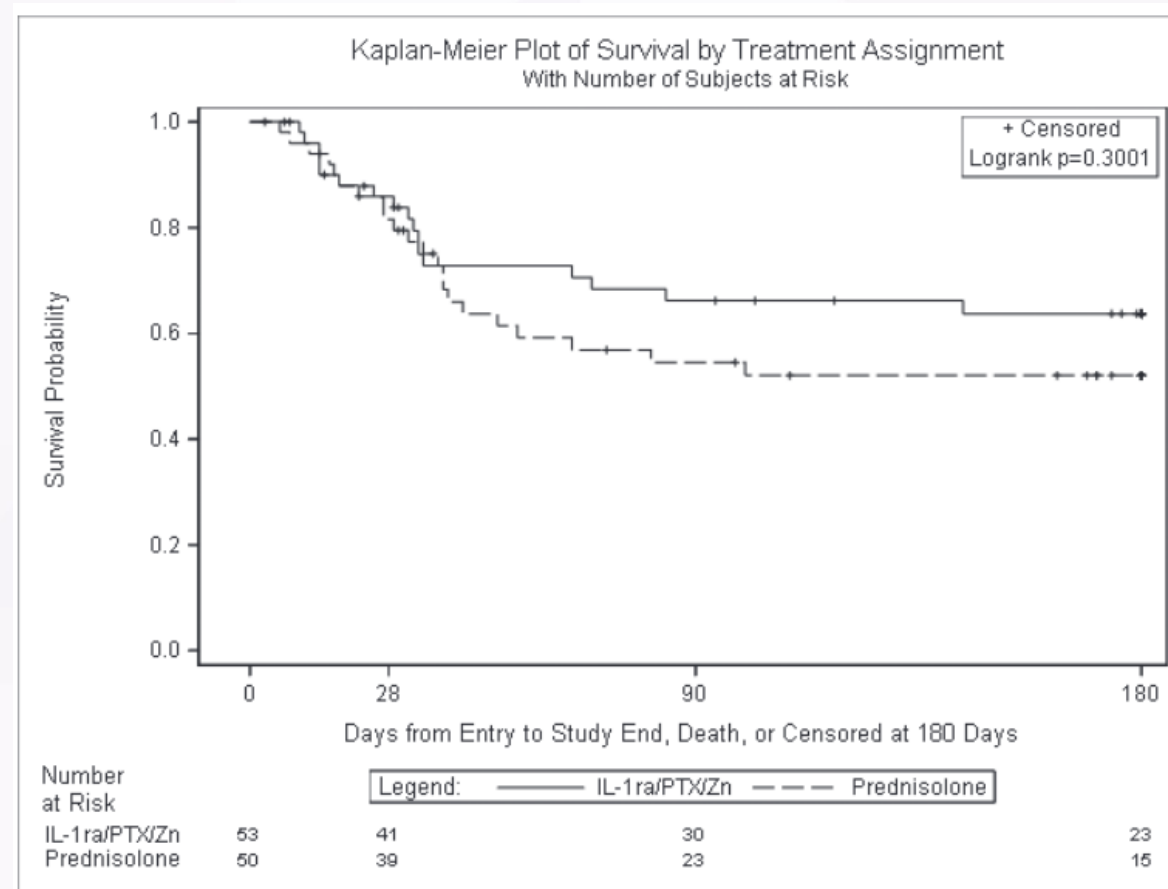


Pathogenesis of Alcohol-Associated Hepatitis

Augmentin and AH: 180-Day Cumulative Incidence of All-Cause Mortality, 60-Day Cumulative Incidence of Infection, and 60-Day Cumulative Incidence of Hepatorenal Syndrome

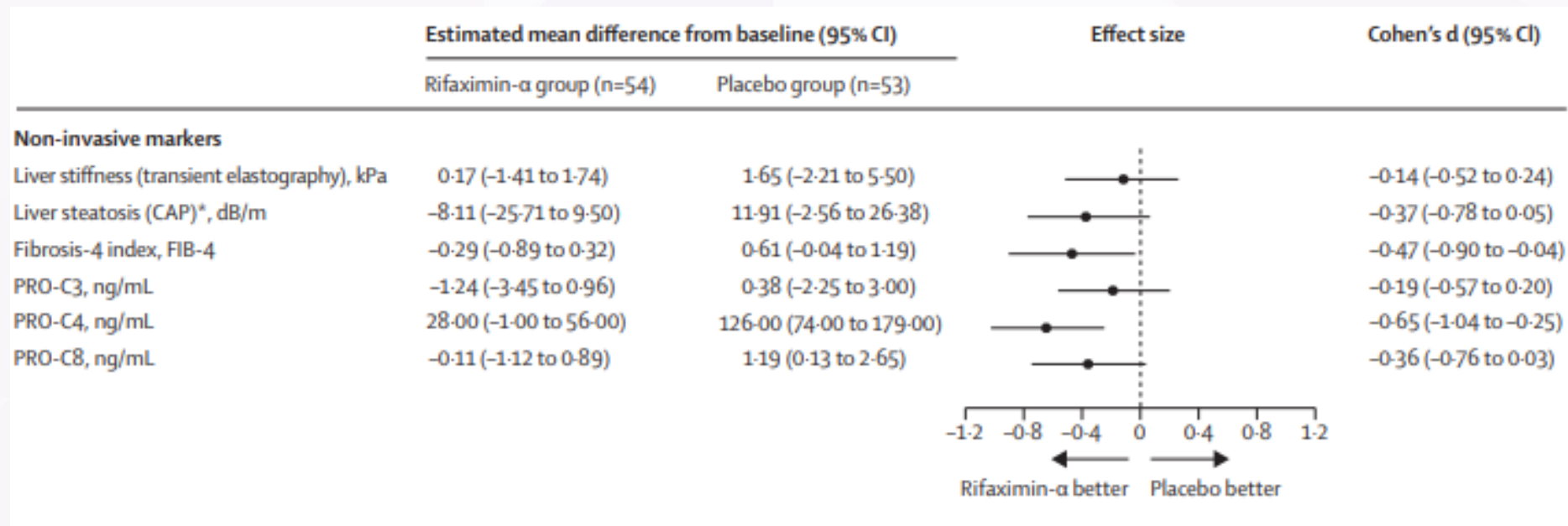


Anikinra: Kaplan-Meier survival plot by treatment assignment of all patients enrolled, by treatment assignment and disease severity in MELD 20–25 group

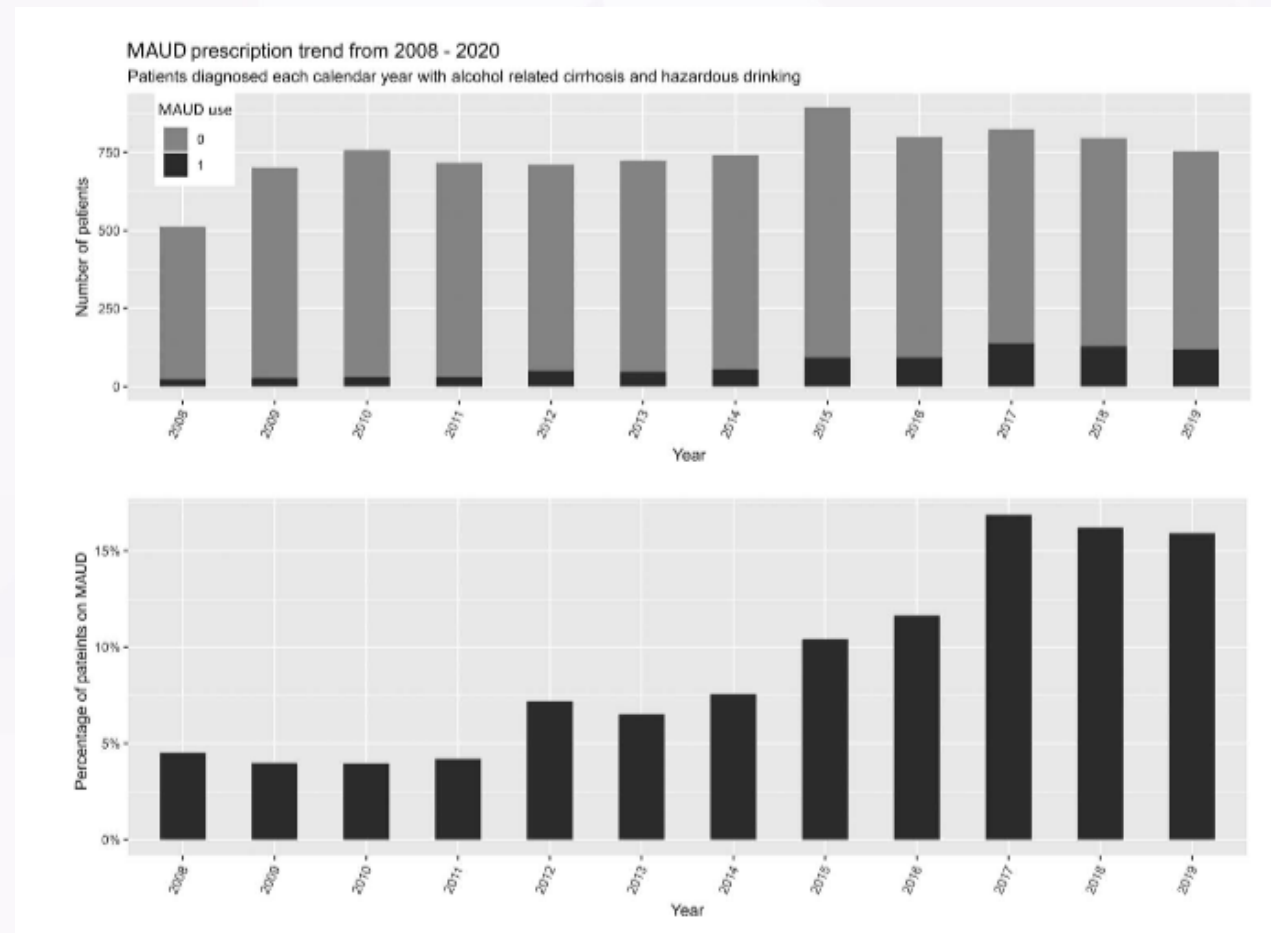


Rifaximin: Changes in non-invasive fibrosis markers, liver enzymes, and self-reported alcohol consumption for the per-protocol population

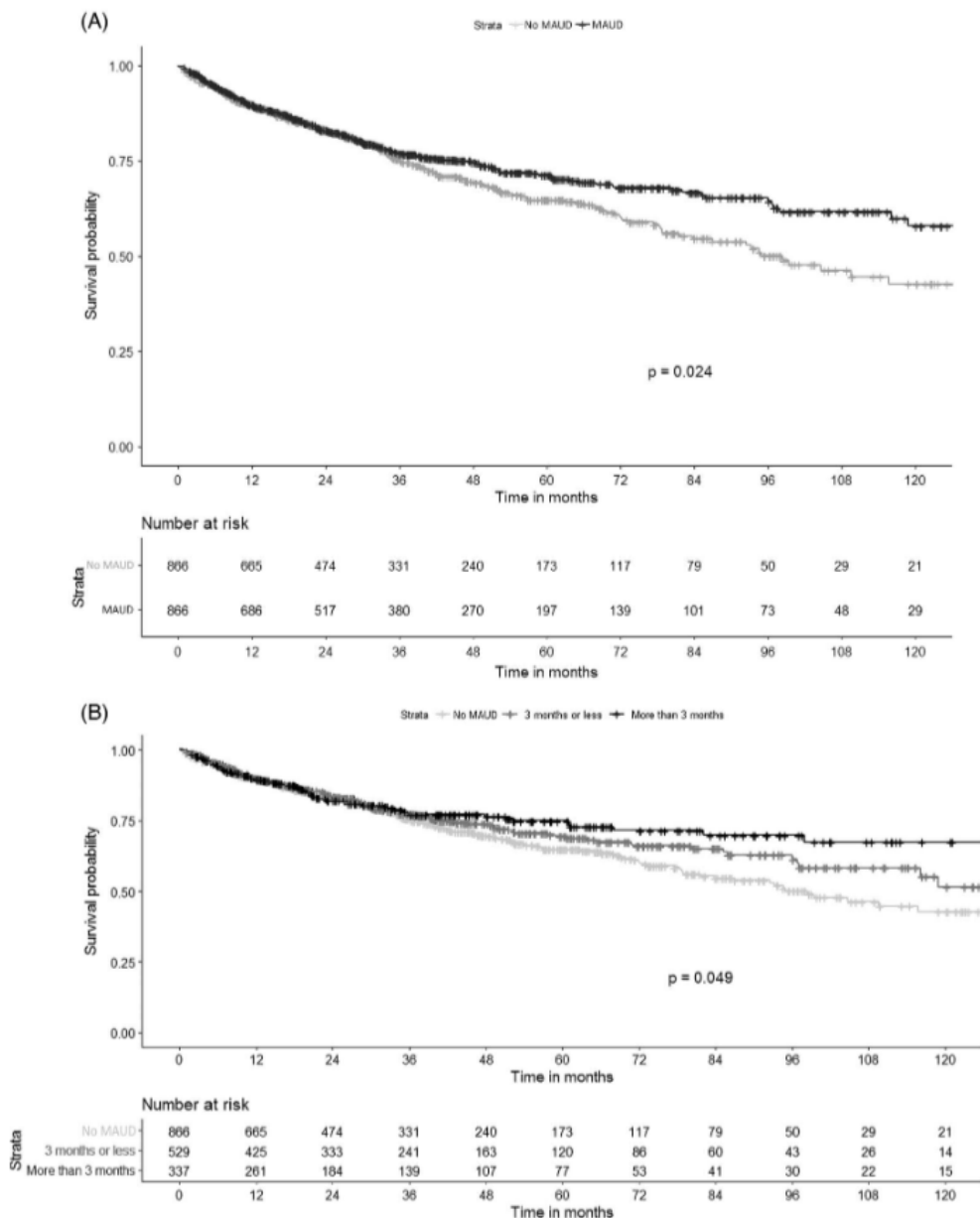
Forest plot of effect sizes and corresponding 95 % CIs for changes in non-invasive secondary endpoints between baseline and 18 months



Temporal Changes in MAUD Prescription Patterns



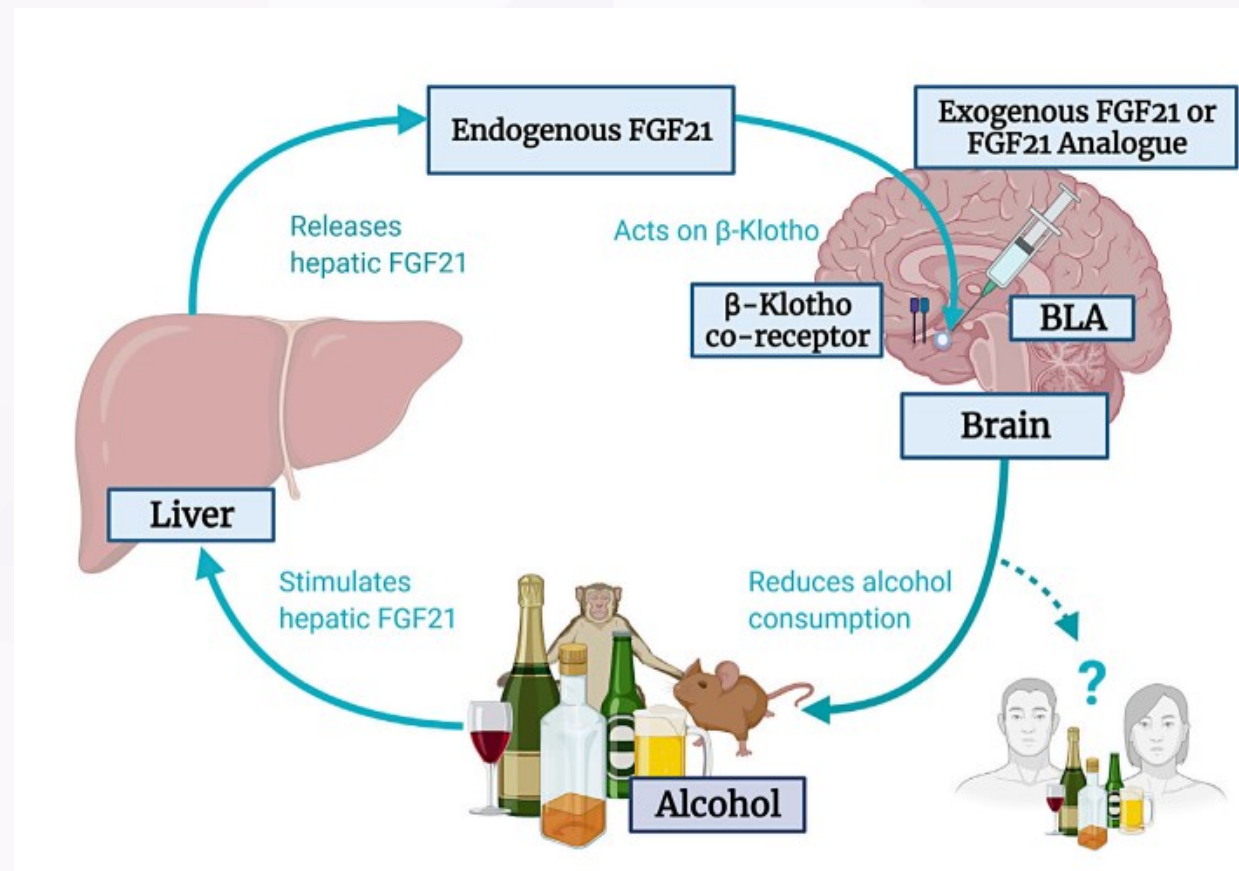
MAUD Improves Survival in Alcoholic Cirrhosis



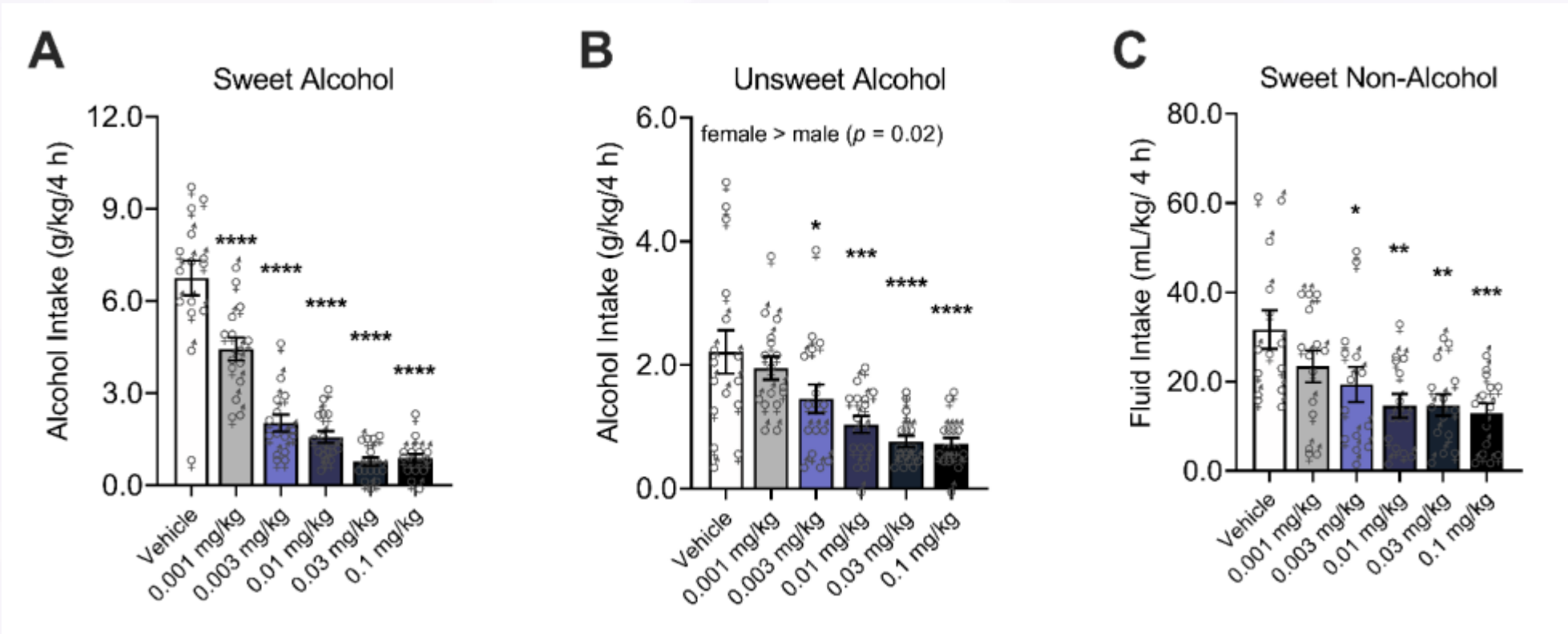
(A) Kaplan-Meier analysis comparing the survival curve among patients who received MAUD in the first year after diagnosis of cirrhosis versus the propensity score–matched controls. (B) Kaplan-Meier analysis comparing the survival curve among patients who did not receive MAUD received 3 months or less, or >3 months, in the first year after diagnosis of cirrhosis in the propensity score–matched cohort.

(B) Abbreviation: MAUD, medications for alcohol use disorder.

Schematic outline of the potential bidirectional relationship between FGF21 and alcohol use



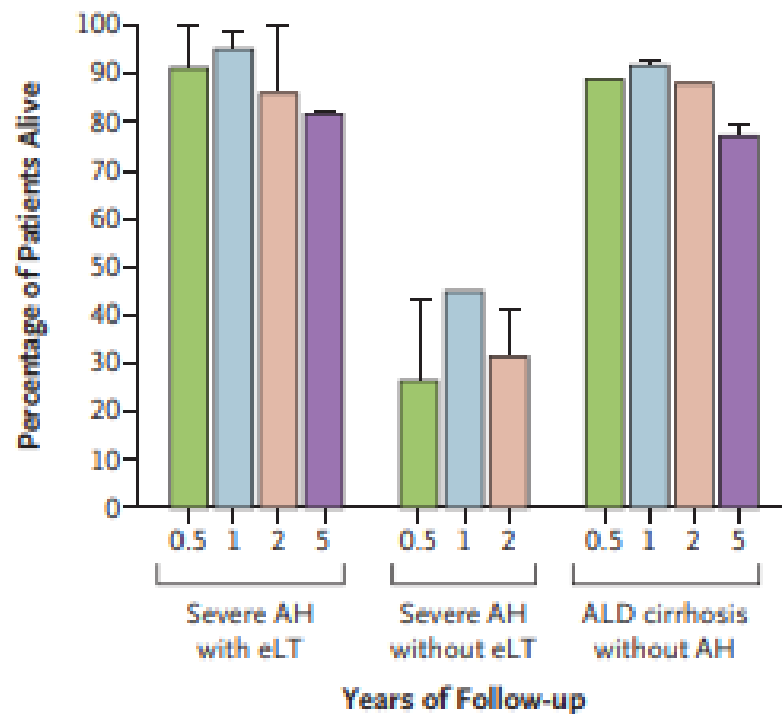
Semaglutide reduces binge-like alcohol drinking in mice



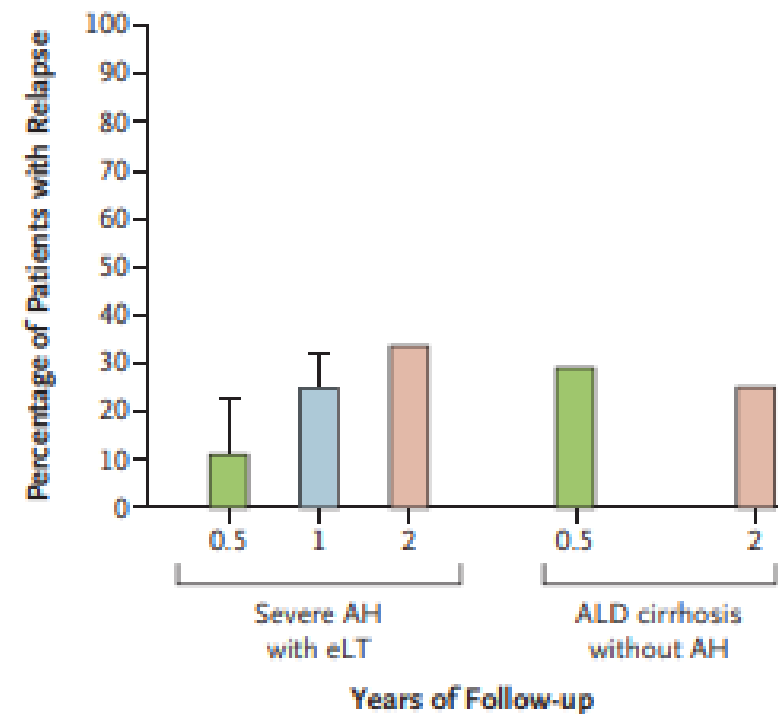
Liver Transplantation

Summary of Studies Assessing Early Liver Transplantation (eLT) for Severe Alcohol-Associated Hepatitis (AH)

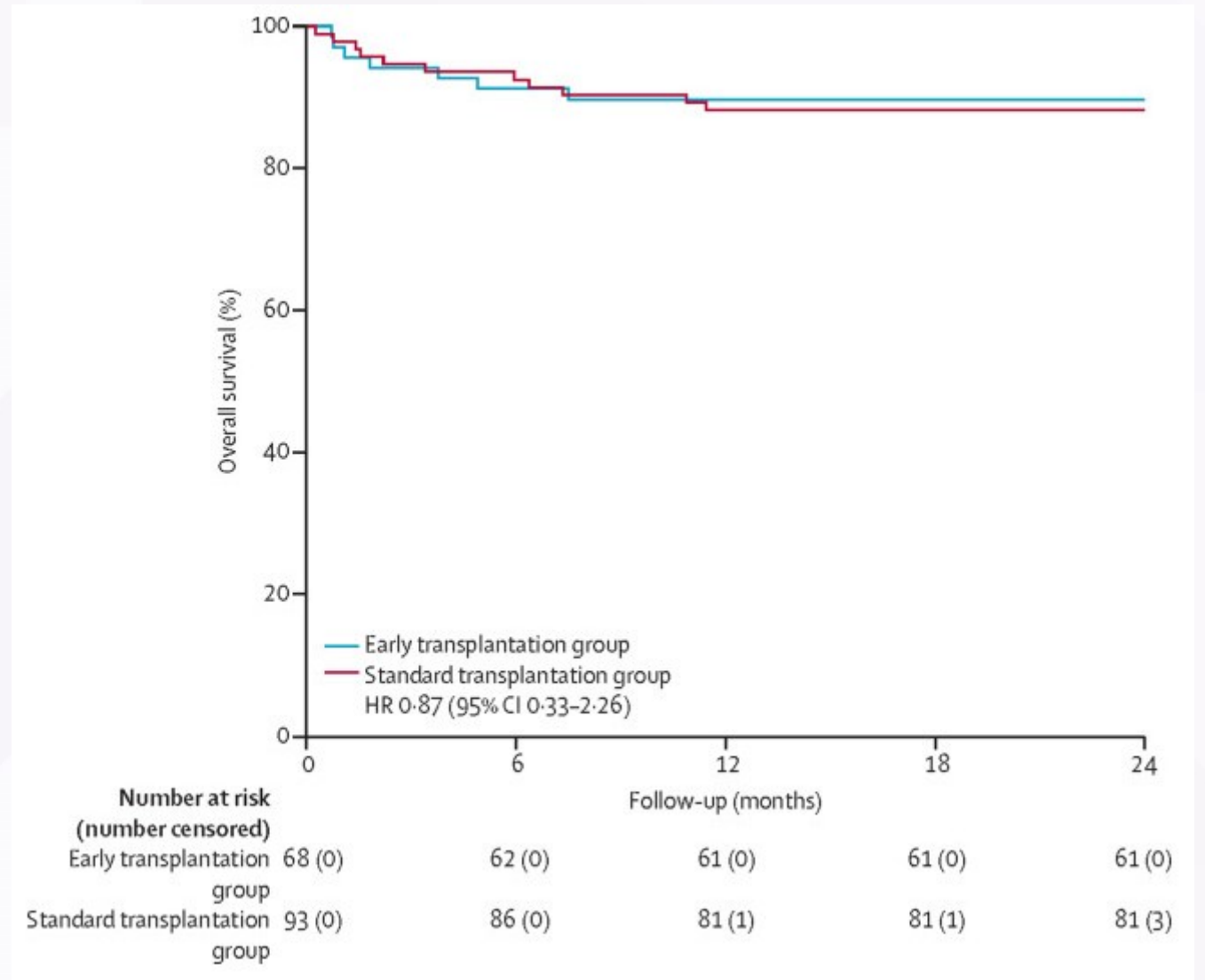
B Survival after Liver Transplantation in Patients with AH and ALD



C Alcohol Relapse after Liver Transplantation in Patients with AH and ALD

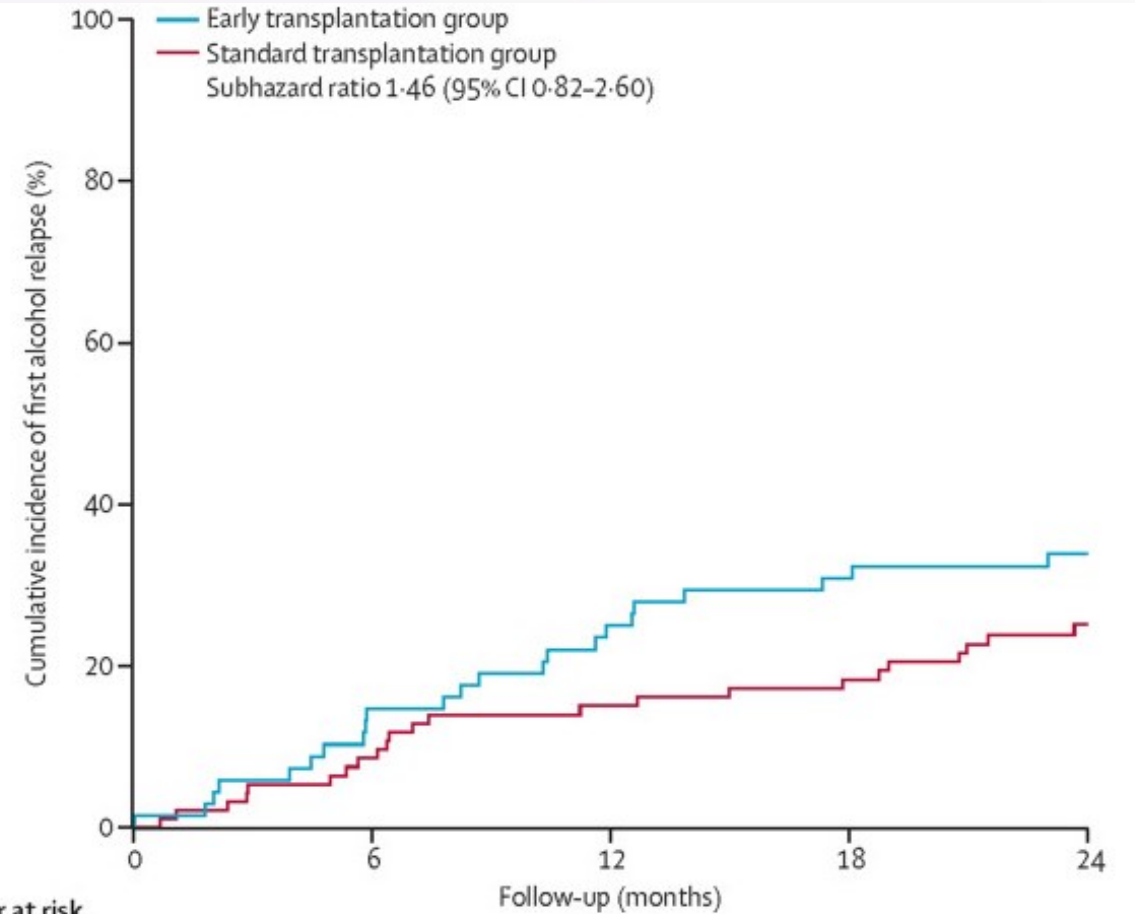


2-year overall survival after liver transplantation in the early liver transplantation group compared with the standard transplantation group in the QuickTrans study



2-year cumulative incidence of first alcohol relapse after liver transplantation in the early transplantation group and standard transplantation group enrolled in the QuickTrans study

A Louvet et al *Lancet Gastroenterol Hepatol* 2022



	0	6	12	18	24
Number at risk (number censored)					
Early transplantation group	68 (0)	52 (0)	44 (0)	40 (0)	37 (1)
Standard transplantation group	93 (0)	78 (1)	68 (1)	65 (1)	57 (3)
Death					
Early transplantation group	0	6	7	7	7
Standard transplantation group	0	7	10	10	10

Key Takeaways

- Worrisome epidemiologic trends in ALD/AH
- Studies are ongoing to target new pathways for therapeutic benefit
- Need to integrate AUD tx w ALD tx
- Efforts to liberalize liver transplantation for ALD/AH